



Anti Viral Agents

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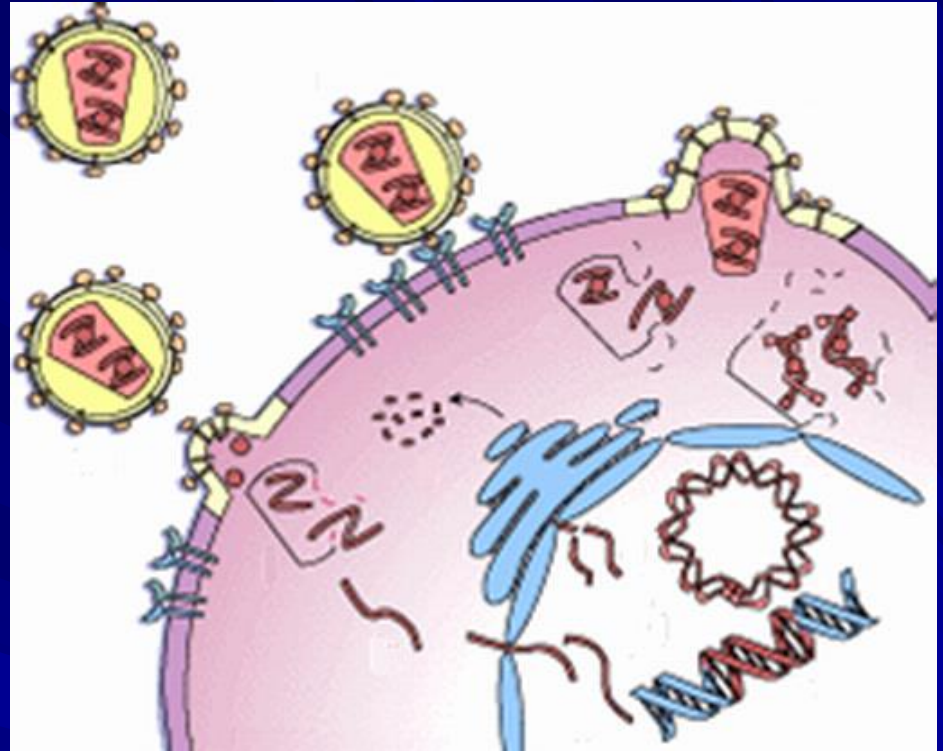
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Antiviral Agents

