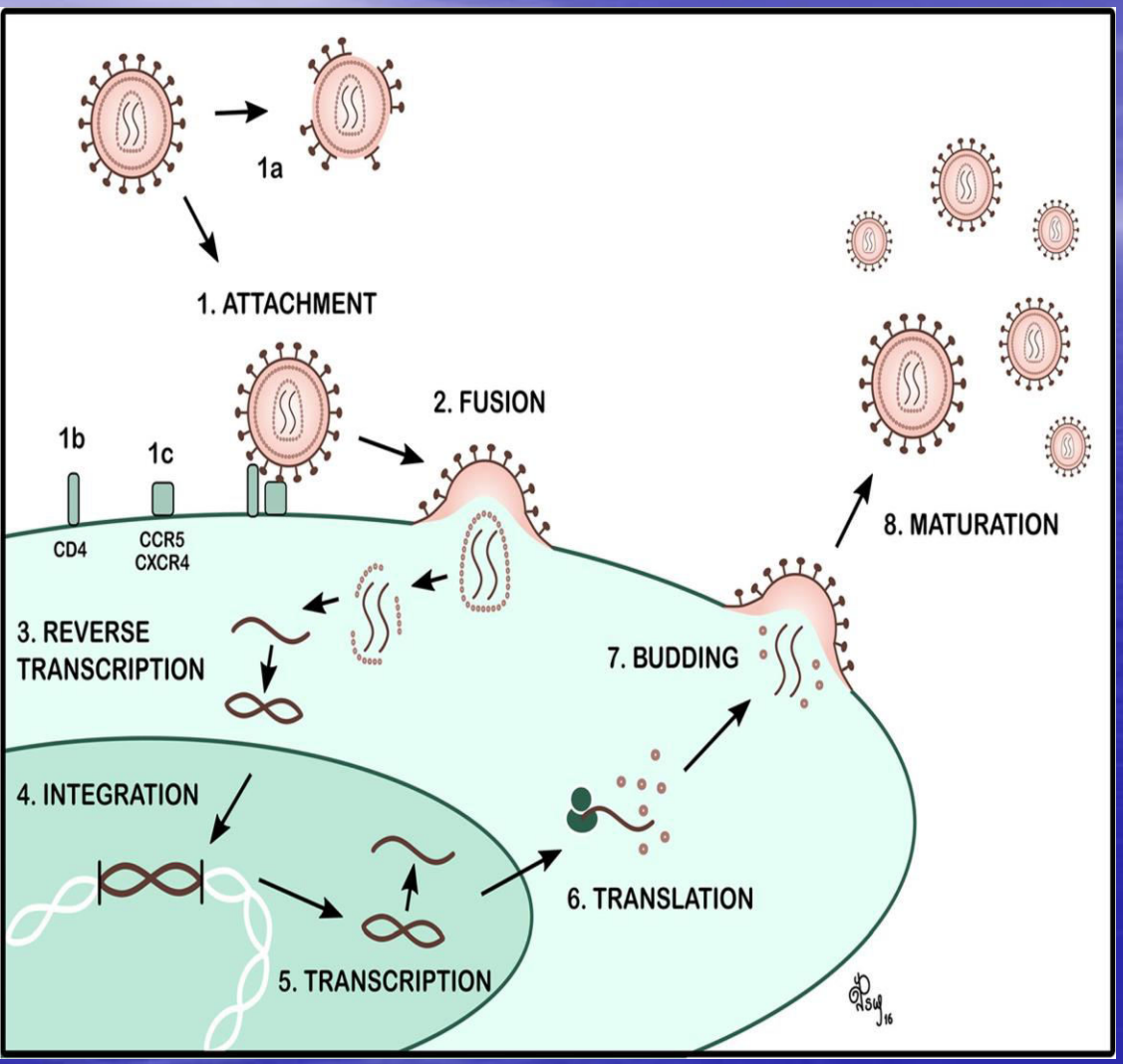
Antiviral Agents

- Viruses are obligate intracellular microbes
- use many of the host cell's biochemical mechanisms and products to sustain their viability

- A mature virus(virion) can exist outside a host cell and still retain its infective properties.



