REPLICATION OF VIRUSES

Viruses multiply only in living cells. The host cell must provide the energy and synthetic machinery and the low molecular- weight precursors for the synthesis of viral proteins and nucleic acids. The viral nucleic acid carries the genetic specificity to code for all of the virus-specific macromolecules in a highly organized fashion.

The unique feature of viral multiplication is that soon after interaction with a host cell the infecting virion is disrupted and its measurable infectivity is lost. This phase of the growth cycle is called the **eclipse period;** its duration varies depending on both the particular virus and the host cell, and it is followed by an interval of rapid accumulation of infectious progeny virus particles. In some cases, as soon as the viral nucleic acid enters the host cell, the cellular metabolism is redirected exclusively toward the synthesis of new virus particles and the cell is destroyed. In other cases, the metabolic processes of the host cell are not altered significantly, although the cell synthesizes viral proteins and nucleic acids, and the cell is not killed. After the synthesis of viral nucleic acid and viral proteins, the components assemble to form new infectious virions. The yield of infectious virus per cell ranges widely, from modest numbers to more than 100,000 particles. Not all infections lead to new progeny virus. **Productive** infections occur in **permissive** cells and result in the production of infectious virus. **Abortive** infections fail to produce infectious progeny, either because the cell may be **nonpermissive** and unable to support the expression of all viral genes or because the infecting virus may be **defective**, lacking some functional viral gene. A **latent** infection may ensue, with the persistence of viral genomes, the expression of no or a few viral genes, and the survival of the infected cell.

General Steps in Viral Replication Cycles

A variety of different viral strategies have evolved for accomplishing multiplication in parasitized host cells. The growth cycles of a double stranded DNA virus and a positive-sense, single-stranded RNA virus are diagrammed in Figure -1.

A. Attachment, Penetration, and Uncoating

The first step in viral infection is **attachment**, interaction of a virion with a specific receptor site on the surface of a cell. Receptor molecules differ for different viruses but are generally glycoproteins. In some cases, the virus binds protein sequences and in others oligosaccharides. Receptor binding is

believed to reflect fortuitous configurational homologies between a virion surface structure and a cell surface component.
After binding, the virus particle is taken up inside the cell. This step is referred to as **penetration** or engulfment. In some systems, this is accomplished by receptor-mediated endocytosis, with uptake of the ingested virus particles within endosomes. There are also examples of direct penetration of virus particles across the plasma membrane. In other cases, there is fusion of the virion envelope with the plasma membrane of the cell.
Uncoating occurs concomitantly with or shortly after penetration. Uncoating is the physical separation of the viral nucleic acid from the outer structural components of the virion so that it can function. The genome may be released as free nucleic acid or as a nucleocapsid. The nucleocapsids usually contain polymerases.

B. Expression of Viral Genomes and Synthesis of Viral Components

The synthetic phase of the viral replicative cycle ensues after uncoating of the viral genome. The essential theme in viral replication is that specific mRNAs must be transcribed from the viral nucleic acid for successful expression and duplication of genetic information. After this is accomplished, viruses use cell components to translate the mRNA. Various classes of viruses use different pathways to synthesize the
mRNAs depending on the structure of the viral nucleic acid.

