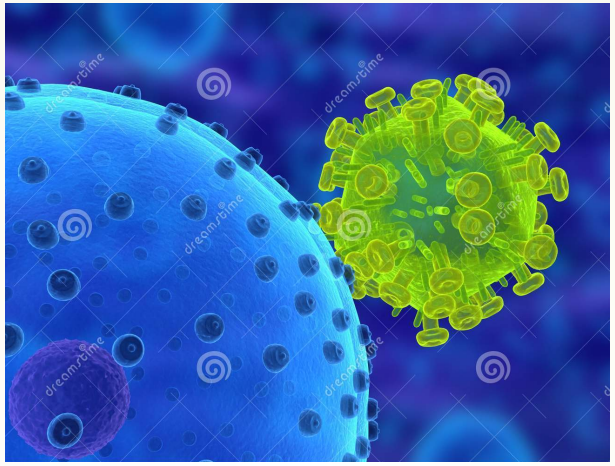

Virus-Cell Interactions

Faculty

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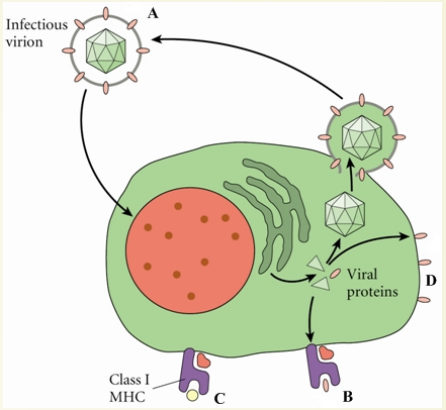
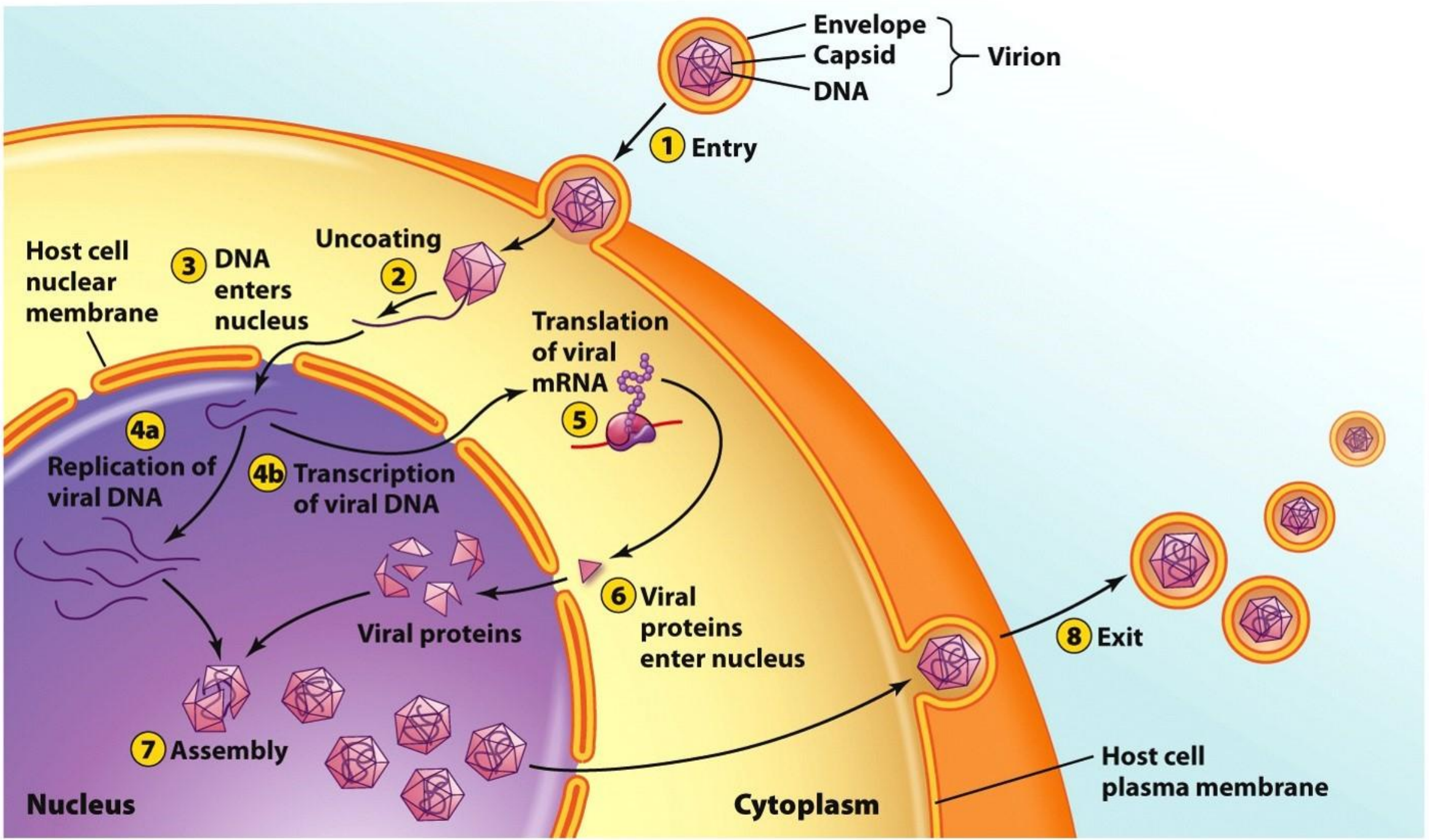
Introduction



