

Anti Viral Drugs

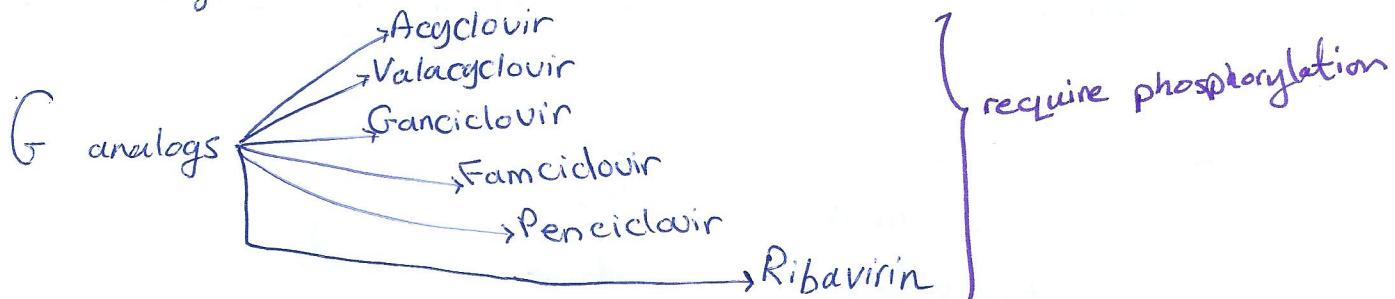
- **Viruses**
 - have no cell wall
 - made up of nucleic acid components
 - enveloped viruses are antigenic in nature
 - Don't have metabolic machinery of their own - use host enzymes
 - Some multiply in the cytoplasm
 - Some multiply in the nucleus
 - are obligate intracellular parasites
 - multiplication take place before diagnosis is made.

* Symptoms & diagnosis after the replication had started.
so you should treat as early as possible.

- **Anti Viral drugs**
 - (they mimic nucleotides)
 - Purine analogs (A & G) ^{sarcyclovir}
 - Pyrimidine analogs (C & T) ^{trifluridine}
 - many of them are Prodrugs. (inactive)
 - Activated by phosphorylation by
 - viral enzymes (better)
 - cellular enzymes
 - Inhibit active replication
 - Don't affect Dormant viruses
 - Viral growth resumes after drug removal.
 - So that the patient mustn't stop taking the ^{anti-} viral drug even if he felt better, if he did (stopped taking AVD) the virus will replicate again and give more resistant form.
 - For Immuno competent people → humoral & cellular immunity are enough for acute infection
 - For Immuno compromised people → the anti viral drug will help in clearing the virus & minimize the symptoms in case of chronic infection.
 - effective host immune response is essential
(~~humeral~~ + cellular immunity) + anti viral drug
 - Clinical efficacy depends on achieving inhibitory conc. at the site of infection within the infected cell.

* Valacyclovir (prodrug) \rightarrow Acyclovir (better bioavailability)

+ Famciclovir (\uparrow bioavailability) $\xrightarrow[\text{to}]{\text{hydrolyzed}}$ Penciclovir
can be administered
Orally



A analog \rightarrow Vidarabine (A: adenosine)

C analog \rightarrow Cidofovir [no phosphorylation required]

C & T analog \rightarrow Trifluridine [pyrimidine]

* Acyclovir & related compounds mechanism of action:

① phosphorylated by \rightarrow Thymidine-Kinase (viral enzyme)