Viral Replication

- Adsorption
- Penetration
- Uncoating
- Biosynthesis
- Maturation
- Release

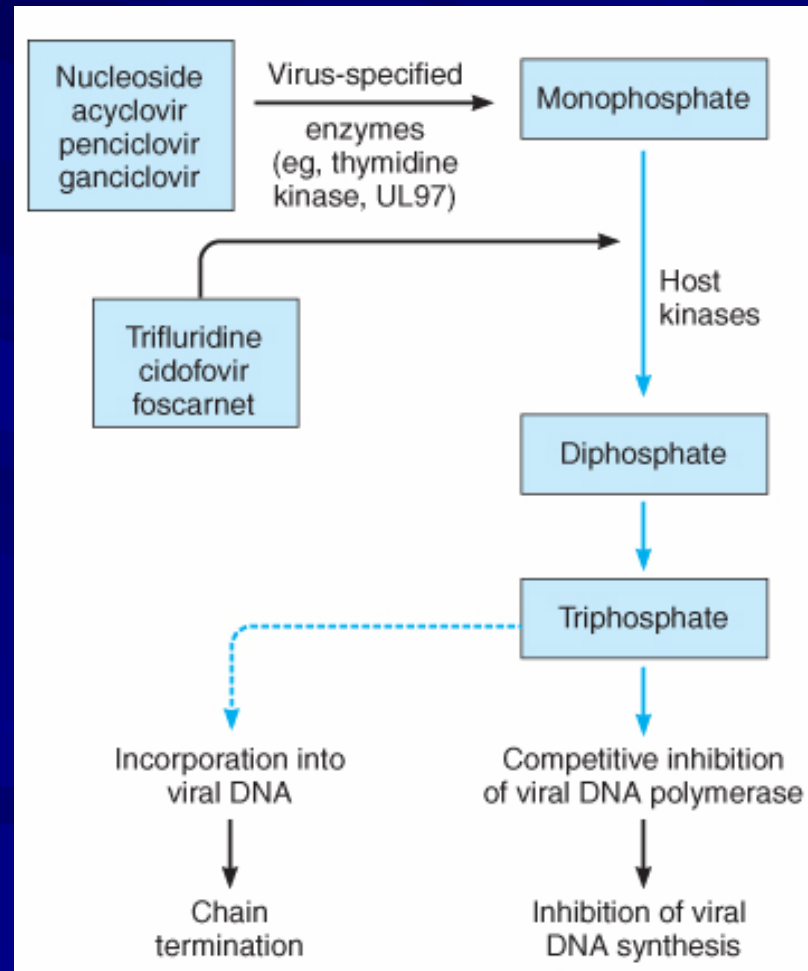


Antiviral Drugs

Classification of Antiviral Drugs:

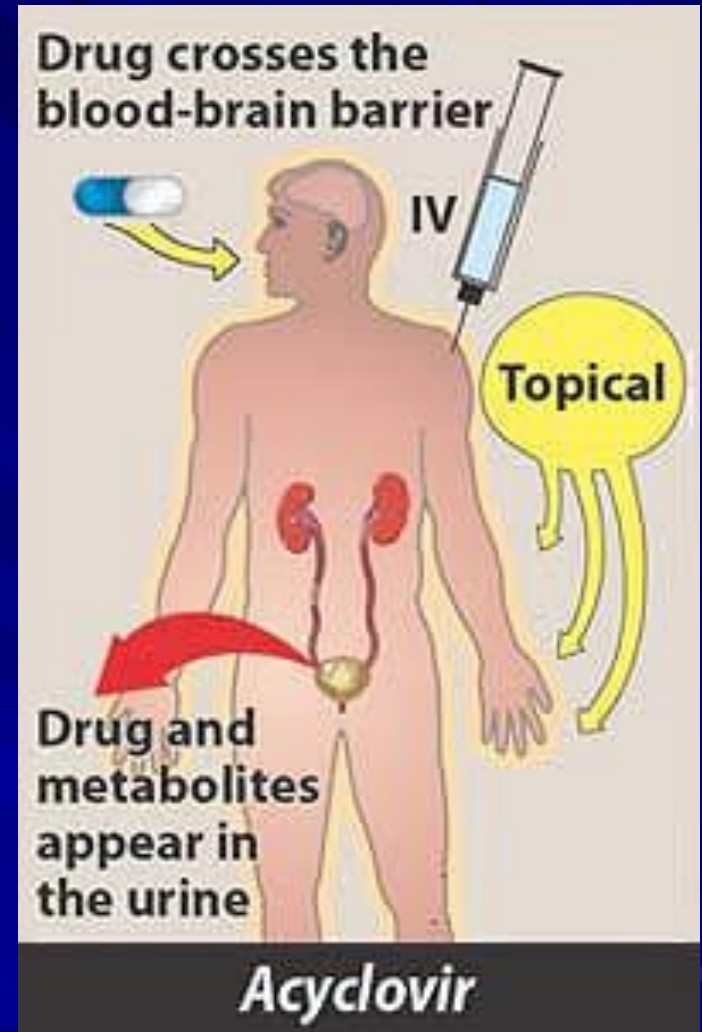
- Drugs directly impair viral replication
- Drugs modulate the host I - system

Agents to treat HSV and VZV infections (Acyclovir, Valacyclovir and Famciclovir)



Pharmacokinetic of Acyclovir

- Oral, i.v, topical.
- Bioavailability is 15-20%.
- Cleared primarily by glomerular filtration and tubular secretion.
- $T_{1/2} = 3\text{hr}$
- Cerebrospinal fluid concentrations are 50% of serum values.