- Virus infection causes a wide variety of potentiality victorious changes in the many different kinds of cells that occur in the animal host.
- Disruption of cellular function
- Induction of cell death
- Transformation
- Activation of an inappropriate immune response



Types of Virus-Cell Interations

- Cytolytic infection – Cell die
- Non cytolytic infection – Cell remain intact
- Productive Infections – Virus replicate and viral progeny produce and they are fully infective
- Non productive Infections/ abortive infections – Virus replicate inside the cell but defective virus or incomplete progeny will produce
- Permissive cells – They support the complete replication of viruses
- Non permissive cells – Not allow the replication of virus. viral replication may be blocked at any point from viral attachment through to the final stages of virion assembly and release.

TYPE OF INFECTION	EFFECTS ON CELL	PRODUCTION OF INFECTIOUS VIRIONS	EXAMPLES
Cytocidal	Morphologic changes in cells (cytopathic effects); inhibition of protein, RNA and DNA synthesis; cell death	Yes	Alphaherpesviruses, enteroviruses, reoviruses
Persistent, productive	No cytopathic effect; little metabolic disturbance; cells continue to divide; may be loss of the special functions of some differentiated cells	Yes	Pestiviruses, Arena viruses, rabies virus, most retroviruses
Persistent, nonproductive	Usually nil	No, but virus may Be induced	Canine distemper virus in brain Polyomavirus, adenoviruses
Transformation	Alteration in cell morphology; cells can be passaged indefinitely; may produce tumors when transplanted to experimental animals	Yes, oncogenic retroviruses	Murine, avian leukosis, and sarcoma viruses

Cytocidal changes in virus-infected cells

- Cytopathic viruses kill the cells in which they replicate and leads to cell damage.
- Cell damage is known as a *cytopathic effect* (CPE).
- CPE can usually be observed by low-power light microscopy of unstained cell cultures.
- Cytopathic effect is often characteristic of the particular virus involved

Mechanisms of Cell Damage

- Inhibition of Host Cell Nucleic Acid Synthesis
- Inhibition of Host Cell RNA Transcription
- Inhibition of Processing of Host Cell mRNAs
- Inhibition of Host Cell Protein Synthesis
- Inviting immune cells

Inhibition of Host Cell Nucleic Acid Synthesis

- Common in viral infections.
- It is an inevitable consequence of viral inhibition of host cell protein synthesis
- Eg. poxviruses produce a DNAse that degrades cellular DNA,
- Herpes viruses specifically displace the synthesis of host cell DNA with their own synthetic processes.

Inhibition of Host Cell RNA Transcription

- Poxviruses, rhabdoviruses, reoviruses, paramyxoviruses, and picornaviruses, inhibit host cell RNA transcription.
- Indirect consequence of viral effects on host cell protein synthesis:, which decrease availability of transcription factors.
- Viruses encode specific transcription factors for the purpose of regulating the expression of their own genes
- Eg. herpesviruses encode proteins that bind directly to specific viral DNA sequences, thereby regulating the transcription of viral genes.

Inhibition of Processing of Host Cell mRNAs

- Interference with the splicing of cellular primary mRNA transcripts Ex. vesicular stomatitis viruses, influenza viruses, and herpesviruses.
- Spliceosomes are formed, but subsequent catalytic steps are inhibited.
- Eg: a protein synthesized in herpesvirus- infected cells suppresses RNA splicing and leads to reduced amounts of cellular mRNAs and the accumulation of primary mRNA transcripts.

