Antiviral Drugs

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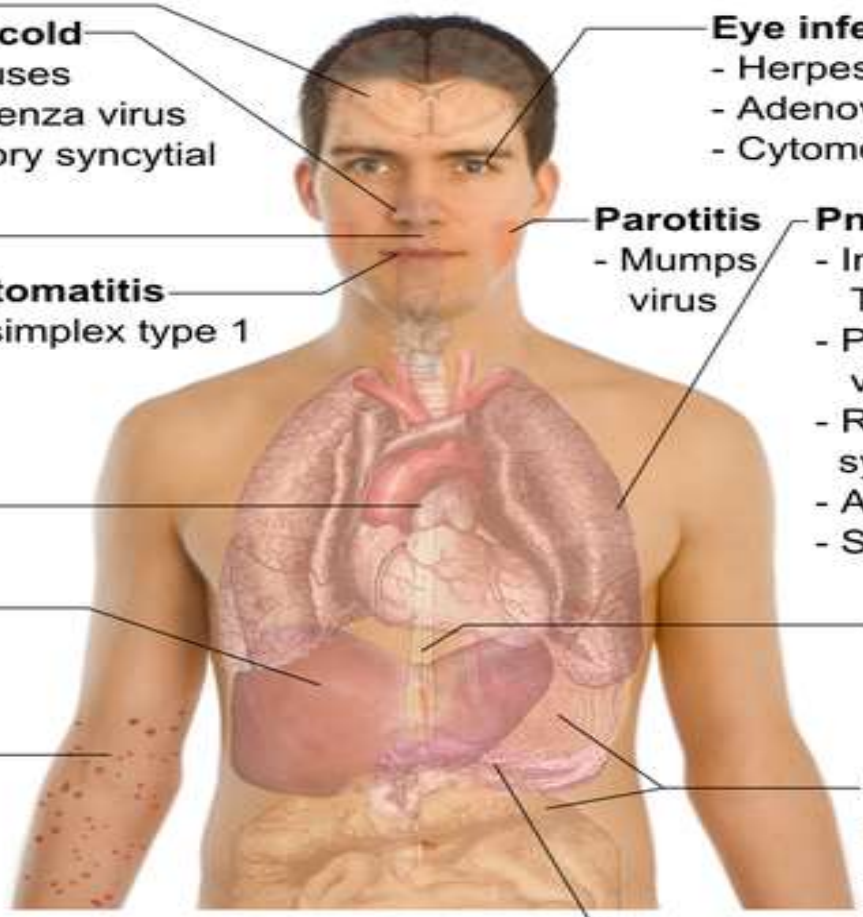
Viral infections

- **Viruses lack both cell wall & cell membrane**
- **Clinical symptoms of viral infection appear late in course of disease**, at time that most viral particles have replicated
- Administration of **antiviral drugs have limited effectiveness**
- Some antiviral are use as **prophylaxis**

Overview of Viral infections



Encephalitis/ meningitis
- JC virus
- Measles
- LCM virus
- Arbovirus
- Rabies

Common cold
- Rhinoviruses
- Parainfluenza virus
- Respiratory syncytial virus

Eye infections
- Herpes simplex virus
- Adenovirus
- Cytomegalovirus

Parotitis
- Mumps virus

Pneumonia
- Influenza virus, Types A and B
- Parainfluenza virus
- Respiratory syncytial virus
- Adenovirus
- SARS coronavirus

