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
<table>
<thead>
<tr>
<th>Agent</th>
<th>Antiviral Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guanines</td>
<td>HSV-1, HSV-2, VZV</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>CMV infection</td>
</tr>
<tr>
<td>Ganciclovir (DHPG)</td>
<td>CMV retinitis and systemic</td>
</tr>
<tr>
<td>Ribavirin (RTCD)</td>
<td>Influenza types A and B, RSV, LV, HV</td>
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<tr>
<td>Adenosines</td>
<td></td>
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<tr>
<td>Didanosine (ddl)</td>
<td>HIV</td>
</tr>
<tr>
<td>Vidarabine (Ara-A)</td>
<td>HSV, herpes zoster</td>
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</table>
Antivirals: Pyrimidine Nucleosides

<table>
<thead>
<tr>
<th>Agent</th>
<th>Antiviral Activity</th>
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<tbody>
<tr>
<td>Cytosines</td>
<td></td>
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<tr>
<td>lamivudine (3TC)</td>
<td>HIV</td>
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<tr>
<td>zalcitabine (ddC)</td>
<td>HIV</td>
</tr>
<tr>
<td>Thymine</td>
<td></td>
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<tr>
<td>idoxuridine (IDU)</td>
<td>HSV</td>
</tr>
<tr>
<td>stavudine (d4T)</td>
<td>HIV</td>
</tr>
<tr>
<td>trifluridine</td>
<td>HSV</td>
</tr>
<tr>
<td>zidovudine (AZT)</td>
<td>HIV</td>
</tr>
</tbody>
</table>

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
- 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.)

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.)

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.)

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

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

Opportunistic Infections
- Protozoal
  - Toxoplasmosis of the brain, others
- Fungal
  - Candidiasis of the lungs, esophagus, trachea
  - PCP, others
- Viral
  - CMV disease, HSV infection, others
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 flu-like symptoms, decreased frequency of herpes-like flare-ups, or crusting over of herpetic lesions