Inhibition of Host Cell Protein Synthesis

- Shutdown of host cell protein synthesis, while viral protein synthesis continues. Eg. Picorna virus, togavirus, influenzavirus, rhabdovirus, poxvirus, and herpesvirus infections.
- The mechanisms underlying the shutdown of host cell protein synthesis are:
  - viral enzymes that degrade cellular mRNAs
  - Factors that bind to ribosomes and inhibit cellular mRNA translation
  - alteration of the intracellular environment favouring the translation of viral mRNAs .
- Viral proteins may also inhibit the processing, transport of cellular proteins from the endoplasmic reticulum, and this inhibition may lead to their degradation. Ex. lentiviruses

Inviting immune cells

Virus infect Healthy cells

During replication of virus some viral protein leaks

Leak protein attach to the cell membrane

Killer cells detect that protein in abnormal cells

Perforin released by killer cells and make hole in mb

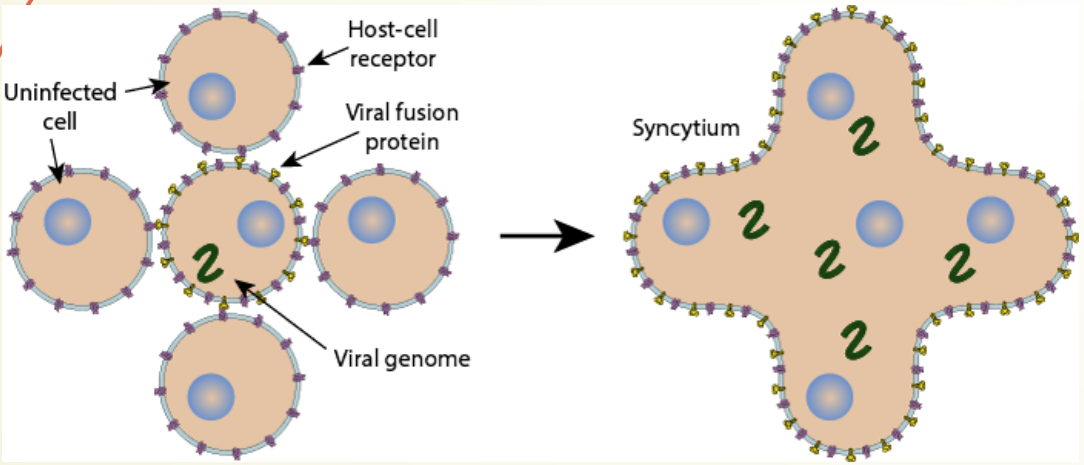
Cytoplasm will come out and cell become die

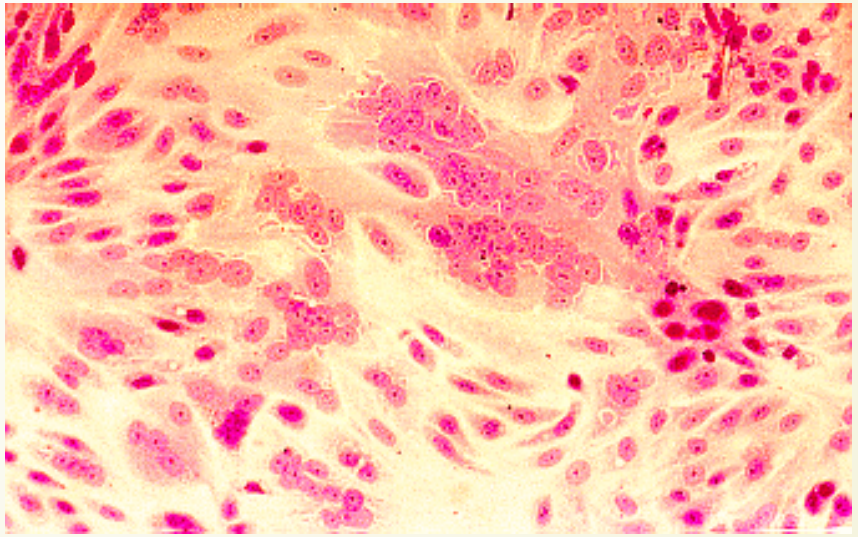
Cytopathic Changes Involving Cell Membranes

- viral attachment ➡ entry, formation of replication complexes, ➡ virion assembly.
- Alter plasma membrane permeability, affect ion exchange and membrane potential.
- Enveloped viruses leads to insertion of fusion protein in C.Mb., often leading to membrane fusion and syncytium formation.
  - **Cell Membrane Fusion and Syncytium Formation**
  - **Hemadsorption**
  - **Hemagglutination**

Cell Membrane Fusion and Syncytium Formation

- Syncytia formation ex. lentiviruses, paramyxoviruses, morbilliviruses, pneumoviruses, and some herpesviruses etc.
- fusion of an infected cell with uninfected cells.
- Cell membrane fusion : viral fusion proteins or fusion domains.

