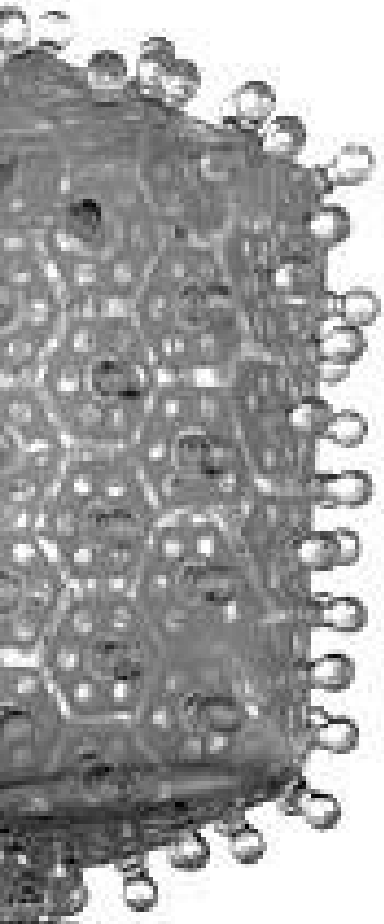
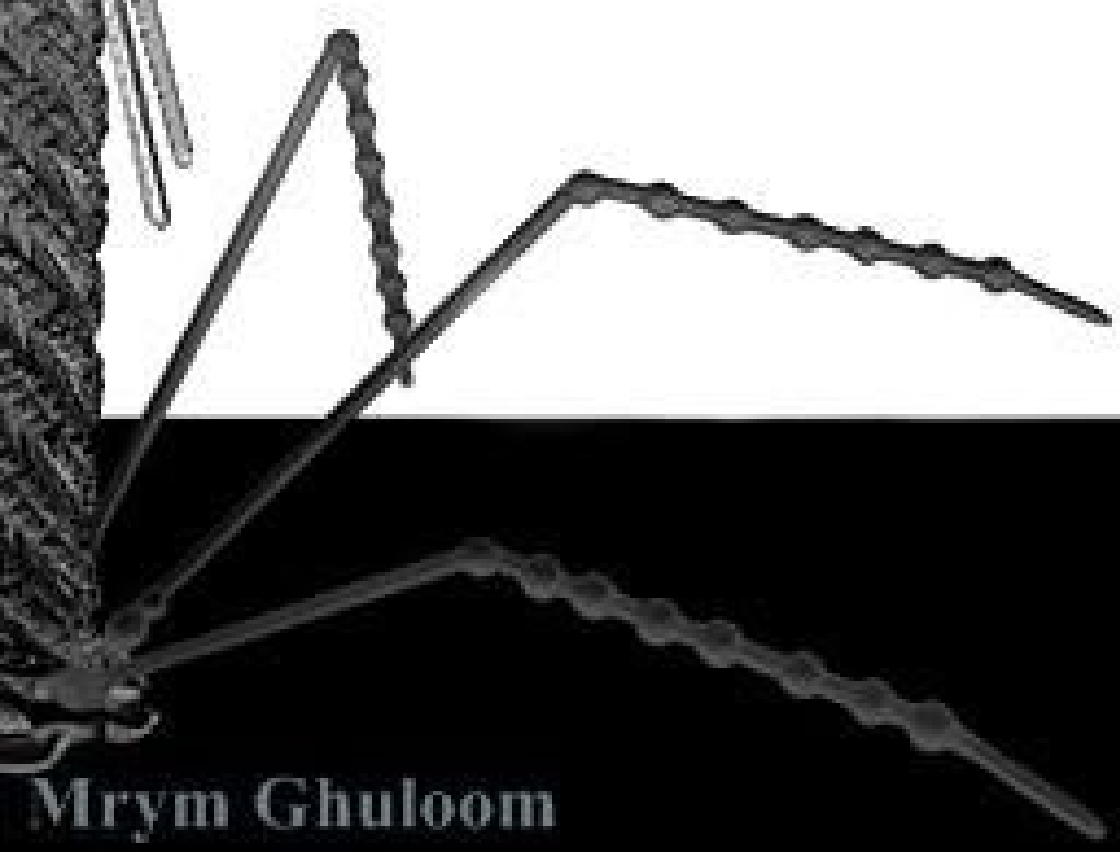