Pharyngitis
- Adenovirus
- Epstein-Barr virus
- Cytomegalovirus

Gingivostomatitis
- Herpes simplex type 1

Cardiovascular
- Coxsackie B virus

Hepatitis
- Hepatitis virus types A, B, C, D, E

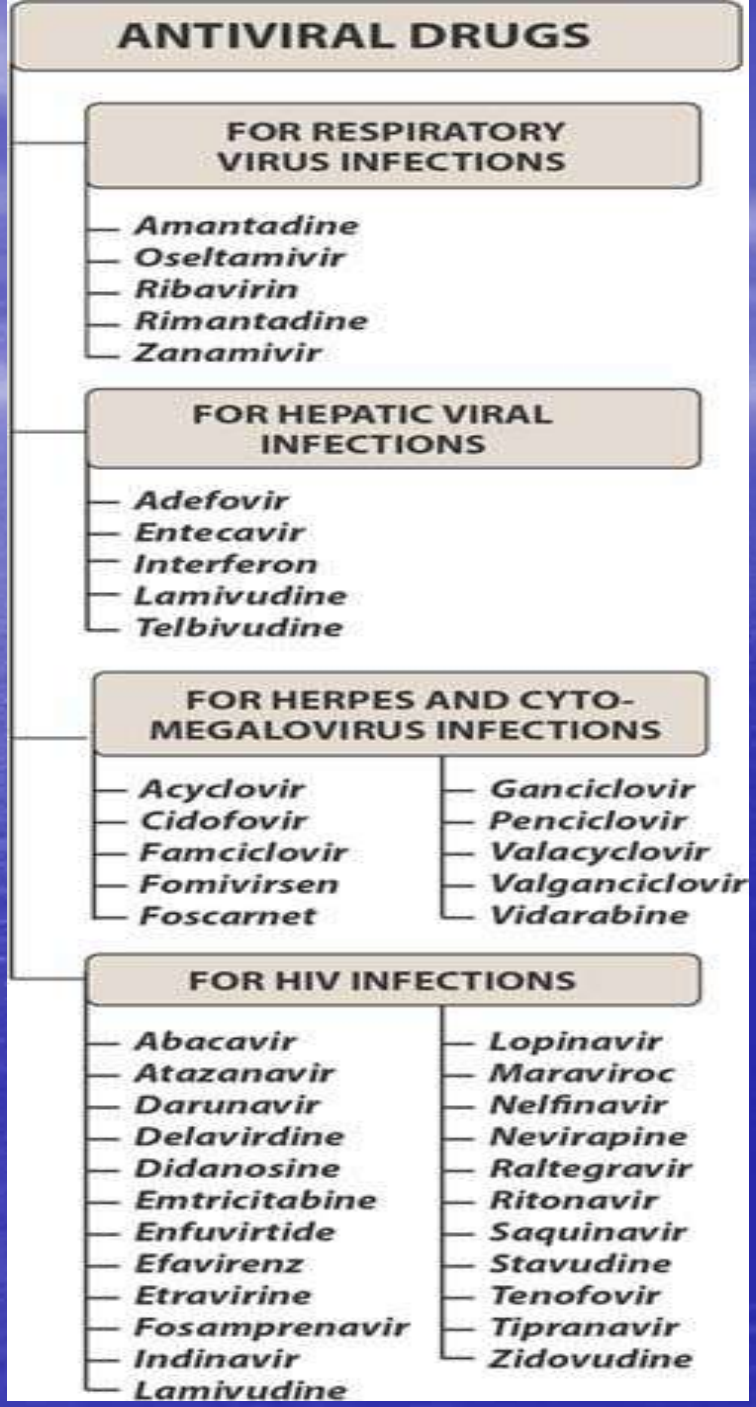
Myelitis
- Poliovirus
- HTLV-I

Skin infections
- Varicella zoster virus
- Human herpesvirus 6
- Smallpox
- Molluscum contagiosum
- Human papillomavirus
- Parvovirus B19
- Rubella
- Measles
- Coxsackie A virus

Gastroenteritis
- Adenovirus
- Rotavirus
- Norovirus
- Astrovirus
- Coronavirus

Sexually transmitted diseases
- Herpes simplex type 2
- Human papillomavirus
- HIV

Pancreatitis
- Coxsackie B virus


ANTIVIRAL DRUGS
FOR RESPIRATORY VIRUS INFECTIONS
Amantadine
Oseltamivir
Ribavirin
Rimantadine
Zanamivir
FOR HEPATIC VIRAL INFECTIONS
Adefovir
Entecavir
Interferon
Lamivudine
Telbivudine
FOR HERPES AND CYTO-MEGALOVIRUS INFECTIONS
Acyclovir
Cidofovir
Famciclovir
Fomivirsen
Foscarnet
Ganciclovir
Penciclovir
Valacyclovir
Valganciclovir
Vidarabine
FOR HIV INFECTIONS
Abacavir
Atazanavir
Darunavir
Delavirdine
Didanosine
Emtricitabine
Enfuvirtide
Efavirenz
Etravirine
Fosamprenavir
Indinavir
Lamivudine
Lopinavir
Maraviroc
Nelfinavir
Nevirapine
Raltegravir
Ritonavir
Saquinavir
Stavudine
Tenofovir
Tipranavir
Zidovudine