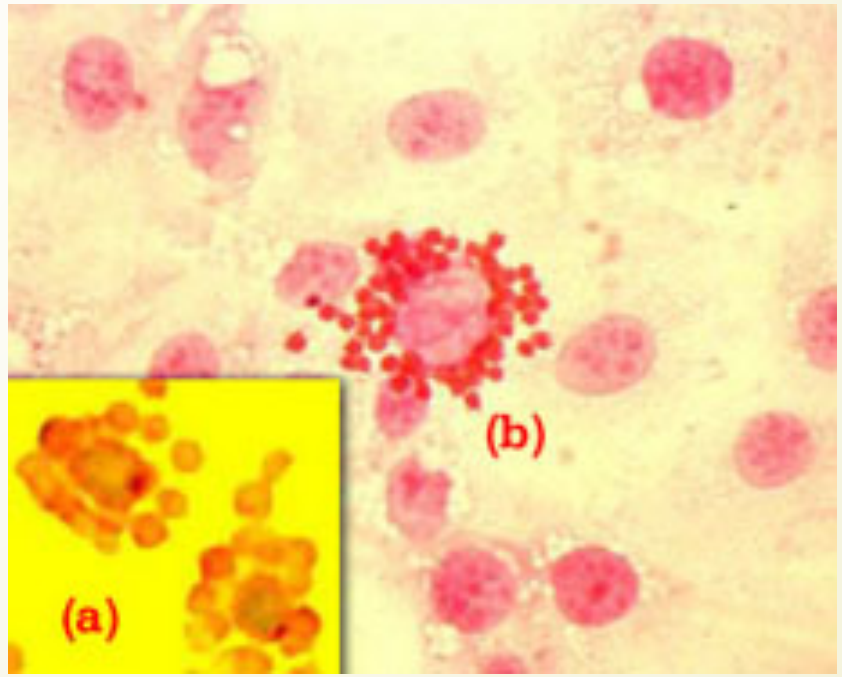




Hemadsorption

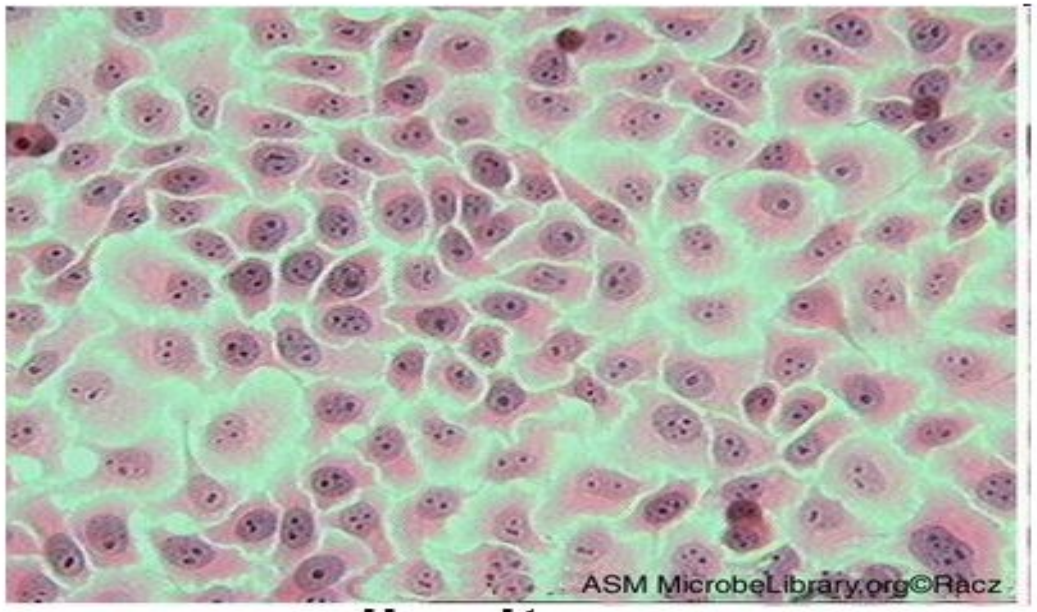
- Infective cell produce some proteins which have the ability to adsorb erythrocytes phenomenon known as *Haemadsorption* .
- Incorporation of viral glycoprotein peplomers into the plasma membrane of infected cells where they serve as receptors for ligands on the surface of erythrocytes.