Microbiology

Lecture No:2- Virology

Dr Name:Hamed Al-Zoubi

Sheet ☐ Slide ■



Mrym Ghuloom

Virology – Introduction
JU- 2nd Year Medical Students

By

Dr Hamed AlZoubi – Microbiology and Immunology Department – Mutah University.

MBBS (J.U.S.T)

MSc, PhD medical microbiology (UK).

FRCPath (associate, medical microbiology).

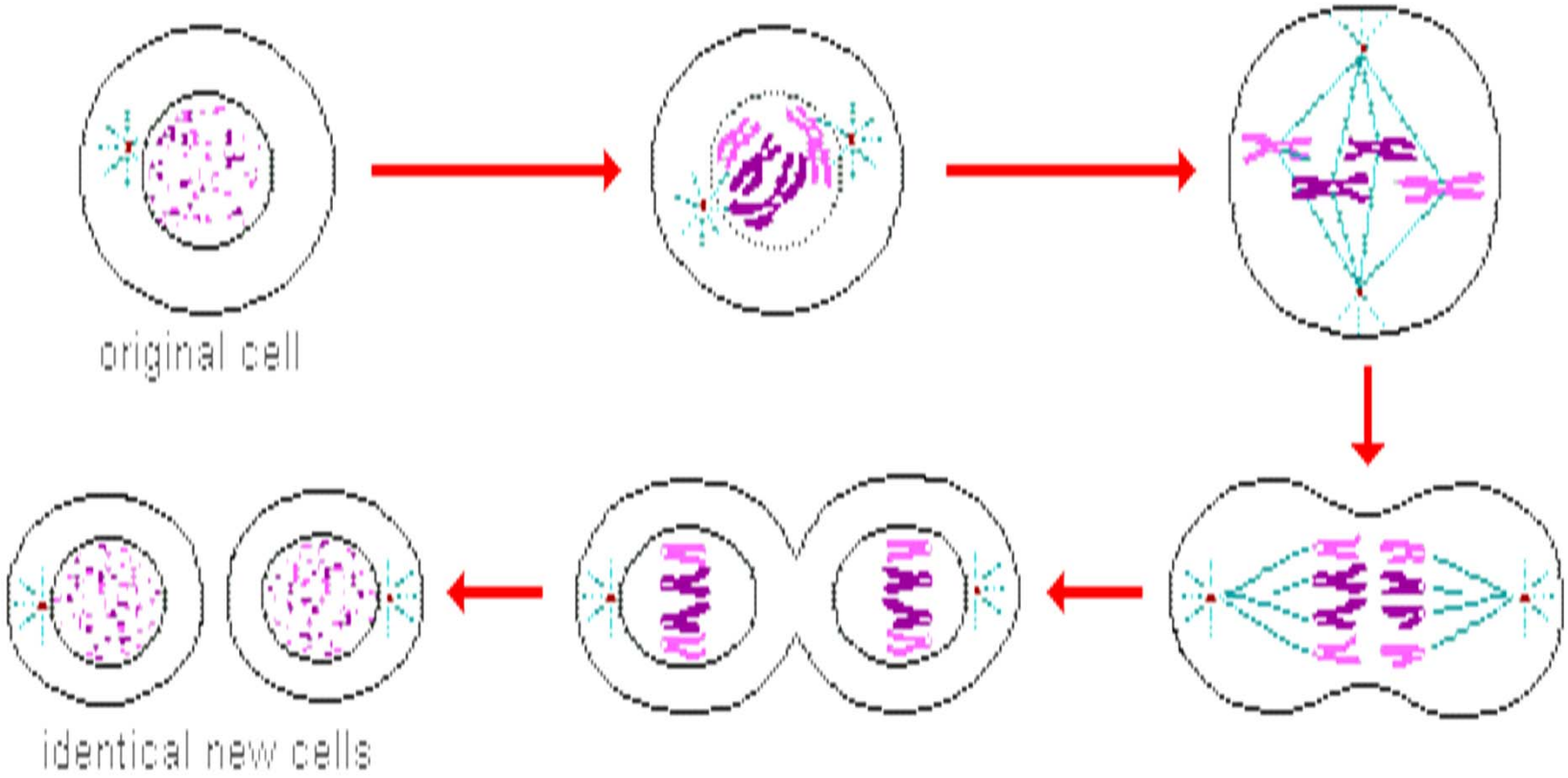
Virology – replication and genetics

- Non-viral forms of life multiply by fission leading to a daughter cell with genetics material and enzymes that are necessary for replication and metabolism

- Viruses enters cell with nearly only 20 genes (cell has 100000 genes)

- so it must rely on cellular mechanism (complicated life cycle)

- Viral replication is not fully understood


original cell
identical new cells

Virology – replication and genetics

- ❑ Molecular biology of mammalian cell:
- ✓ Structure
- dsDNA in an enveloped nucleus

- Nuclear pores
- Cytoplasm that contains proteins ad chemicals

- Golgi apparatus, lysosomes (intracellular digestion)

Virology – replication and genetics

- Ribosomes (proteins factory)
- Plasma membrane (has receptors for nutrients and hormones that are necessary for cell)
- These receptors, might be used by viruses