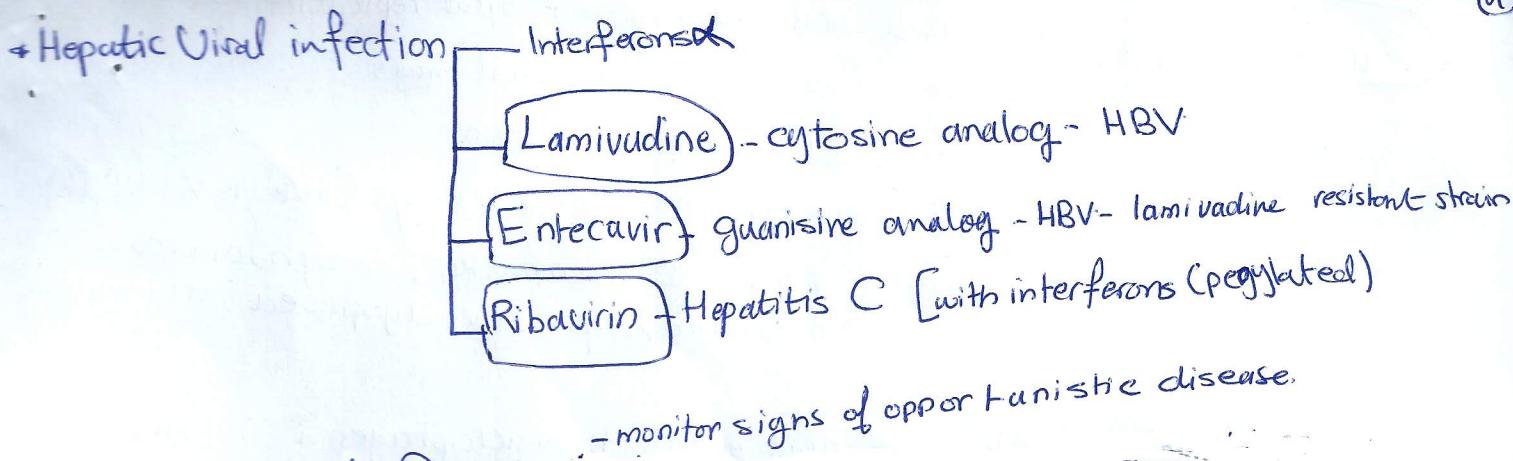
② metabolized by \rightarrow host cell Kinases to nucleotide analogs

③ the analog inhibits Viral-DNA polymerase

④ Incorporation of acyclovir triphosphate into the growing viral DNA chain \Rightarrow blocks the elongation!