Eg. orthomyxoviruses,
paramyxoviruses, and togaviruses,

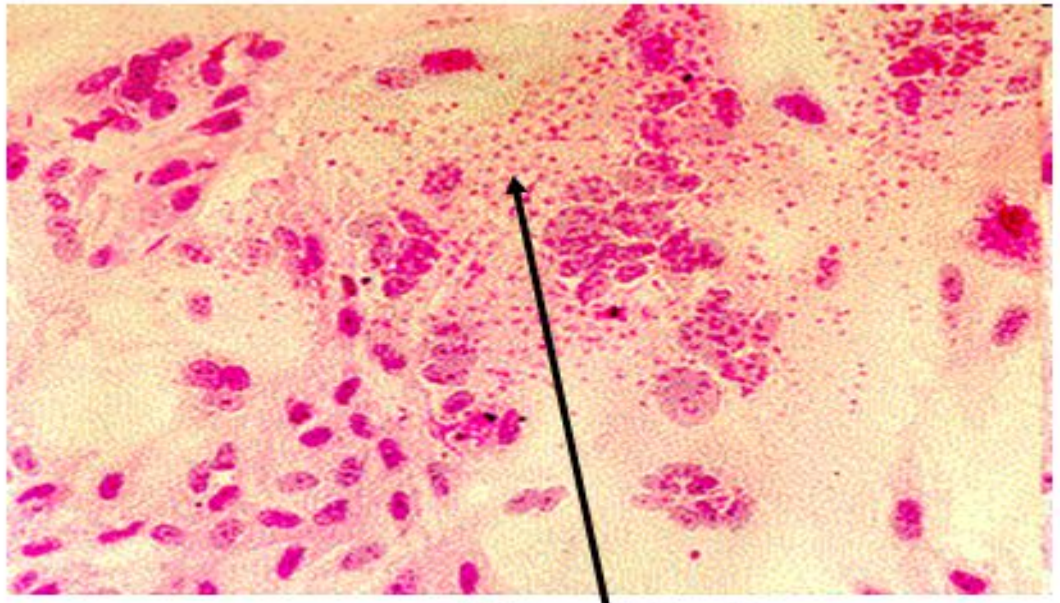


Hemadsorption (Hads)

- Virus growth in cell cultures is detected by testing for hemadsorption: red cells are added to the culture and adhere to virus budding from infected cells.
- If the culture tests positive, hemadsorption inhibition test with specific antisera is used to identify the virus.