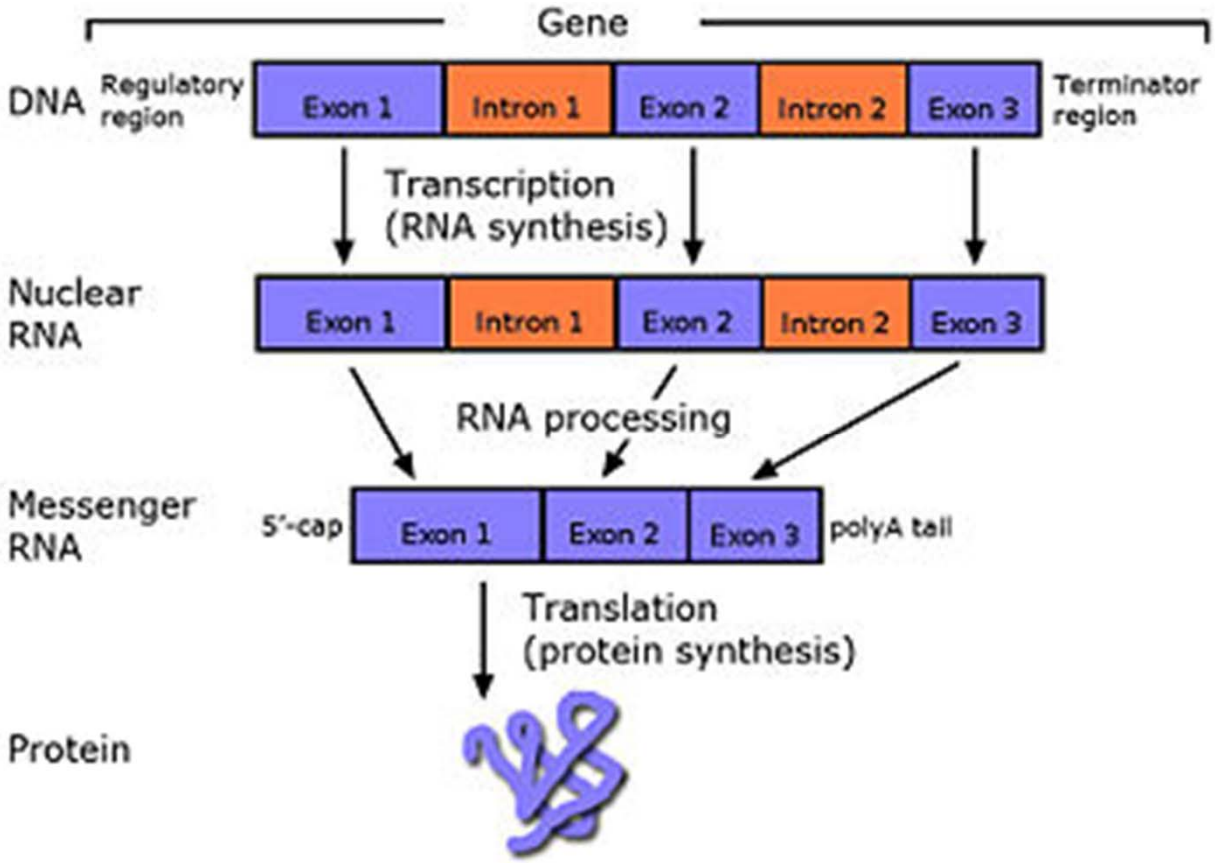
Virology – replication and genetics

✓ DNA

- ds DNA $3x10^9$ nucleotides
- Replication: DNA polymerase in the cell uses a template strand to build a complementary strand

✓ Transcription and processing:

- DNA is copied into mRNA
- m RNA is then processed (5'guanine cap and 3' poly A tail)
- introns are removed (spliced by small nuclear ribonucleoprotein particles) – translation of redaing frame into proteins