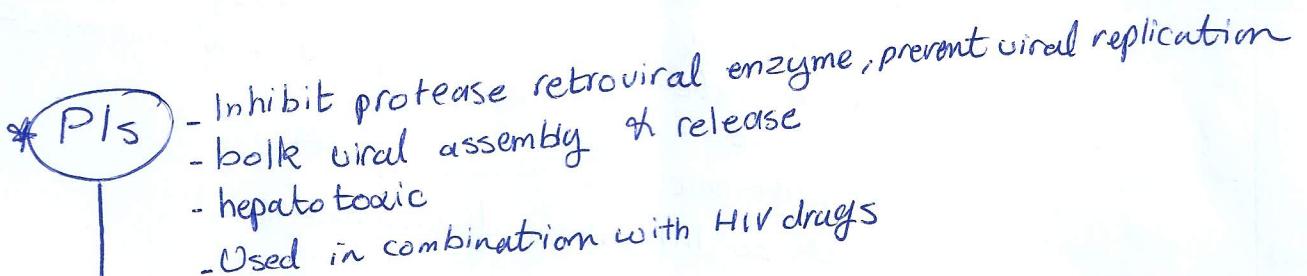
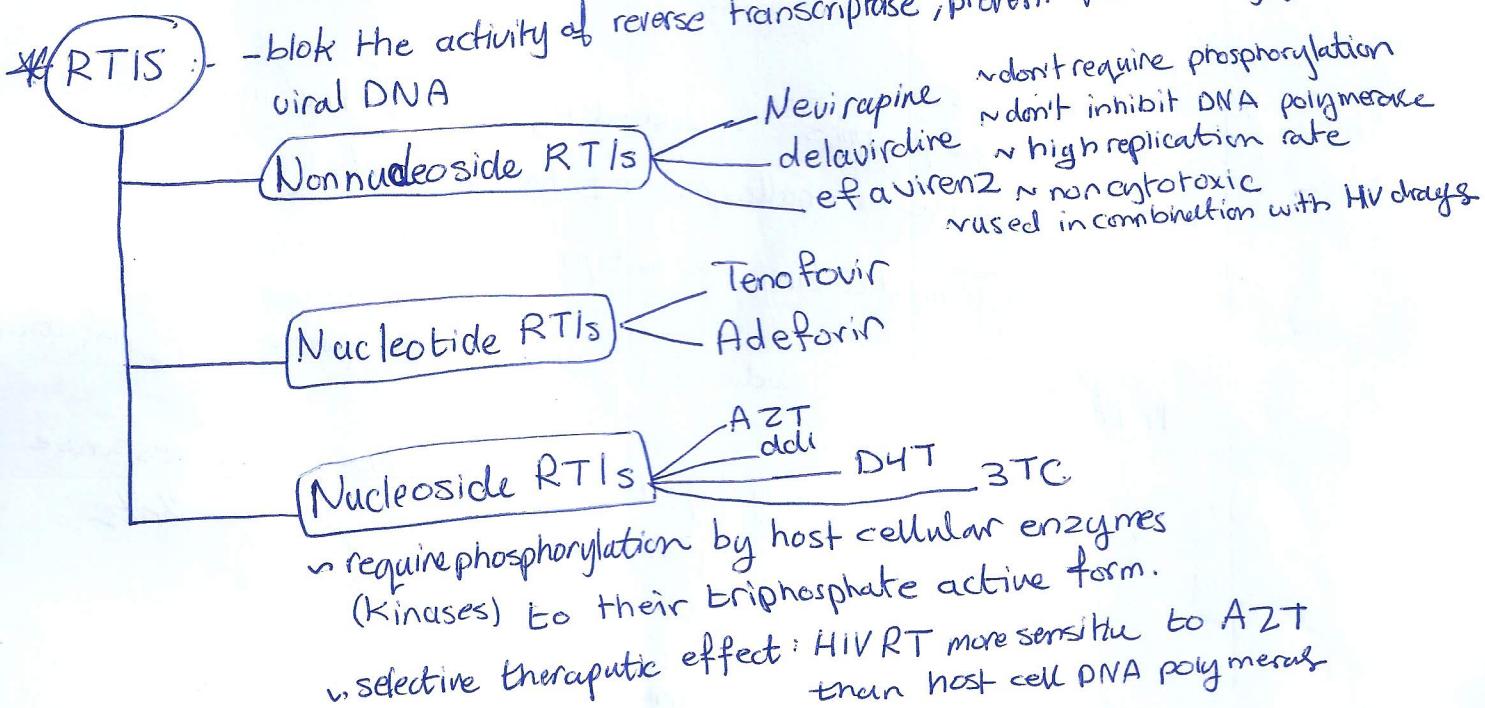
Foscarnet \rightarrow pyrophosphate inorganic analog

Dose	Adult blood, Adminstration	Distribution	ADverse effects	therapeutic use	Extraintest.
Aldolour	~20-30 %	Topical, Oral	Nausea, diarrhoea	HSV encephalitis oral ulcers herpetic eye disease	half life 2-5 hrs oral excretion >80%. shedding HSV-1, HSV-2, HSV-3 shingles
Ganciclovir	IV, topical	CMV retinitis in ICP Nephrotoxicity CMV retinitis in ICP transplant patients lymphoproliferative disease adenovirus infection	CMV retinitis in ICP pneumonitis of CMV in transplant patients lymphoproliferative disease adenovirus infection	CMV retinitis only HSV Keratitis (keratoconjunctivitis) all body tissues	~2% vidarabine foscarnet Trifluridine Amantadine ~50-90% Ribavirin
Vidarabine	IV	Opthalmic cream	S IADH	HSV Keratitis only all body tissues	~10-20 %
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Ribavirin	Oral, IV	all tissues except CNS	Inhalation in HSV	Anemia, jaundice	-RSV bronchitis & pneumonia in hospitalized children (by aerosol) -loss of fever
Zanamivir	Oral	Inhalation	Inhalation	Influenza A or B	-inhibits viral membrane pro M2 -inhibits viral nucleocapsid
Neuramindase inhibitors in inhibitory	Not advised in pregnancy			Influenza A or B	(prevent + the release)



Antiretroviral Drugs

- includes at least 3 medications "cocktails"
- these medications work in different ways to reduce the viral load.
- Adverse effects vary and may be severe [monitor for dose-limiting toxicities]



- amprenavir (Agenerase)
- nelfinavir (Viracept)
- ~~saquinavir~~
- indinavir (crizivac)
- ritonavir (norvir)
- Saquinavir (Invirase)