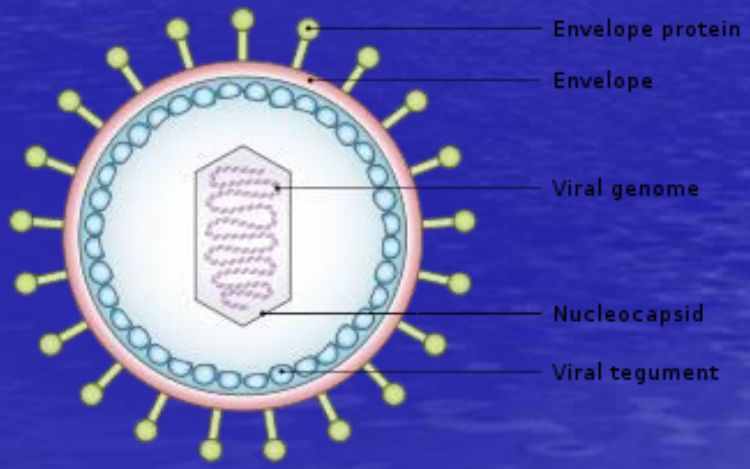
- the virus must enter the host cell, take over the host cell's mechanisms for nucleic acid and protein synthesis, and direct the host cell to make new viral particles

Classification of Viruses

- Viruses are composed of one or more strands of a nucleic acid (core) enclosed by a protein coat (capsid).

- Many viruses possess an outer envelope of protein or lipoprotein.

- Viral cores can contain either DNA or RNA



- viruses may be classified as DNA viruses or RNA viruses.

- Further classification is usually based on morphology, cellular site of viral multiplication, or other characteristics.

DNA viruses

- adenoviruses (colds, conjunctivitis)
- hepadnaviruses (hepatitis B);
- herpesviruses (cytomegalovirus chickenpox)
- papillomaviruses (warts)

RNA viruses

- arborviruses (yellow fever)
- arenaviruses (meningitis);
- orthomyxoviruses(influenza);
- paramyxoviruses (measles, mumps);
- picornaviruses (meningitis, colds);
- rubella virus (German measles)
- retroviruses (AIDS).

Antiviral Agents

Viruses live intracellular, so drugs should be able to enter the human cells.

ANTIHERPESVIRUS AGENTS

Used primarily in the treatment of herpesviruses.

Acyclovir

- Wide spectrum antiviral agent.
- Herpes virus.
- Available as oral tablets, IV injections, eye drops and ointment, or as a cream.
- In Varicella= Chicken Pox, use is restricted to immunocompromized patients.
- Side Effects: N, V, Skin rashes.