Gene
DNA
Regulatory region
Exon 1
Intron 1
Exon 2
Intron 2
Exon 3
Terminator region
Transcription (RNA synthesis)
Nuclear RNA
Exon 1
Intron 1
Exon 2
Intron 2
Exon 3
RNA processing
Messenger RNA
5'-cap
Exon 1
Exon 2
Exon 3
polyA tail
Translation (protein synthesis)
Protein

Virology – replication and genetics

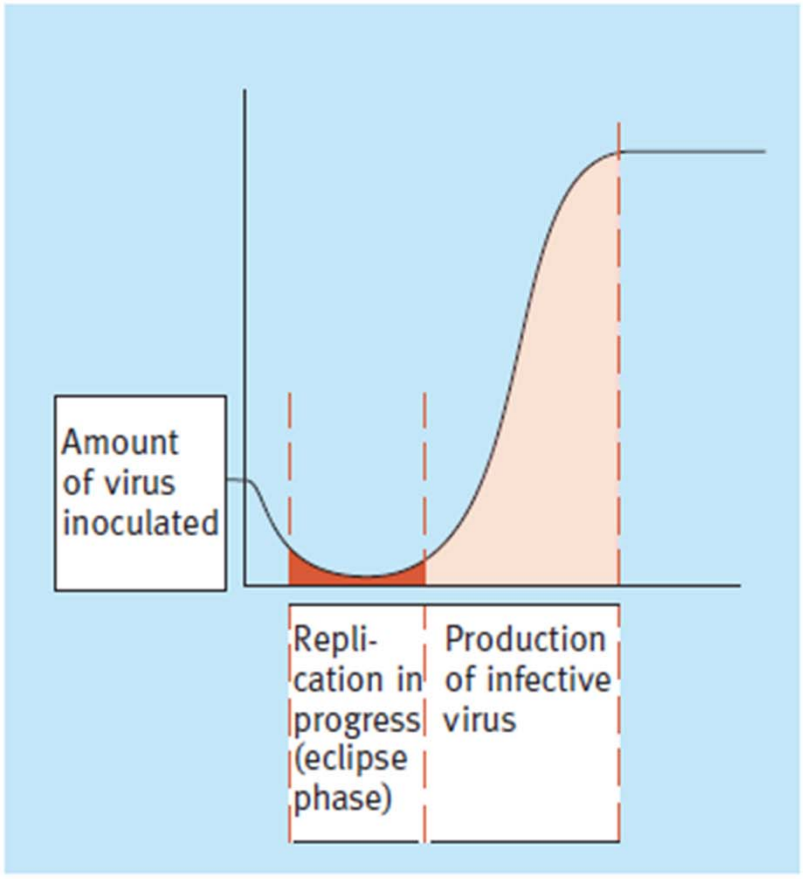
✓ Translation into proteins:

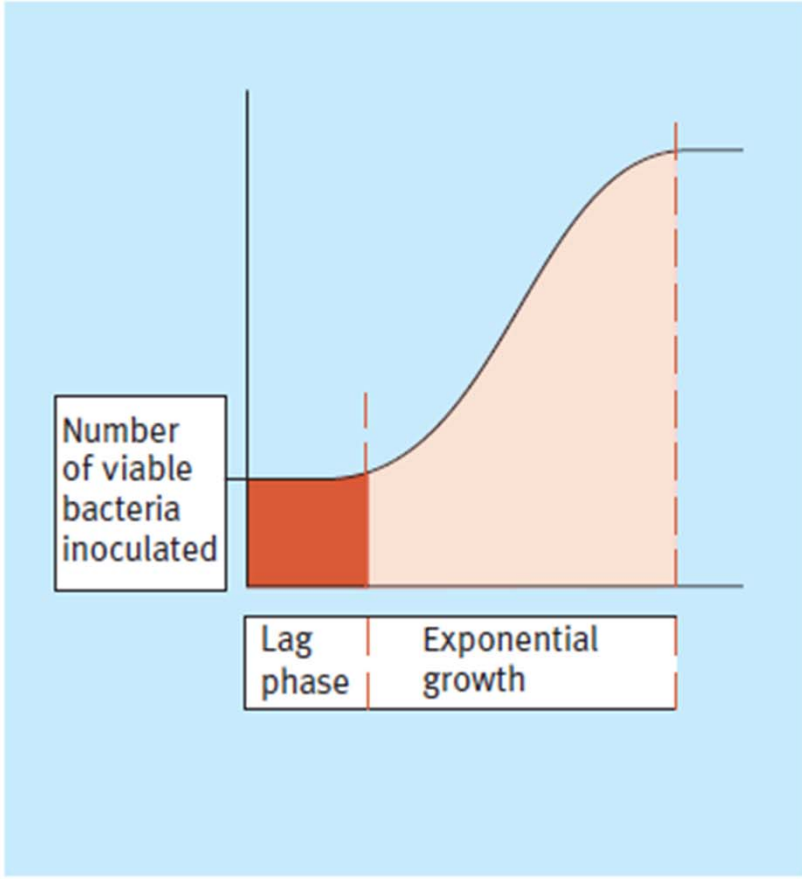
- Codon , ribosomes, amino acids
- Start (AUG) and stop codons (UAG UGA UAA)

❑ Viral replication and infection:

- Hit or miss, chance of contact (receptor and number)
- Few viral particles to initiate infection

Virology – difference between viral and bacterial replication





Virology – replication and genetics

Stages of viral life cycle:

1. Adsorption (attachment).
2. Penetration (internalisation)
3. Uncoating.
4. Transcription to mRNA
5. Translation into early (functional) and late (structural) proteins
6. Assembly in cytoplasm, nucleus or membrane
7. Release – lytic or budding

These stages can be divided into three phases

I – Initiation phase

-Attachment

-Penetration

-Uncoating

II - Replication phase

-DNA Synthesis

-RNA Synthesis

-Protein synthesis

III - Release phase

-Assembly

-Maturation

-Exit from cell

Virology – replication and genetics

- **Adsorption**
- Viral particles have receptor binding proteins (virus attachment proteins/spikes) attach to specific cellular receptors (glycoproteins or glycolipids).