Administration and metabolism of acyclovir

Indications for Acyclovir

1. Herpes simplex virus
2. Varicella - zoster virus:
 - Chickenpox
 - Shingles

Adverse Reactions

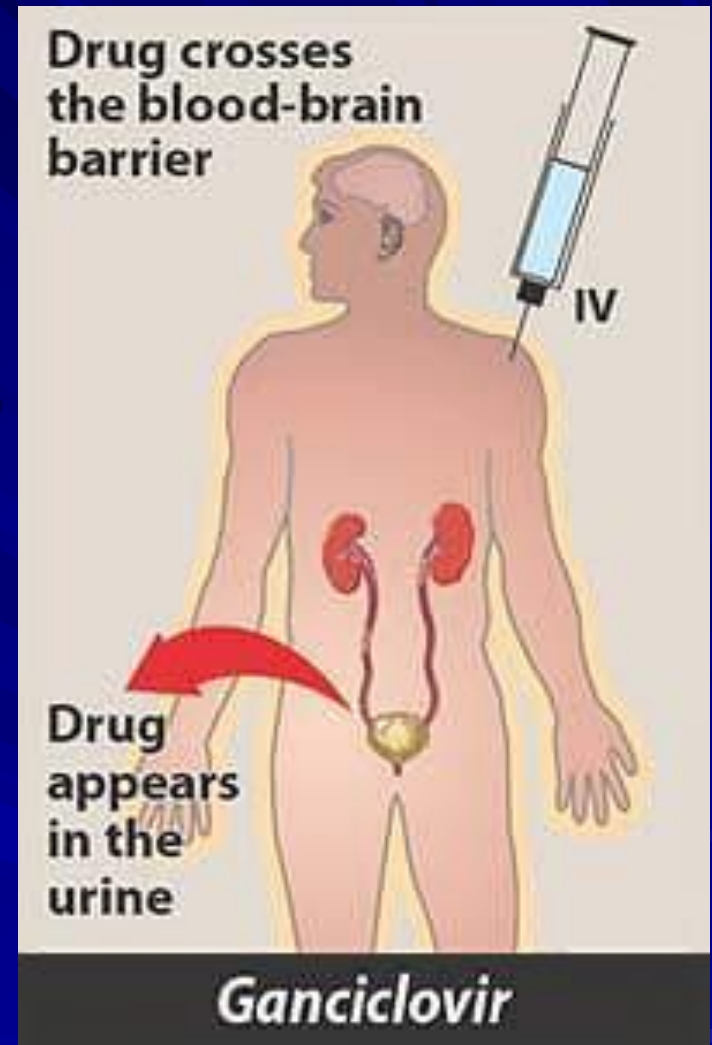
- Stinging sensation and a diffuse superficial punctate keratopathy.
- Gastrointestinal symptoms, headache and neuropsychiatric reactions, severe local inflammation with i.v.

Agents to treat Cytomegalovirus (CMV) Infections

**Ganciclovir, Valganciclovir,
Cidofovir**

Ganciclovir

- Oral or i.v,
- Poor bioavailability.
- Eliminated in the urine, mainly unchanged, ($t_{1/2}$ is 4h).



**Administration and
metabolism of ganciclovir**

Indications for Ganciclovir Include

- Life - threatening (CMV) infection
- For maintenance suppressive treatment of retinitis in patients with AIDS
- Prevention (CMV) following organ transplantation

Adverse Reactions of Ganciclovir

- Neutropenia and thrombocytopenia
fever, rash, gastrointestinal symptoms,
confusion and seizure
- Concomitant use of potential marrow -
depressant drugs, e.g. cotrimoxazole,
zidovudine, should be avoided.