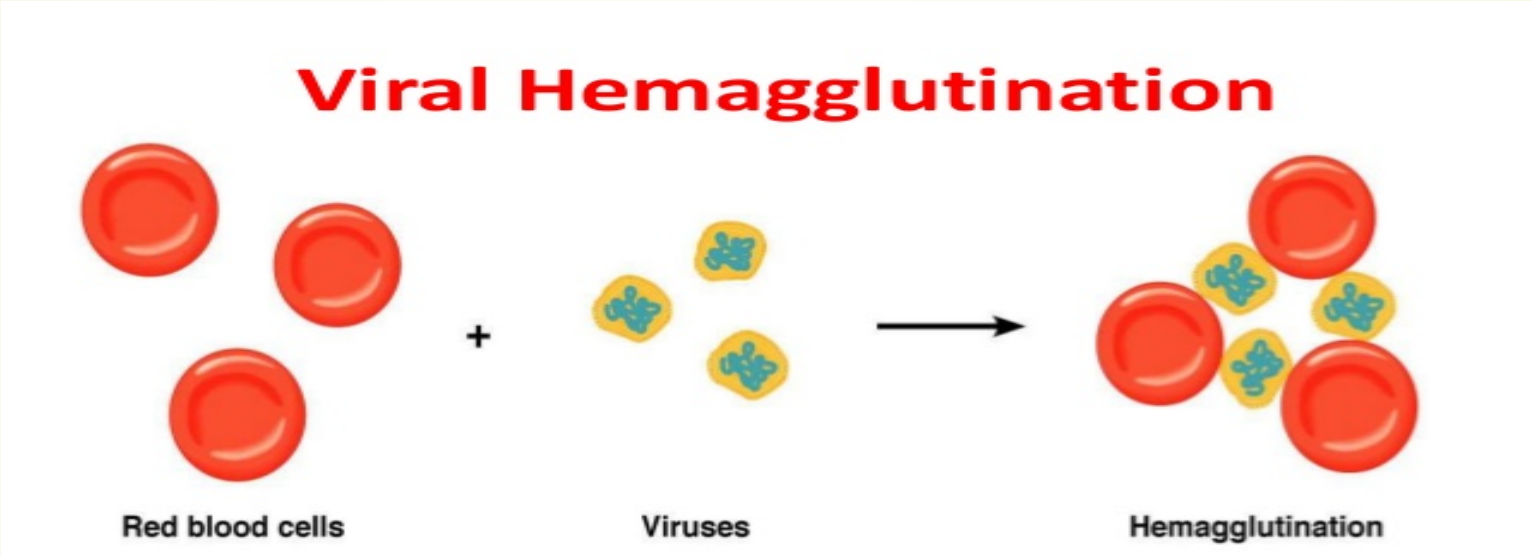
cell culture

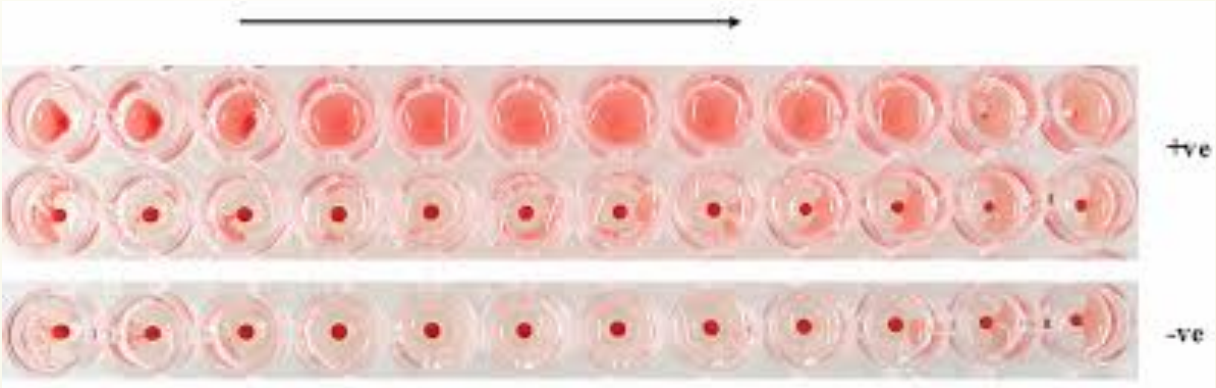


positive Hads

Haemagglutination

- Glycoprotein peplomers (enveloped virus) are responsible for ***hemagglutination,*** *in vitro,* i.e., the agglutination of erythrocytes.
- Virions added to an erythrocyte suspension form cell-virus-cell bridges involving large numbers of erythrocytes.
- Both phenomena are used extensively in laboratory diagnostics
- Haemadsorption – by Infected host cell
- Haemagglutination – by virus


Viral Hemagglutination
+
Red blood cells
Viruses
Hemagglutination


+ve
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Cytopathic Changes Involving the Cytoskeleton

- Responsible for the structural integrity of the cell, for the transport of organelles through the cell, and for certain cell motility activities.
- Microfilaments (actin) and microtubules (tubulin)
- Particular viruses are known to damage specific filament systems

Canine distemper virus, vesicular stomatitis viruses, vaccinia virus, → depolymerization of actin-containing microfilaments

Enteroviruses → extensive damage to microtubules

Noncytocidal Changes in Virus-Infected Cells

- do not kill the cells, cell metabolism not affected
- Infected cells continue to grow and divide
- Mainly occur in RNA Virus
  - **Persistent infection**
  - **Inclusion bodies**
  - **Cells transformation**

Persistence infections

- The virus or its genome is maintained in the cell.
- by the integration of the viral nucleic acid into the host cell DNA,
- by carriage of the viral nucleic acid in the form of an episome.
- In these instances, the cell survives, indeed may divide repeatedly.
- Viral progeny hide in sensory ganglia eg. Herpes virus

