

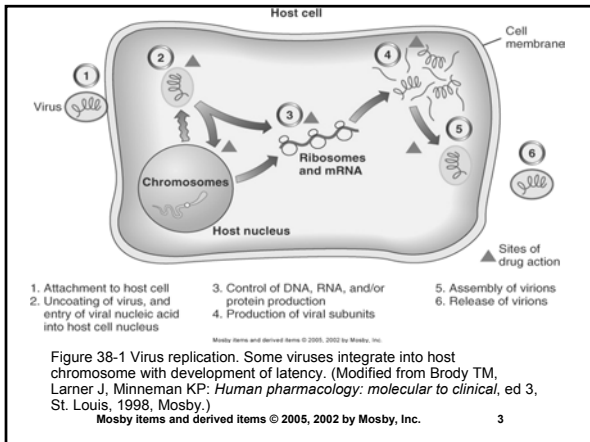
## CHAPTER 38

### Antiviral Agents

## Understanding Viruses

### Viral replication

- 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



## Understanding Viruses (cont'd)

Viruses are difficult to kill because they live inside our cells

- Any drug that kills a virus may also kill our cells

## Viral Infections

Competent immune system:

- Best response to viral infections
- A well-functioning immune system will eliminate or effectively destroy virus replication

## Viral Infections (cont'd)

Immunocompromised patients have frequent viral infections

- Cancer patients, especially leukemia or lymphoma
- Transplant patients, due to pharmacologic therapy
- AIDS patients, disease attacks immune system

## Antivirals

Viruses killed by current antiviral therapy

- Cytomegalovirus (CMV)
- Hepatitis viruses
- Herpes viruses
- Human immunodeficiency virus (HIV)
- Influenza viruses (the “flu”)
- Respiratory syncytial virus (RSV)

## Antivirals (cont'd)

Key characteristics of antiviral drugs

- Able to enter the cells infected with virus
- Interfere with viral nucleic acid synthesis and/or regulation
- Some agents interfere with ability of virus to bind to cells
- Some agents stimulate the body's immune system

## Antiviral Medications

- Antiviral agents
  - Used to treat infections caused by viruses other than HIV
- Antiretroviral agents
  - Used to treat infections caused by HIV, the virus that causes AIDS

## Antiviral Agents: Nonretroviral

- Mechanism of action
  - Inhibit viral replication
- Used to treat non-HIV viral infections
  - Influenza viruses
  - HSV, VZV (another herpesvirus)
  - CMV
  - Hepatitis A, B, C (HAV, HBV, NCV)

## Antivirals: Synthetic Purine Nucleoside Analogues

- Purine nucleosides
  - Guanine
  - Adenosine
- Pyrimidine nucleosides
  - Thymine
  - Cytosine
  - Uracil

## Antivirals: Purine Nucleosides

<u>Agent</u>	<u>Antiviral Activity</u>
<b>Guanines</b>	
acyclovir	HSV-1, HSV-2, VZV
ganciclovir (DHPG)	CMV retinitis and systemic
CMV infection	
ribavirin (RTCD)	Influenza types A and B, RSV, LV, HV
<b>Adenosines</b>	
didanosine (ddl)	HIV
vidarabine (Ara-A)	HSV, herpes zoster

## Antivirals: Pyrimidine Nucleosides

Agent	Antiviral Activity
<b>Cytosines</b>	
lamivudine (3TC)	HIV
zalcitabine (ddC)	HIV
<b>Thymine</b>	
idoxuridine (IDU)	HSV
stavudine (d4T)	HIV
trifluridine	HSV
zidovudine (AZT)	HIV

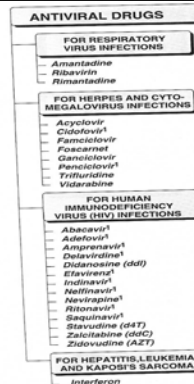


Figure 37.1 Summary of antiviral drugs. <sup>1</sup>Described in *Pharmacology update*, p. 457.