- Adsorption is a random process determined by diffusion (Viruses do not have any capacity for locomotion)

- Determined by the concentrations of both, the virions and the cells.

Virology – replication and genetics

- Small viral amount (down to one virus) interacting with the receptors is enough to establish infection.

- A cell can have between 10^4-10^5 receptors on its surface.

- Mutations in the genes specifying anti-receptors may cause loss of the capacity to interact with certain receptors.

Virology – replication and genetics

- Example:

- Influenza virus – sialic acid
- HIV1: Primary receptoe CD4 on Tcells

  Secondary receptors: CXCR4 and CCR5

Virology – replication and genetics

- Presence of receptors determines:

1. Host range: e.g Measles (humans only),

Arboviruses (many hosts including animals)

2. Tissue tropism: e.g Rabies (brain), Hepatitis (Liver)

- The neutralizing antibodies can prevent infection by blocking adsorption to receptors.

Virology – replication and genetics

- Penetration:

❑ Direct membrane fusion (fusion from without)

- For the enveloped viruses Paramyxoviruses (eg, Parainfluenza), some retroviruses (eg, HIV-1), and herpesviruses
- The virus envelop fuses with the cell membrane and left there
- Mediated by hydrophobic amino acids of fusion proteins

Virology – replication and genetics

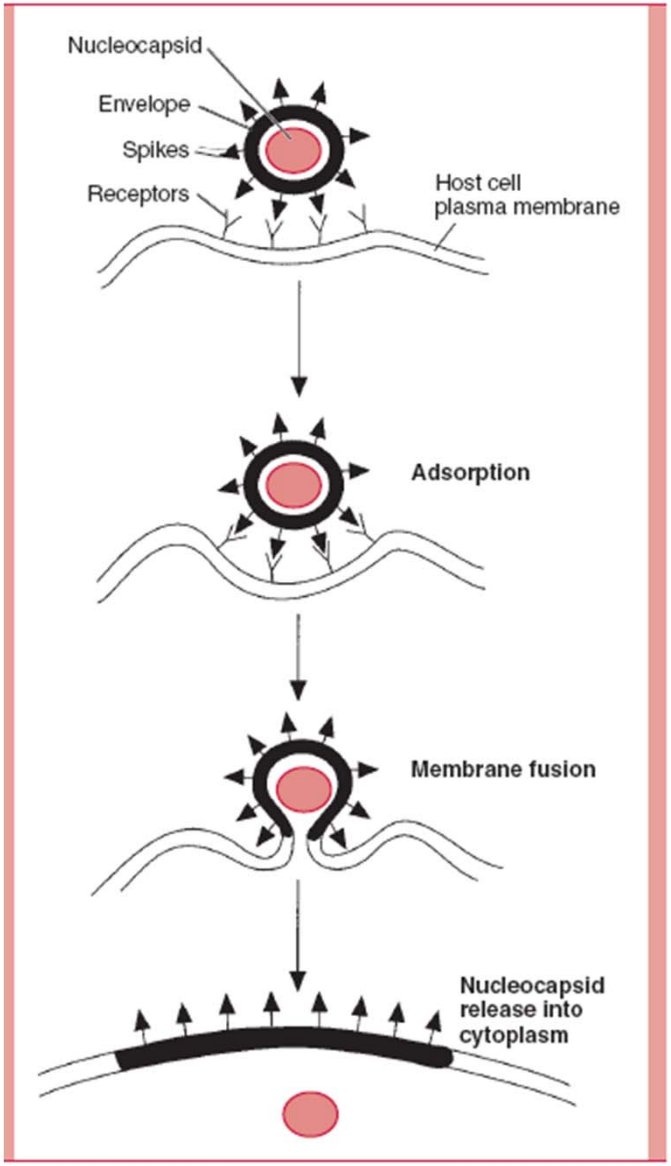
- Nucleocapsid released into cellular cytoplasm > capsid digested by cytoplasmic protease