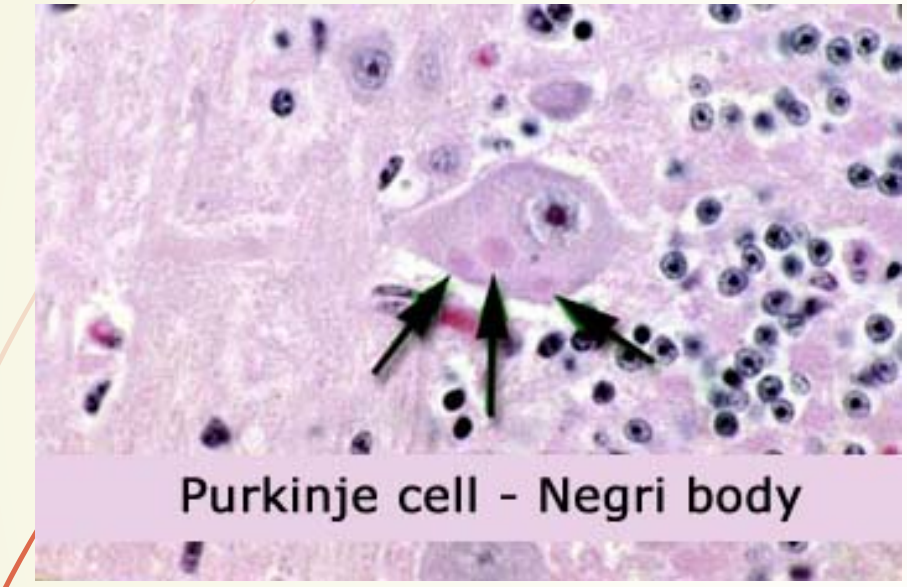
Inclusion bodies

- Certain morphological changes are produced in the infected cell in the form of inclusion bodies
- *Inclusion Bodies are the remnant of virus particle or viral protein*
- Intranuclear/ Intracytoplasmic, also found both
- single / multiple, Large/ small, round/ irregular in shape
- Acidophilic (pink, stained by eosin) or basophilic (blue, stained by hematoxylin).

Continue.....

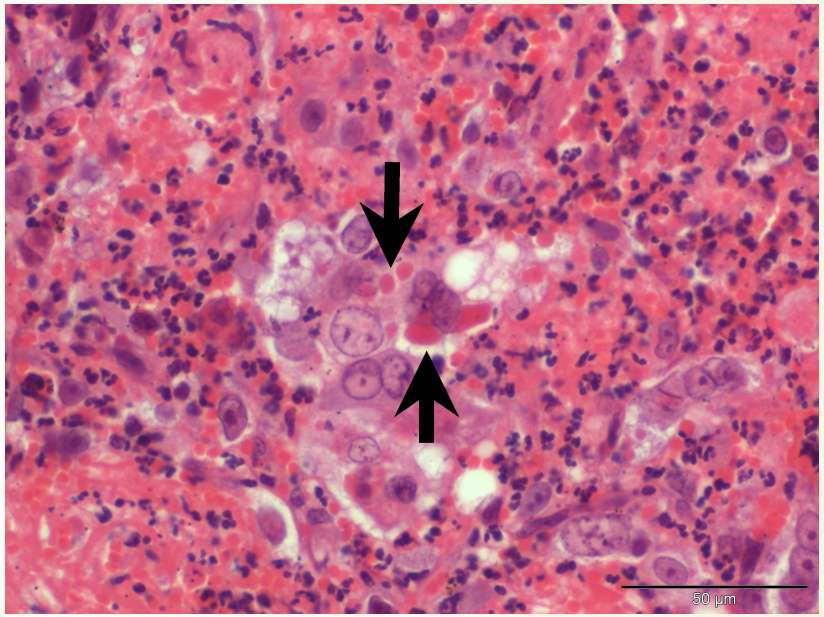
- Intracytoplasmic Inclusion bodies – Pox virus, Reovirus, Paramyxo virus and Rabies virus
- Intranuclear Inclusion bodies – Herpes virus, Adeno virus and Parvo virus
- Both IB – Canine distemper virus and porcine cytomegalo virus

Negri bodies in Rabies Virus



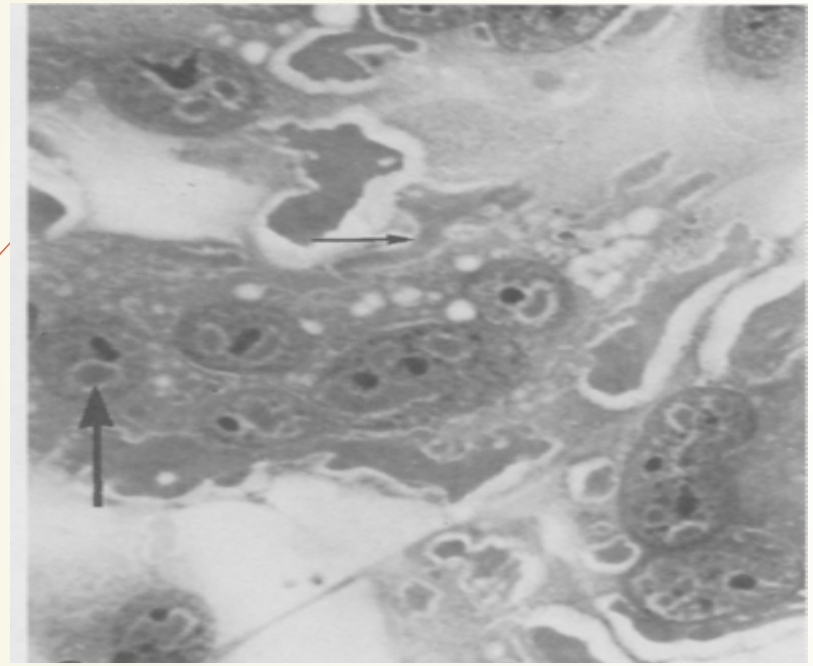
Negri bodies: masses of viral nucleocapsids, (Intracytoplasmic Inclusion bodies)