## Other Antivirals: Nonretroviral

- amantadine (Symmetrel) and rimantadine (Flumadine)
  - Influenza A
- foscarnet (Foscavir)
  - CMV (retinitis and systemic)
  - HSV infections

## Nonretrovirals: Neuraminidase Inhibitors

- oseltamivir (Tamiflu) and zanamivir (Relenza)
  - Influenza types A and B
- acyclovir (Zovirax)
  - HSV-1 and HSV-2, VZV (chickenpox or shingles)
- ganciclovir (Cytovene)
  - CMV infections
- ribavirin (Copegus)
  - Lower respiratory RSV infections in infants – not indicated for adults

## Antivirals: Side Effects

- acyclovir
  - Burning when topically applied, nausea, vomiting, diarrhea, headache
- amantadine and rimantadine
  - Anticholinergic effects, insomnia, lightheadedness, anorexia, nausea, others
- didanosine
  - Pancreatitis, peripheral neuropathies, seizures

## Antivirals: Side Effects (cont'd)

- zidovudine
  - Bone marrow suppression, nausea, headache
- foscarnet
  - Headache, seizures, acute renal failure, nausea, vomiting, diarrhea, others
- ganciclovir
  - Bone marrow toxicity, nausea, anorexia, vomiting

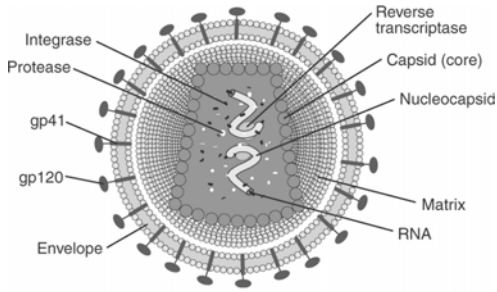


Figure 38-02 Human immunodeficiency virus (HIV). Within the core capsid, the diploid, single-stranded, positive-sense RNA is complexed to nucleoprotein. (From *Dorland's illustrated medical dictionary*, ed 30, Philadelphia, 2003, WB Saunders.)

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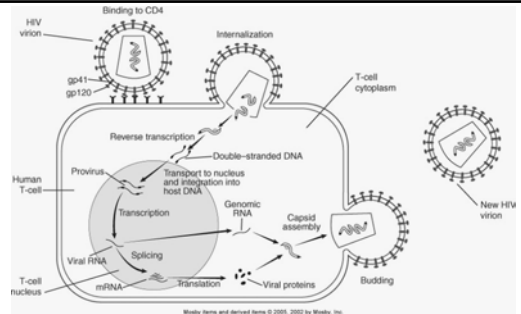
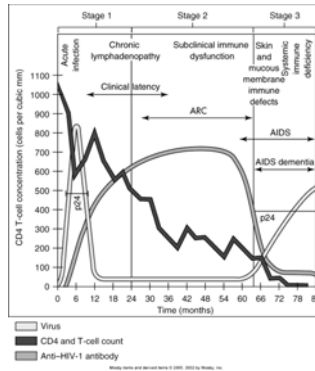


Figure 38-03 Life cycle of the HIV virus. The extracellular envelope protein gp120 binds to CD4 on the surface of T-lymphocytes or mononuclear phagocytes, while the transmembrane protein gp41 mediates the fusion of the viral envelope with the cell membrane. *gp*, Glycoprotein. (From *Dorland's illustrated medical dictionary*, ed 30, Philadelphia, 2003, WB Saunders.)

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Figure 38-04 Time course and stages of HIV disease. A long clinical latency period follows the initial mononucleosis-like symptoms. The progressive decrease in the number of CD4 T-cells, even during the latency period, allows opportunistic infections to occur. The stages (World Health Organization and Centers for Disease Control and Prevention) in HIV disease are defined by the CD4 T-cell levels and occurrence of opportunistic disease. ARC, Acquired immunodeficiency syndrome (AIDS)-related complex. (Redrawn from Redfield RR, Buske DS: HIV infection: the clinical picture, *Sci Am* 259:90-98, 1988, updated 1996. In Murray PR et al: *Medical microbiology*, St. Louis, 2002, Mosby.)