Respiratory Virus Infections

- **Antiviral drugs** for **influenza types A & B** and **respiratory syncytial virus (RSV)**
- **Immunization** against **influenza A is the preferred approach**

Antiviral drugs for Respiratory Virus Infections

- **Neuraminidase inhibitors:**
  oseltamivir & zanamivir
- **Inhibitor of viral uncoating:**
  Amandatine
- **Ribavarin**

1. Neuraminidase inhibitors

- At surface of influenza virus **two glycoproteins: hemagglutinin (HA)& neuraminidase (NA)**
- **Neuraminidase** enzyme that is essential for release of virus particles from surface of infected cell
- **Neuraminidase can be inhibited** by **sialic acid analogs:**
- **oseltamivir (Tamiflu) & Zanamivir (Relanza)**

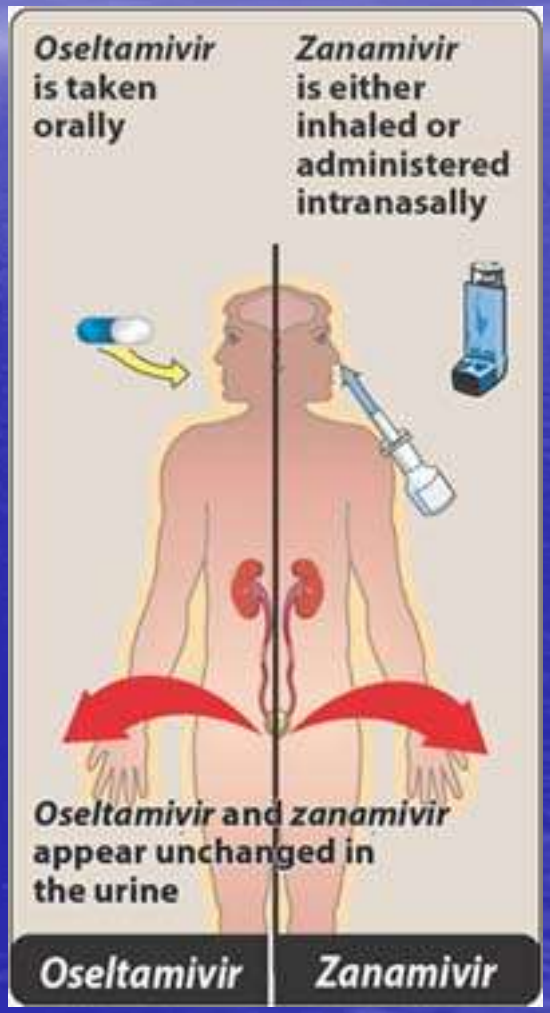
- These drugs **prevent release of new virions** & **their spread from cell to cell**
- **Oseltamivir & zanamivir** are **effective against influenza types A & B**

1. Neuraminidase inhibitors

- **Neuraminidase inhibitors prevent infection if administered prior exposure**
- They are **most effective for treatment of influenza if given within few hours of onset of symptoms**
- When administered within **first 24-48 hrs of onset of infection**, they have **modest effect on intensity & duration of symptoms**

1. Neuraminidase inhibitors

- They reduce risk of complications in **elderly & in patients with chronic diseases**
- **Oseltamivir** is given **orally for 5 days**
- **Zanamivir** is administered either inhaled or intranasally for 5 days



1. Neuraminidase inhibitors

- **Adverse effects:**
- **Oseltamivir:** GI discomfort, nausea
- **Zanamivir:** irritation of respiratory tract, bronchospasm, **should be avoided in patients with asthma, COPD**