Antiretroviral Agents

- Nucleoside reverse transcriptase inhibitors (NRTIs).
- Non nucleoside reverse transcriptase inhibitors (NNRTIs).
- Protease inhibitors (PIs).

Zidovudine (NRTIs)

- Well absorbed
- Distributed to most body tissues and fluids.
- Eliminated primarily by renal excretion following glucuronidation in the liver.

Indications for Zidovudine

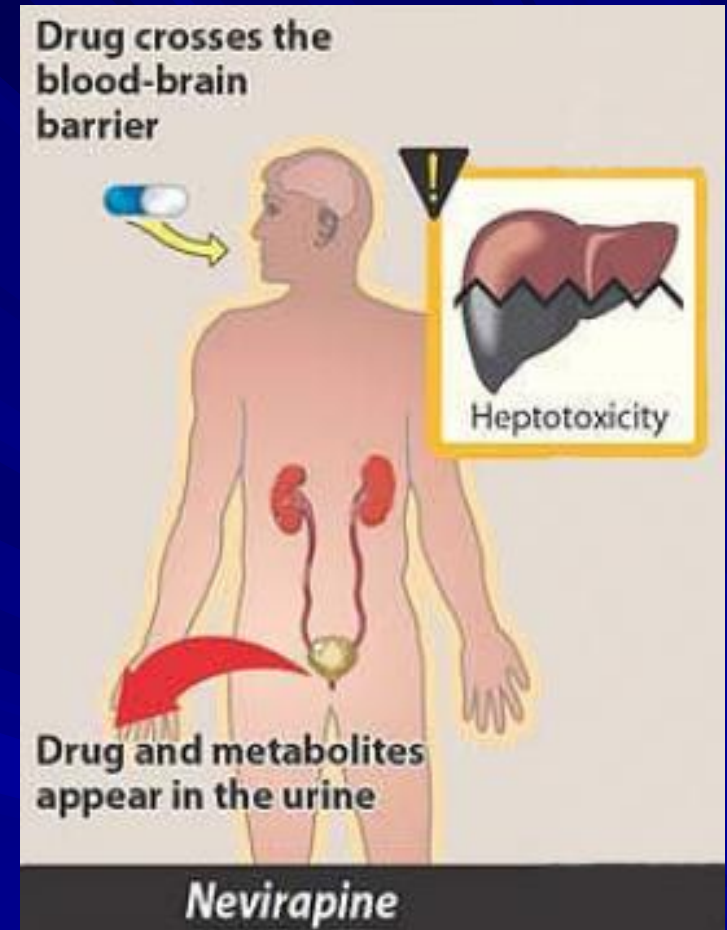
- HIV infection in patients with acquired immunodeficiency syndrome (AIDS) or AIDS related complex.

Drug Interaction of Zidovudine

- Myelosuppressive drugs such as ganciclovir, ribavirin and cytotoxic agents ↑ toxicity.
- Probenecid, ↑ Serum levels of zidovudine acid through decreased its clearance.

(NNRTIs) Nevirapine

- It used in combination with at least two other antiretroviral
- It penetrates the CSF
- Hepatic metabolism.
- Rash and hepatitis are the commonest side effects.

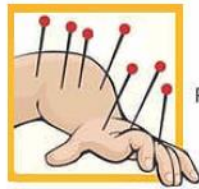


Administration, metabolism, and toxicity of nevirapine

Protease Inhibitors (Ritronavir, Indinavir, Saquinavir)

HIV produces protein and also a protease which cleaves the protein into component parts that are subsequently reassembled into virus particles; protease inhibitors disrupt this essential process.

Some Adverse effect of HIV protease inhibitors



Paresthesias

Diarrhea



Nausea and vomiting

Hypertriglyceridemia



Hyperglycemia

Hypercholesterolemia



Drug Interactions with Protease Inhibitors

1. Enzyme inducer P450 (e.g) rifampicin.
2. Enzyme inhibitors (e.g) ketoconazole, cimetidine.

Anti-influenza Agents

Amantadine

- Active against influenza A virus
- Mechanism of action: interfering with the uncoating and release of viral genome into the host cell.