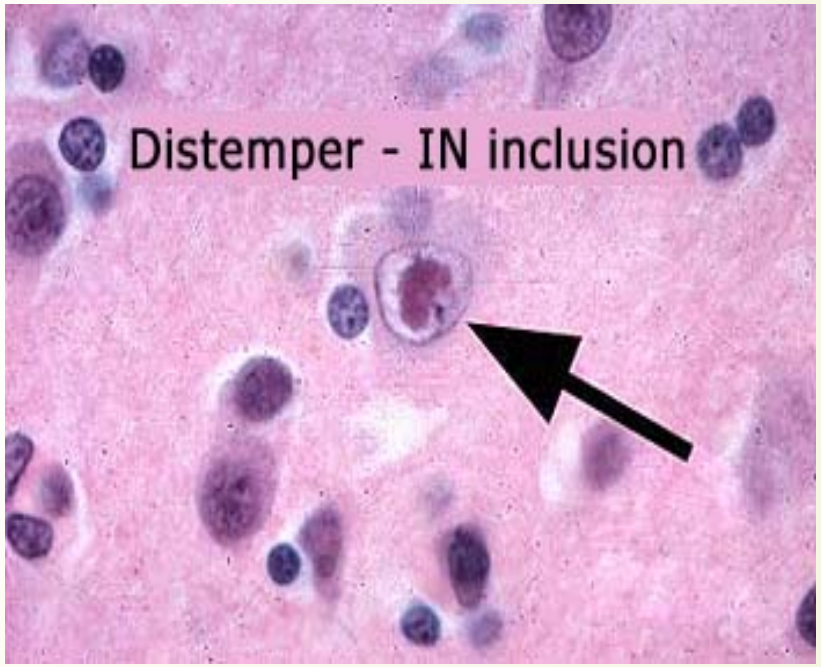
Elementary bodies in Pox virus



Intracytoplasmic inclusion bodies in Pox virus

Inclusion bodies in Canine diestemper virus





Virus-Induced Cell Death (Apoptosis / Necrosis)

- Viruses kill cells by direct means, by usurping cellular machinery, disrupting membrane integrity, etc.
- Cell die due to Necrosis or Apoptosis (Programmed cell Death)
- When a virus induces cell death by necrosis, it usually does so late, after progeny virus production is complete. (Viral strategy) eg. Picorna virus
- when a cell induces its own death, by apoptosis, it usually does so early, before progeny virus production is complete. (Host defence mechanism)

Continue.....

- Some viruses induce apoptosis by the direct action of a specific protein ex. adenoviruses, alphaviruses, and the circovirus, chicken anemia virus,
- Viruses induce apoptosis indirectly through their effects on cellular processes.
- Chromatin condensation and margination and eventually break up into membrane-bound bodies
- Cellular endonuclease is activated and cleaves cellular DNA into 180- to 200-bp fragments.

Interferons

- Viral *interference* - virus-infected cell resists superinfection
- Isaacs and Lindenmann 1954 - influenza virus release a nonviral protein into the medium , "interferon," that protects uninfected cells against infection
- Antiviral effects
- Species specific but not virus specific
- RNA viruses are better inducer than DNA viruses

Properties of Interferons

Property	Interferon α	Interferon β	Interferon γ
Principal source	Leukocytes, many other cells	Fibroblasts Epithelial cells	T lymphocytes, NK cells
Inducing agent	Virus infection	Virus infection	Antigen (or mitogen)
Number of subtypes	At least 22 in humans, fewer identified in animals	1	1
Glycosylation	No (most subtypes)	Yes	Yes
Functional form	Monomer	Dimer	Tetramer
Principal activity	Antiviral	Antriviral	Immunomodulation
Mechanism of action	Inhibits protein synthesis	Inhibits protein synthesis	Enhances MHC antigens; activates cytotoxic T cells, macrophages, and NK cells

Continue….

- Used in prophylaxis and treatment
- Anti cancer agent in lymphomas
- Used in Hepatitis B and C infections


Thank You!