2. Inhibitor of Viral Uncoating

- **Adamantine derivatives: Amandatine**
- **Effective only against influenza A infections**
- Treatment is useful for **unvaccinated individuals & during epidemics**
- **Amantadine** is also effective in treatment of some cases of **Parkinson's disease**

2. Inhibitor of Viral Uncoating

- drugs are well absorbed **orally**
- **Adverse effects:**
- **Amantadine:** CNS symptoms
  - **Minor neurological symptoms** (insomnia, dizziness, ataxia)
  - **Serious effects** (hallucinations & seizures)
- **should be avoided in pregnancy**

3. Ribavirin

- Effective against RNA & DNA viruses
- Is used in treating **infant & children** with **severe RSV infections**
- Is indicated in **chronic hepatitis C in combination with interferon-alpha-2b**
- Is given **orally or I.V, aerosol**
- **Adverse effects:**

- Transient anemia, elevated bilirubin, teratogenic

Hepatic viral infections

- **Hepatitis viruses** identified **A, B, C, D, E**
- **Hepatitis B & C** are most common causes of **chronic hepatitis, cirrhosis, hepatocellular carcinoma**
- **Therapy is currently available** only **for B & C**
- **Chronic hepatitis B is treated with interferon-α or lamivudine**

Hepatic viral infections

- **Chronic hepatitis C respond to interferon-α & ribavirin**
- **Hepatitis A** is a common infection but **not chronic**

Antiviral drugs for hepatic viral infections:

- Interferon
- Lamivudine

1. Interferon

- A family of naturally occurring, inducible glycoproteins that interfere with ability of viruses to infect cells
- Three types interferon- α, β, γ

- **Pegylated" formulations** has been attached to either **interferon-α-2a or interferon-α-2b to increase size of molecule**
- The larger molecular size **delays absorption from injection site, increase duration of action of drug** & decreases its clearance

Some approved indications for interferons

Interferon-α	*Interferon-β*	*Interferon-γ*
Chronic hepatitis B and C	Relapsing-remitting multiple sclerosis	Chronic granulo-matous disease
Genital warts caused by papilloma-virus		
Leukemia, hairy-cell Leukemia, chronic myelogenous		
Kaposi's sarcoma		

Interferon

- **Interferon** is **not active orally**
- **Is administered intralesionally, SC & I.V**
- **Adverse effects:**

- Flu-like symptoms: fever, chills, myalgias, arthralgias
- Bone marrow suppression
- Neurotoxicity (severe fatigue, weight loss, thyroditis)
- Rarely CHF, hypersensitivity reactions (HSR)

2. Lamivudine

- **Cytocine analog** that **inhibits both HBV DNA polymerase & HIV reverse transcriptase**
- **Is given orally**

Herpesvirus infections

- Acyclovir, Ganciclovir, famciclovir, penciclovir

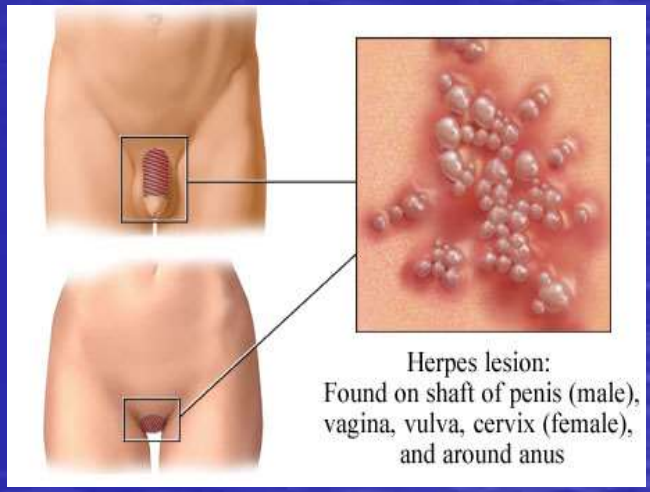
- Two most important herpes viruses:
  - Herpes simplex viruses type 1 & 2 (HSV-1 & HSV-2)

  - Varecilla-zoster virus (VZV)

Herpesvirus infections

- **Herpes simplex infections:**
  - Mouth, lips (cold sores) & eye are associated with HSV-1,
  - are treated with topical antiviral