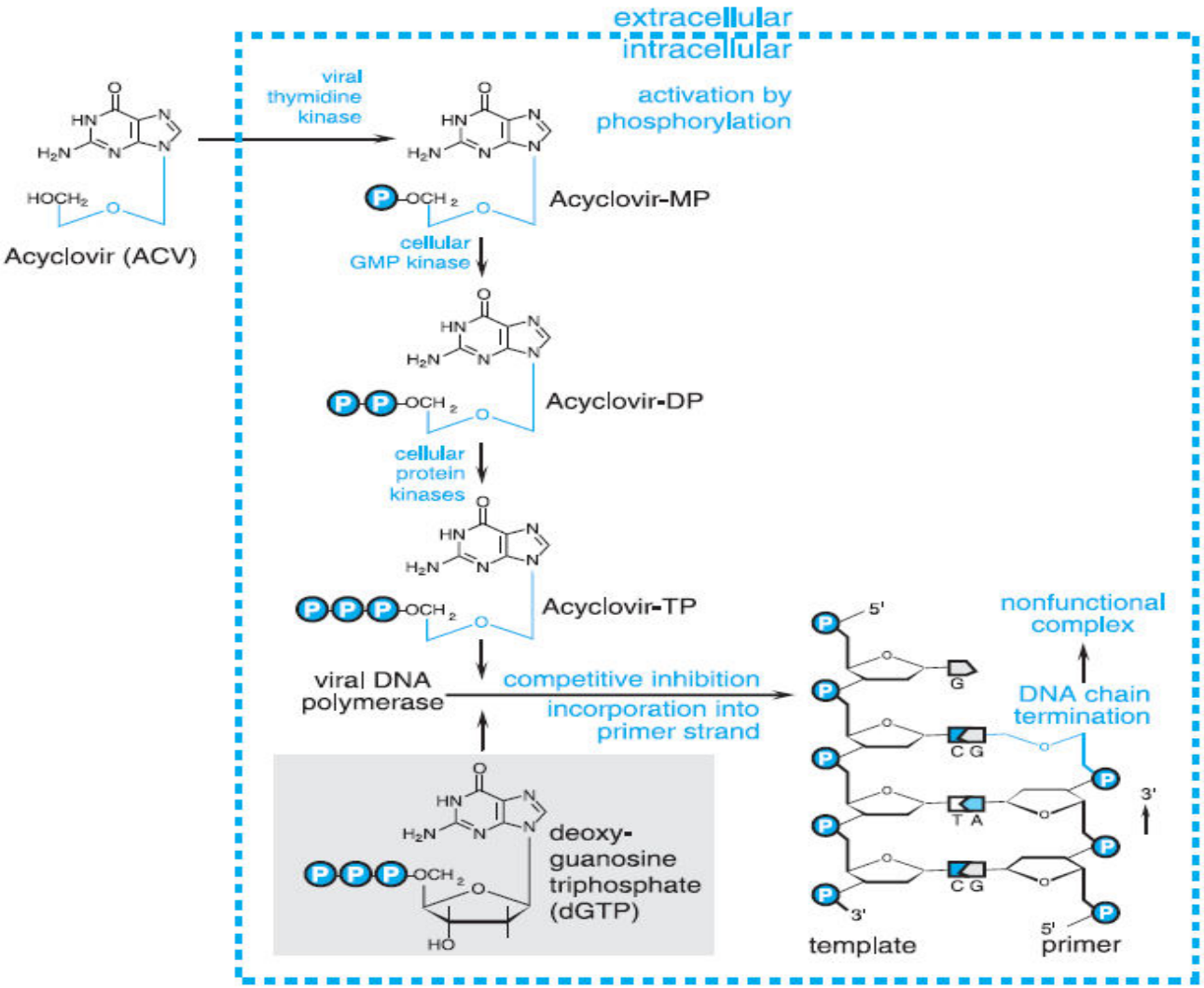


Figure 49–2. ***Conversion of acyclovir to acyclovir triphosphate leading to DNA chain termination.*** Acyclovir is converted to the monophosphate (MP) derivative by a herpesvirus thymidine kinase. Acyclovir-MP is then phosphorylated to acyclovir-DP and acyclovir-TP by cellular enzymes. Uninfected cells convert very little or no drug to the phosphorylated derivatives. Thus, acyclovir is selectively activated in cells infected with herpesviruses that code for appropriate thymidine kinases. Incorporation of acyclovir-MP from acyclovir-TP into the primer strand during viral DNA replication leads to chain termination and formation of an inactive complex with the viral DNA polymerase. (Adapted from Elion, 1986, with permission.)

ANTIINFLUENZA AGENTS

- *Amantadine*
- *Rimantadine*
- *Oseltamivir*
- *Zanamivir*

- Amantadine (*Symmetrel*) is a synthetic tricyclic amine,
- rimantadine (*Flumadine*) is its -methyl derivative.

- *Their mechanism of action involves inhibition of the viral M2 protein, an integral membrane protein that acts as a H channel.*

- Blockade of the M2 protein prevents the acid-mediated dissociation of the ribonucleoprotein complex
- the pH changes that result from M2 inhibition inhibit viral assembly.