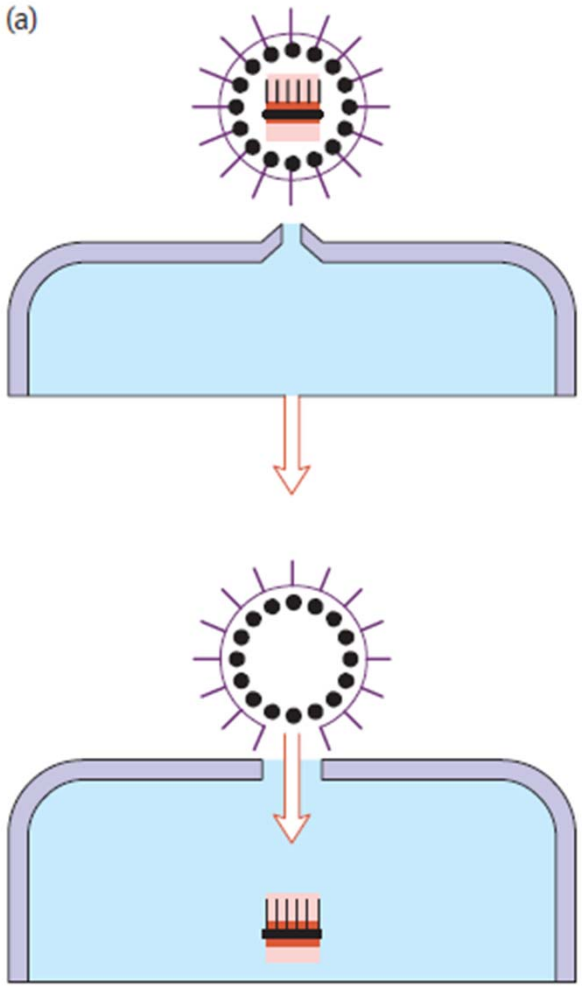
- Presence of the envelop fusion proteins in the cell membrane

  > Immune target

  > enhances infected cell – non infected cell fusion.

Virology – replication and genetics





Virology – replication and genetics

❑ Receptor mediated endocytosis (viropexis)

- For remaining enveloped viruses and for the naked viruses.

