

Antiviral therapy

Viruses

Viruses are the smallest infective agents, consisting essentially of nucleic acid (either RNA or DNA) enclosed in a protein coat or capsid. A virus cannot replicate on its own. It must attach to and enter a host cell. It then uses the host cell's energy to synthesize protein, DNA, and RNA. Viruses are difficult to kill because they live inside the cells. Any drug that kills a virus may also kill cells.

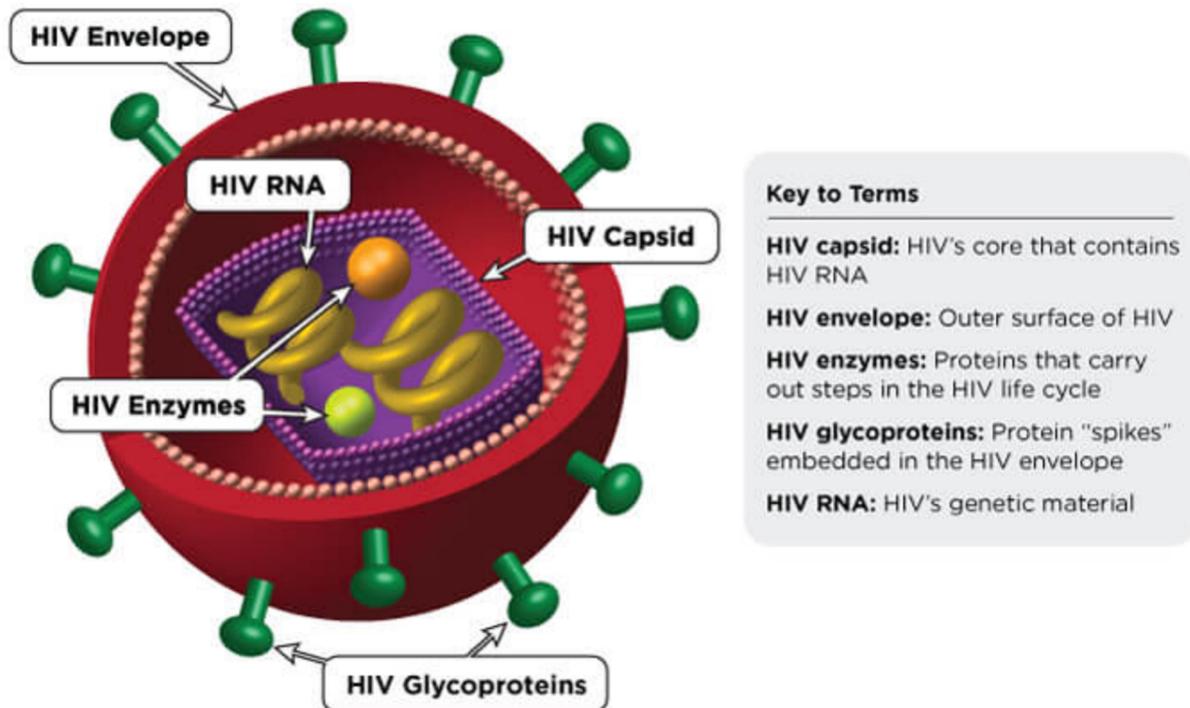


Figure: viral structure.