Ribonucleoprotein an association that combines a RNA and an RNA-binding protein together.

During the replication of many **viruses**, hundreds to thousands of proteins assemble around the **viral** nucleic acid to form a protein shell called a capsid.

OTHER ANTIVIRAL AGENTS

Used in the treatment of

HBV
hepatitis C virus (HCV)
respiratory syncytial virus (RSV)
human papilloma virus (HPV)
HIV infection

Anti HIV Agents

Zidovudine

- Inhibits viral DNA production.
- Expensive.
- Causes N, V, muscle pain, and bone marrow suppression.

Anti HIV Agents

Indinavir

- **Protease inhibitor.**
- block the part of HIV called protease. HIV-1 protease is an enzyme required for the proteolytic cleavage of the viral polyprotein precursors into the individual functional proteins found in infectious HIV-1. Indinavir binds to the protease active site and inhibits the activity of the enzyme
- **Expensive.**

- **Causes N, V, Diarrhea, Renal stone formation.**
- indinavir wears off quickly after dosing, so requires very precise dosing every eight hours to prevent HIV from forming drug-resistant mutations, including resistances to other protease inhibitors

Interferones

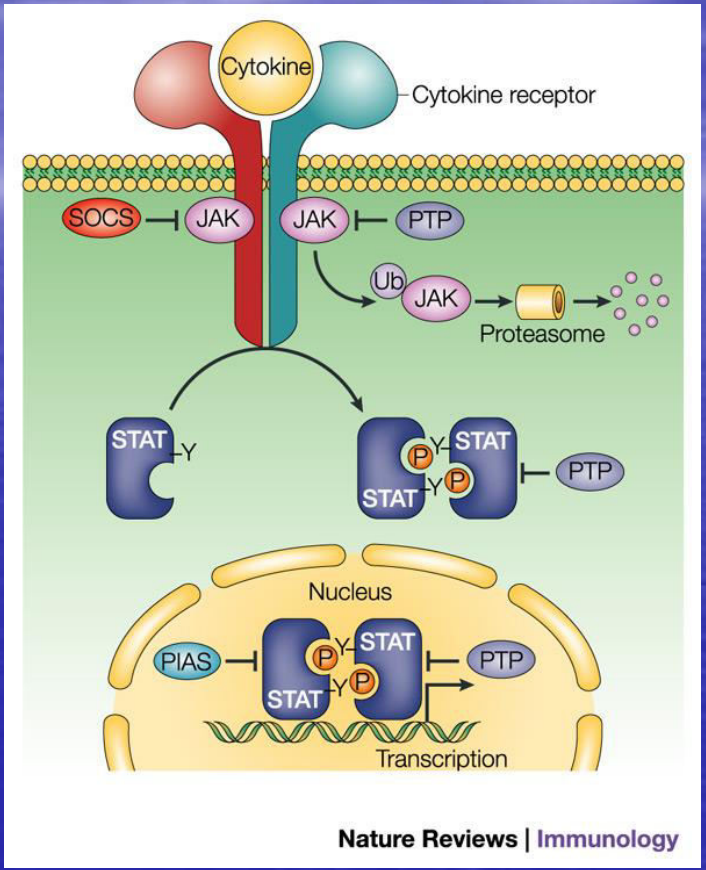
- Interferons (IFNs) are potent cytokines that possess antiviral, immunomodulating, and antiproliferative activities
- Natural substances produced by virally infected cells.
- Viral infection gives immunity for variable duration.
- Modify the immune response to increase resistance to viral infection, and control growth of the virus.

- Obtained in small amounts form donor WBCs.
- Nowadays, obtained commercially by recombinant DNA technology.
- Used in Hepatitis C, and some leukemias.
- Can cause nausea, fever, and malaise (flu-like symptoms).

Mechanisms of Action.

Following binding to specific cellular receptors, IFNs activate the JAK-STAT signal transduction pathway

This, in turn, leads to synthesis of over two dozen proteins that contribute to viral resistance mediated at different stages of viral penetration



- 7