- receptor attachment followed by plasma membrane inversion

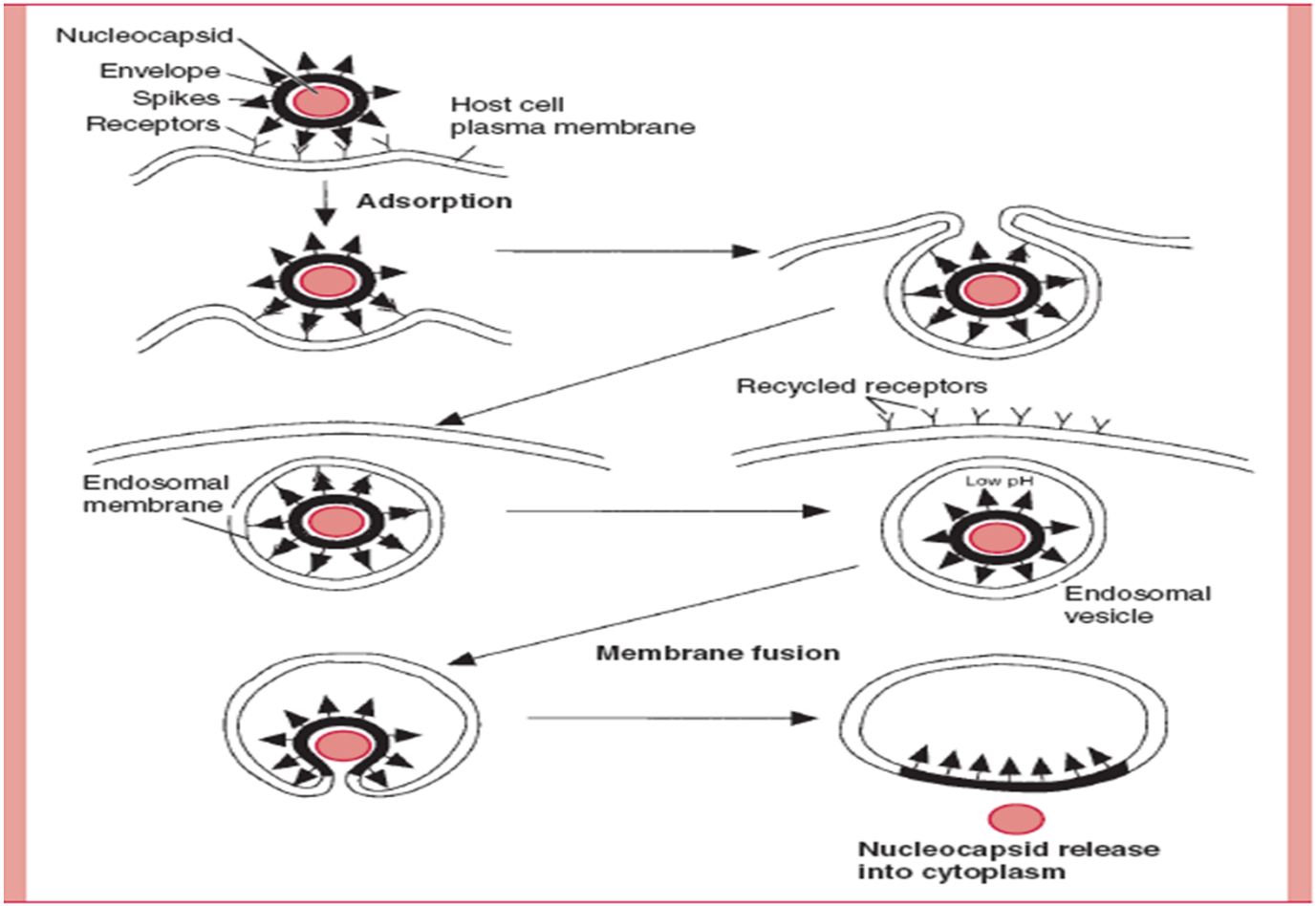
- Clathrin coated pit

Virology – replication and genetics

- Viruses attach to receptors then become surrounded by a plasma membrane invagination (pseudopodia)

> Pinching off of the cellular membrane encloses the virion in a cytoplasmic vesicle are formed > termed the **endosomal vesicle**

- Virus (nucleocapsid) is then released by acidity changes in the vesicle/endosomal lysis


Nucleocapsid
Envelope
Spikes
Receptors
Host cell
plasma membrane
Adsorption
Recycled receptors
Endosomal
membrane
Low pH
Endosomal
vesicle
Membrane fusion
Nucleocapsid release
into cytoplasm

Virology – replication and genetics

- In case of influenza:

- fusion from within
- PH and haemagglutinin mediated

- ❑ Some viruses use Non-clathrin mediated endocytosis (Caveolae)

Virology – replication and genetics

- **Formation of viral mRNAs**
- Synthesis of mRNA is a crucial step in replication

✓ mRNA is transcribed from dsDNA using cellular DNA dependent RNA polymerase (POXVIRUS?)

✓ +ve ssRNA recognised as mRNA and translated directly by cellular ribosomes (POLIOVIRUS, FLAVIVIRUS) (+ - +)

- directly infectious to cells by itself

✓ -ve ssRNA? antigenome (RABIES, INFLUENZA)

Virology – replication and genetics

- For many other viruses, translation is not straightforward:

1. Poxviruses replicate in the cytoplasm where no cellular RNA polymerase is available to transcribe the DNA genome > therefore, poxviruses carry its DNA dependent - RNA polymerase with it.

2. No cellular machinery exists that can use either single-stranded DNA or double-stranded RNA as a template to synthesize mRNA.

The End