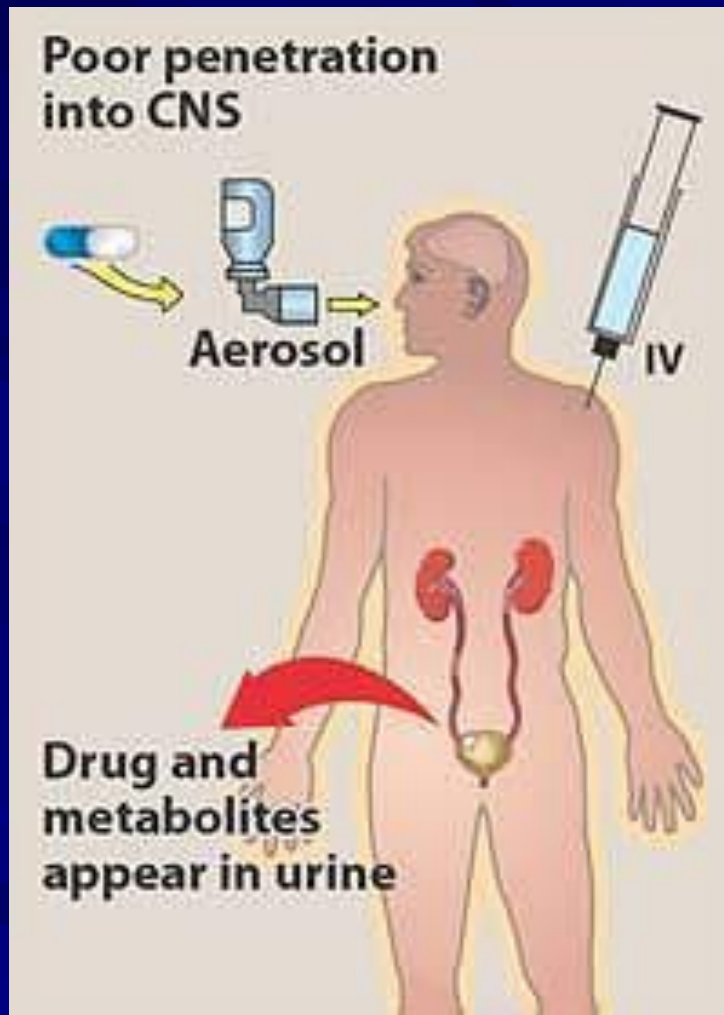
PK:

- Well absorbed from the GIT.
- It is eliminated in the urine.

Amantadine Adverse Reactions

- Dizziness, insomnia, headedness and nervousness, Drowsiness, hallucinations, delirium, coma may occur in patients with impaired renal function. Convulsions may be induced and amantadine should be avoided in epileptic patients.

Respiratory Syncytial Virus (RIBAVIRIN)



Interferons (Hepatic Viral Infection)

1. Directly on uninfected cells to induce enzymes that degrade viral RNA.
2. Indirectly by stimulating the immune system.

Uses of Interferon

- Alfa Interferon used for hairy cell leukaemia, recurrent or metastatic renal cell carcinoma, Kaposi's sarcoma in AIDS patients
- Alfa-2 α and -2b improve the manifestations of viral hepatitis, B and C. hepatitis C may need prolonged therapy.

Adverse Reactions of Interferon

- An influenza-like syndrome
- Fatigue & anorexia
- Convulsions, depression
- Hypotension, hypertension and cardiac arrhythmias
- Bone marrow depression.
- It inhibits the metabolism of theophylline

Inosine Pranobex

- Mucocutaneous herpes simplex and genital warts.
- It is administered by mouth and metabolised to uric acid.