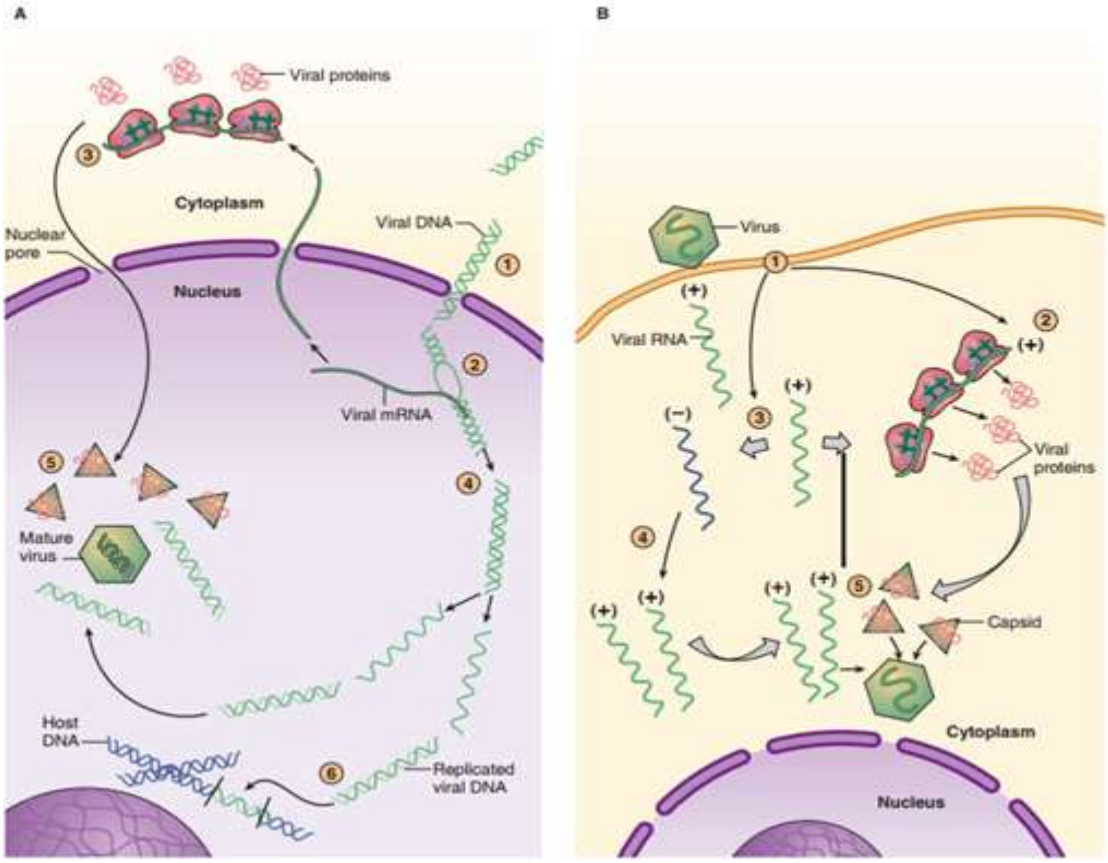

Figure 1: Example of viral growth cycles. **A:** The growth cycle of a nonenveloped, double-stranded DNA virus. In this example multiple steps in the replication cycle take place in the nucleus. (1) After penetrating the host cell, viral DNA is uncoated and enters the nucleus. (2) Viral genes are transcribed. (3) The mRNAs are translated in the cytoplasm. Newly synthesized proteins enter the nucleus. (4) Viral DNA is replicated in the nucleus, sometimes with the help of newly synthesized viral replication proteins. (5) Viral DNA and viral structural proteins assemble in the nucleus to produce new progeny virions. (6) On rare occasions, viral DNA may be incorporated into cellular DNA as a side-effect of infection. **B:** The growth cycle of a positive-sense, single-stranded RNA virus. In this example the replication cycle occurs in the cytoplasm. (1) The virus enters the cell and the viral RNA genome is uncoated. (2) As a positive-sense, single-stranded genome, the RNA is directly translated, producing viral proteins. (3) A negative-sense RNA copy of the positive template is synthesized. (4) It is used to produce many positive-sense copies. (5) The newly synthesized positive-sense RNA molecules are assembled with viral structural proteins to produce new progeny virions.

C. Morphogenesis and Release

Newly synthesized viral genomes and capsid polypeptides assemble together to form progeny viruses. Nonenveloped viruses accumulate in infected cells, and the cells eventually lyse and release the virus particles.
Enveloped viruses mature by a budding process. Virus specific envelope glycoproteins are inserted into cellular membranes; viral nucleocapsids then bud through the membrane at these modified sites and in so doing acquire an envelope.
Budding frequently occurs at the plasma membrane. Enveloped viruses are not infectious until they have acquired their envelopes.
Therefore, infectious progeny virions typically do not accumulate within the infected cell.
Viral maturation is sometimes an inefficient process. Excess amounts of viral components may accumulate and be involved in the formation of inclusion bodies in the cell. As a result of the profound deleterious effects of viral replication, cellular cytopathic effects eventually develop and the cell dies.
However, there are instances in which the cell is not damaged by the virus and long-term, persistent infections evolve.

Prepared by Assist Prof. Dr. Zainab Khudhur Ahmad