- Genital infection is associated with HSV-2,
- are treated with oral antiviral



Herpesvirus infections

- **Varecilla-zoster virus:**

- **Chickenpox in healthy children** **mild & antiviral drug is not required**
- **Chikenpox in adults is more severe, required antiviral therapy**

- In **herpes zoster (shingles)** **systemic antiviral treatment** can reduce severity, duration of pain & reduce complications

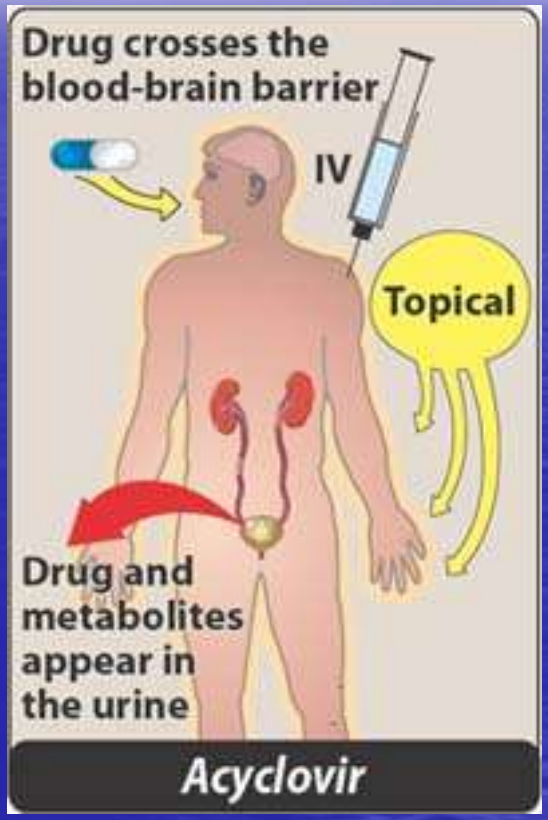
1. Acyclovir (Zovirax)

- Is a **prototypic antiherpetic agent**
- **The most common use of acyclovir** is in therapy for **genital herpes infections**
- **Herpes simplex virus type 1 & 2 (HSV-1 & HSV-2), varecilla-zoster virus (VZV), mediated infections are sensitive to acyclovir**
- **Drug of choice in HSV encephalitis**

1. Acyclovir

- **Route of administrations: I.V, orally or topical route**

- **Adverse effects:**
  - **Topical:** Local irritation
  - **Oral:** headache, diarrhea, nausea, vomiting
  - **I.V:** renal dysfunction