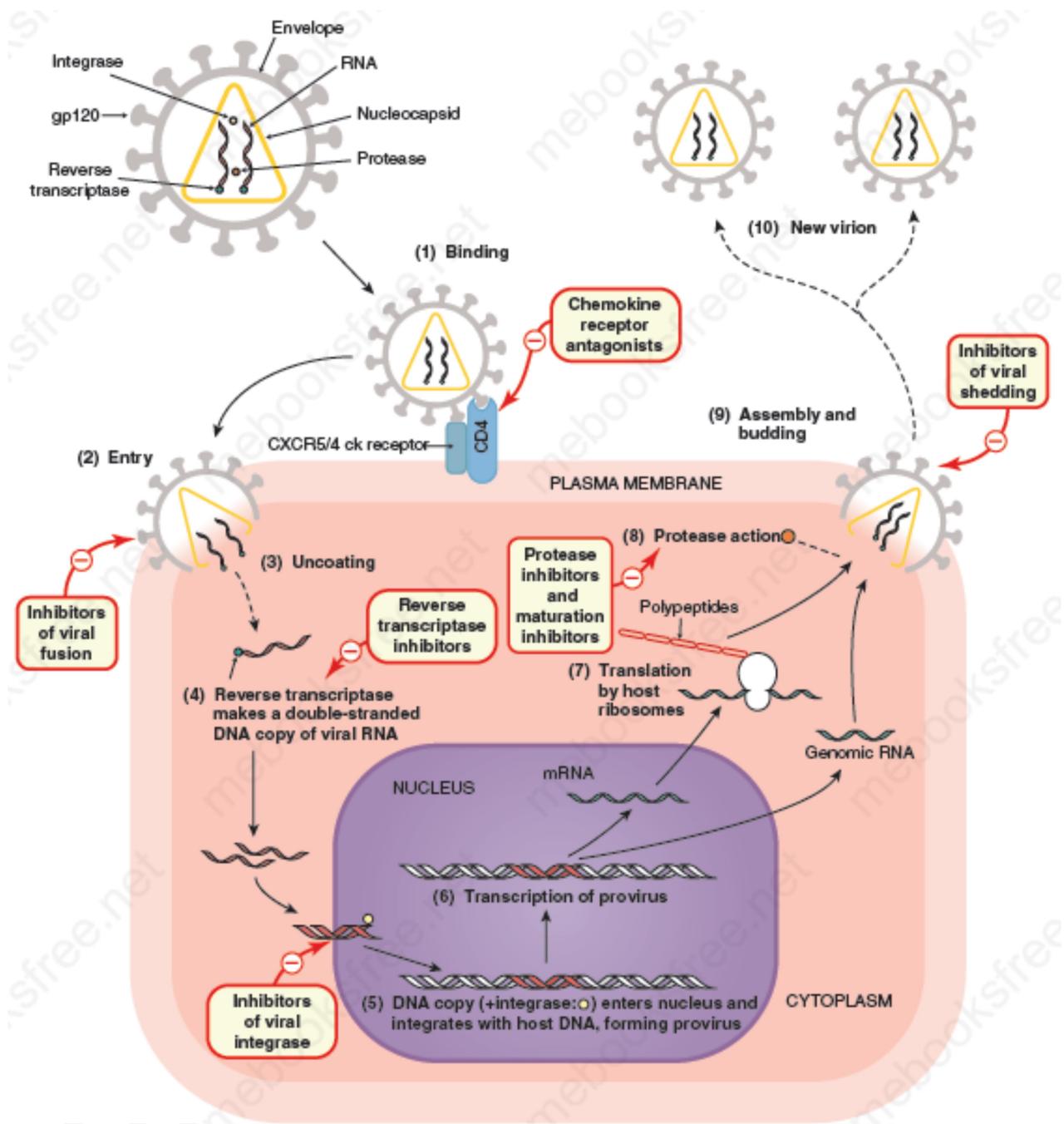


Fig. Schematic diagram of infection of a CD4+ T cell by an HIV virion, with the sites of action of the main classes of anti-HIV drugs.

Antiviral drugs

Antiviral drugs are used to prevent or treat viral infections ranging from influenza to human immunodeficiency virus (HIV). The major antiviral drug classes used to treat systemic infections include:

- synthetic nucleosides
- pyrophosphate analogues
- influenza A and syncytial virus drugs
- nucleoside analogue reverse transcriptase inhibitors (NRTIs)
- non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- nucleotide analogue reverse transcriptase inhibitors
- protease inhibitors.

Synthetic nucleosides

Synthetic nucleosides are a group of drugs used to treat many viral syndromes that can occur in an immunocompromised patient including herpes simplex virus (HSV) and cytomegalovirus (CMV).

Drugs in this class include:

- acyclovir
- famciclovir
- ganciclovir

Acyclovir enters virus-infected cells, where it's changed through a series of steps to acyclovir triphosphate. Acyclovir triphosphate inhibits virus-specific DNA polymerase, an enzyme necessary for viral growth, thus disrupting viral replication. The main adverse effect of Acyclovir is kidney impairment with rapid I.V. injection

Pyrophosphate analogues

An example of these drugs are **Foscarnet**, it prevents viral replication by selectively inhibiting DNA polymerase. Foscarnet's primary therapeutic use is treating CMV retinitis in the patient with AIDS.

Influenza A and syncytial virus drugs

Amantadine and its derivative, rimantadine hydrochloride, are used to prevent or treat influenza A infections. Ribavirin is used to treat respiratory syncytial virus (RSV) infections in children.

Although its exact mechanism of action of this group is unknown, it appears that they inhibit an early stage of viral replication, probably by inhibiting viral RNA and protein synthesis.

Nucleoside analogue reverse transcriptase inhibitors (NRTIs)

NRTIs are used to treat the patient with advanced HIV infection. Drugs in this class include:

- abacavir
- didanosine
- emtricitabine
- lamivudine
- stavudine
- zidovudine.

They act by inhibiting viral DNA replication.

Note: Potentially fatal lactic acidosis and severe hepatomegaly with steatosis have occurred in patients taking NRTIs alone or with other antiretrovirals.

Non-nucleoside reverse transcriptase inhibitors

NNRTIs are used in combination with other antiretrovirals to treat HIV infection.

The three agents in this class include:

- delavirdine
- efavirenz
- nevirapine.

They bind to the reverse transcriptase enzyme, preventing it from exerting its effect, and thus preventing viral replication.

Nucleotide analogue reverse transcriptase inhibitors

Nucleotide analogue reverse transcriptase inhibitors are used in combination with other antiretrovirals in the treatment of HIV. The only drug in this class to date is **tenofovir**, and it works much like the NRTIs by inhibiting viral DNA replication.

Protease inhibitors

Protease inhibitors are drugs that act against the enzyme HIV protease, preventing it from dividing a larger viral precursor protein into the active smaller enzymes that the HIV virus needs to fully mature. The result is an immature, noninfectious cell. Drugs in this group include:

- amprenavir
- atazanavir
- darunavir
- fosamprenavir
- indinavir sulfate
- lopinavir and ritonavir
- nelfinavir mesylate
- ritonavir
- saquinavir mesylate
- tipranavir.

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