Fusion Inhibitors

- inhibit viral fusion, prevent viral replication
- newest class of antiretroviral drugs
- ex:- enfuvirtide (Fuzeon)
- used in combination with HIV drugs (like PIs & NNRTIs)
- side effect: peripheral neuropathy, cough, anorexia, insomnia, depression, dyspnoea, arthralgia

Entry Inhibitors

- inhibit viral entry to macrophages & T-cells

- CCR 5 receptor antagonist

- FDA approved in 2007

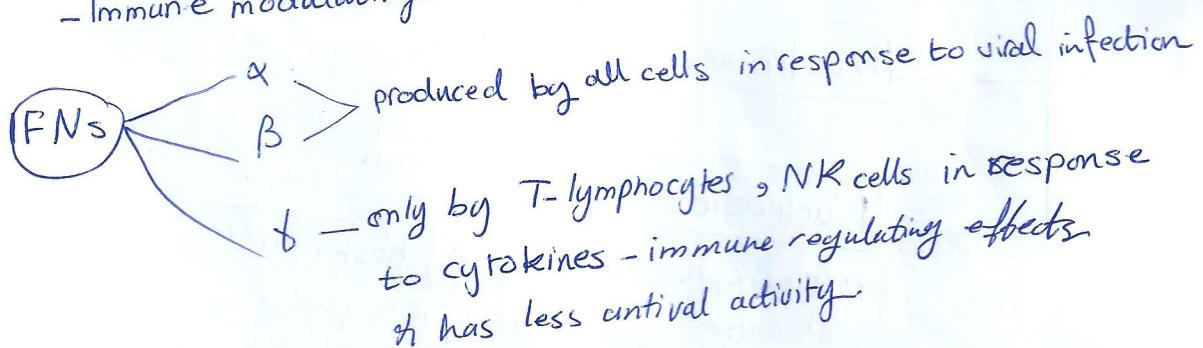
- used in combination with HIV drugs

- ex: Maraviroc (Selzentry, Celsentri)

Interferons

IFNs
- natural proteins - produced by cells of the immune system
in response to challenges by foreign agents (viruses, bacteria, parasites, tumor cells)

- immune modulating & antiproliferative actions



- Mechanism:- Induction in → Inhibits

- protein kinase → protein synthesis
- oligo-adenylate → degradation of viral mRNA
- synthase
- phosphodiesterase → tRNA
- ∴ leads to Inhibition of translation

- spectrum :- Interferon δ

- HBV, HCV (pegylated IFN), HPV

- pegylation (addition of polyethylene glycol to INF)
enhances the half-life.

- Anti-proliferative action may inhibit growth of
certain cancers like:- Kaposi sarcoma
hairy cell leukemia

Virus	Disease	Drug of choice	Alternative drugs
Flu A	Influenza	Amantadine	Rimantadine
RSV	pneumonia bronchiolitis	Ribavirin (aerosol)	
HSV	genital herpes	acyclovir	Foscarnet
	keratitis conjunctivitis	Trifluridine	Idoxuridine Vidarabine
	encephalitis	acyclovir	
	Neonatal HSV infection	Aцикловир	Vidarabine
	herpes infection in IC	Aцикловир	Foscarnet
VZV	normal host	no therapy	
	In ICP → pregnancy	Aцикловир	Foscarnet
CMV	Retinitis	Ganciclovir	Foscarnet
HIV	AIDS	Zidovudine + PIs	Didanosine Stavudine
HBV	HB	Interferon	
HCV	HC		

(IFN) - Oral bioavailability < 1%

administration: IV, SC, Intralesionally

distribution: all body tissues except CNS, eye.

- half life 1-4 hrs

- Adverse effects
 - Acute flu-like syndrome (fever, headache)
 - bone marrow suppression (granulocytopenia, thrombocytopenia)
 - Neurotoxicity (confusion, seizures)
 - Cardiotoxicity - arrhythmia
 - Impairment of fertility

- Therapeutic uses
 - chronic hepatitis B & C
 - HZV infection in cancer patients
 - CMV in renal transplant patients
 - AIDS related Kaposi's sarcoma
 - Hairy cell leukaemia
 - Condylomata acuminata