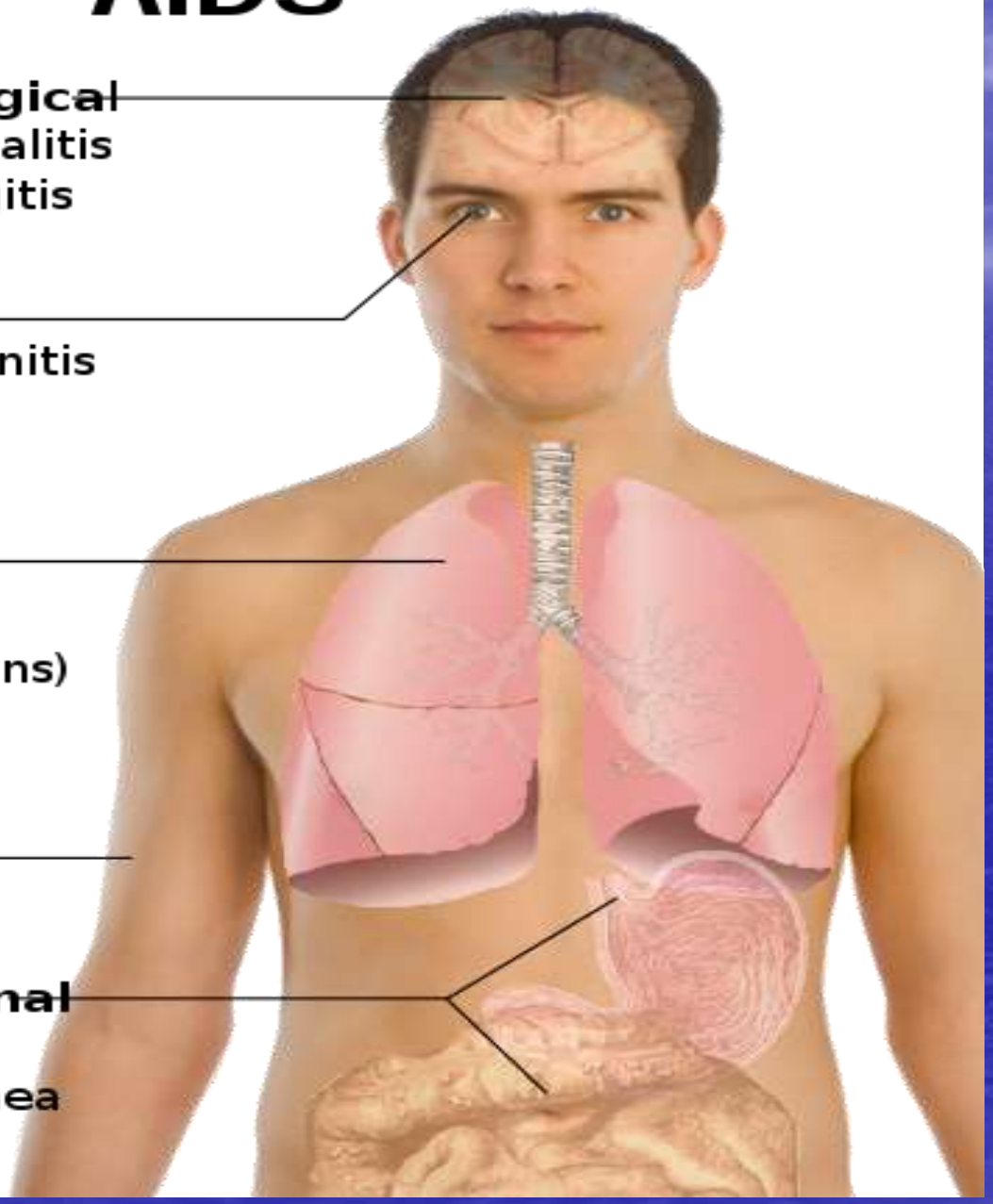


AIDS

- Aquired immunodeficiency syndrome
- Is disease of human immune system caused by HIV (Human immunodeficiency virus)
- 33.2 million live with AIDS worldwide

Main symptoms of

AIDS



Neurological
- Encephalitis
- Meningitis

Eyes
- Retinitis

Lungs
- Pneumocystis pneumonia
- Tuberculosis (multiple organs)
- Tumors

Skin
- Tumors

Gastrointestinal
- Esophagitis
- Chronic diarrhea
- Tumors

Treatment of AIDS

- A highly active regimen that **uses combinations of drugs to suppress replication of HIV** & **to restore immunocompetency of host**

Treatment of AIDS

- Highly Active AntiRetroviral Therapy (HAART)
  1. Nucleoside & nucleotide reverse transcriptase inhibitors (NRTIs)
  2. Non-Nucleoside reverse transcriptase inhibitors (NNRTIs)
  3. Protease inhibitors (PIs)

Treatment of AIDS

- There is no cure for infection caused by HIV
- A number of drugs slow disease progression & increase life expectancy

Treatment of AIDS

- **Current recommendation** for primary therapy **two NRTIs** with either **a PI** or **a NNRTI**

Nucleoside & nucleotide reverse transcriptase inhibitors (NRTIs)

1. Zidovudine (AZT)
2. Didanosine
3. Abacavir

Non-Nucleoside reverse transcriptase inhibitors (NNRTIs)

- Nevirapine

Protease inhibitors (PIs)

- Saquinivir
- Ritonavir
- Indinavir

Protease inhibitors (PIs)

- Adverse effects:

- Lipodystrophy syndrome: metabolic effects include fat redistribution, insulin resistance & dyslipidemia
- Fat redistribution after chronic use including loss of fat from extremities & its accumulation in abdomen & base of neck (buffalo hump)

Buffalo hump