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## HIV

- Human immunodeficiency virus infection
- ELISA (enzyme-linked immunosorbent assay)
  - Detects HIV exposure based on presence of human antibodies to the virus in the blood
- Retrovirus
- Transmitted by:
  - Sexual activity, intravenous drug use, perinatally from mother to child

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## Five Stages of HIV Infection

- Stage 1: primary infection
- Stage 2: asymptomatic infection
- Stage 3: persistent generalized lymphadenopathy
- Stage 4: symptomatic stage
- Stage 5: progression to full-blown AIDS

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## Opportunistic Infections

- Protozoal
  - Toxoplasmosis of the brain, others
- Fungal
  - Candidiasis of the lungs, esophagus, trachea
  - PCP, others
- Viral
  - CMV disease, HSV infection, others

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## Opportunistic Infections (cont'd)

- Bacterial
  - Various mycobacterial infections, others
- Opportunistic neoplasias
  - Kaposi's sarcoma, others
- Others
  - HIV wasting syndrome
  - HIV encephalopathy
  - Lymphoid interstitial pneumonia

## Antiretroviral Agents

- HAART
- Highly active antiretroviral therapy
- Includes at least three medications
- These medications work in different ways to reduce the viral load

## Antiretroviral Agents (cont'd)

- Reverse transcriptase inhibitors (RTIs)
  - Block activity of the enzyme reverse transcriptase, preventing production of new viral DNA
- Protease inhibitors (PIs)
  - Inhibit the protease retroviral enzyme, preventing viral replication
- Fusion inhibitors
  - Inhibit viral fusion, preventing viral replication

## Antiretroviral Agents (cont'd)

- Reverse transcriptase inhibitors (RTIs)
  - Nucleoside RTIs (NRTIs)
  - Nonnucleoside RTIs (NNRTIs)
  - Nucleotide RTIs (NTRTIs)
- Examples
  - abacavir (Ziagen)      delavirdine (Rescriptor)
  - didanosine (Videx)    lamivudine (EpiVir)
  - stavudine (Zerit)      tenofovir (Viread)

## Antiretroviral Agents (cont'd)

- Protease inhibitors (PIs)
  - Inhibit the protease retroviral enzyme, preventing viral replication
  - Examples:
    - amprenavir (Agenerase)    indinavir (Crixivan)
    - nelfinavir (Viracept)      ritonavir (Norvir)
    - saquinavir (Invirase)

## Antiretroviral Agents (cont'd)

- Fusion inhibitors
  - Inhibit viral fusion, preventing viral replication
  - Newest class of antiretroviral drugs
  - Example: enfuvirtide (Fuzeon)

## Antiretroviral Agents: Side Effects

- Numerous and vary with each agent
- Drug therapy may need to be modified because of side effects
- Goal is to find the regimen that will best control the infection with a tolerable side effect profile
- Medication regimens change during the course of the illness

## Antivirals: Nursing Implications

- Before beginning therapy, thoroughly assess underlying disease and medical history, including allergies
- Assess baseline VS and nutritional status
- Assess for contraindications, conditions that may indicate cautious use, and potential drug interactions

## Nursing Implications

- Be sure to teach proper application technique for ointments, aerosol powders, etc.
- Emphasize handwashing before and after administration of medications to prevent site contamination and spread of infection
- Patients should wear a glove or finger cot when applying ointments or solutions to affected areas

## Nursing Implications

- Instruct patients to consult their physician before taking any other medication, including OTCs
- Emphasize the importance of good hygiene
- Inform patients that antiviral agents are not cures but do help to manage symptoms

## Nursing Implications

- Instruct patients on the importance of taking these medications exactly as prescribed and for the full course of treatment
- With zidovudine (AZT, ZDV, Retrovir):
  - Inform patients that hair loss *may* occur so that they are prepared for this rare adverse reaction
  - This medication should be taken on an empty stomach

## Nursing Implications

### Monitor for side effects

- Effects are varied and specific to each agent

## Nursing Implications

### Monitor for therapeutic effects

- Effects will vary depending on the type of viral infection
- Effects range from delayed progression of AIDS and ARC to decrease in flulike symptoms, decreased frequency of herpes-like flare-ups, or crusting over of herpetic lesions