Tikrit University
College of Veterinary Medicine

Pharmacology

Subject name: **Antiviral agents**
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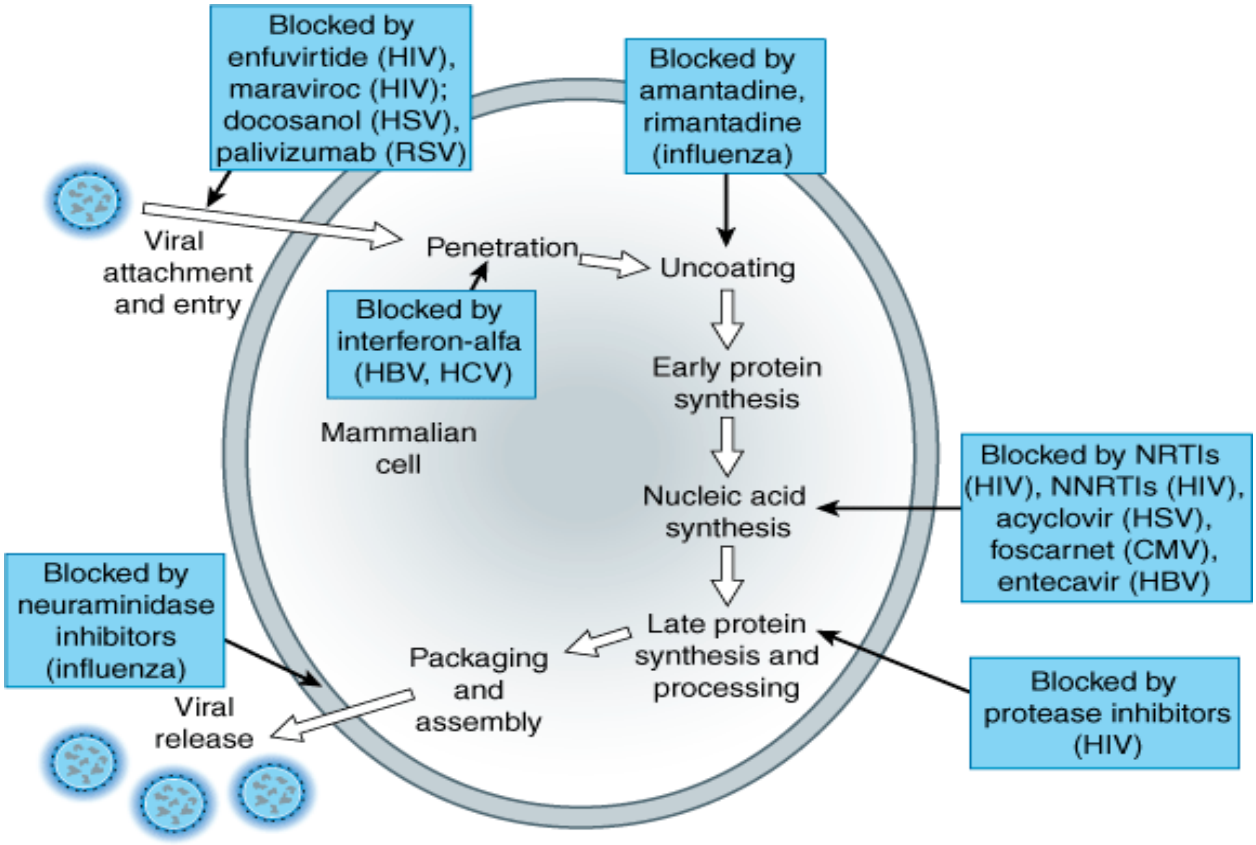
SCAN ME
Lecturers link

Antiviral agents

Viruses essentially consist of genetic material (nucleic acids) and a capsular envelope made up of proteins, often with a coat of a phospholipid (PL) bilayer with embedded proteins. They lack a metabolic system and depend on the infected cell for their growth and replication. Targeted therapeutic suppression of viral replication requires selective inhibition of those metabolic processes
that specifically serve viral replication in infected cells.
Some viruses are as follows:
Hepatitis viruses, herpes viruses , human immunodeficiency virus infection (HIV), influenza viruses , respiratory syncytial virus (RSV).



TREATMENT OF VIRAL RESPIRATORY INFECTIONS:-

1=Amantadine and rimantadine :-

Drugs have a narrow antiviral spectrum, only active against influenza A viruses.

- these drugs are prophylactic against influenza A virus infection with 80% efficacy.
- both drugs are well absorbed orally.
- amantadine distributes throughout the body and readily penetrates into the CNS, rimantadine dose not cross the BBB .

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- **mechanisms**:- amantadine and rimantadine inhibit the first steps in replication of the influenza A virus

2-Ribavirin:-

Is a synthetic gunosine analog. It is effective against a broad spectrum of RNA & DNA viruses.

Ribavirin is contraindicated in pregnancy.

Treatment of herpesvirus infection:-

1-**Acyclovir (acycloguanosine):-** acyclovir is a guanosine analog active against herpes simplex virus (HSV)

Mechanism of action:-. The drug is activated to form acyclovir triphosphate, a competitive substrate for DNA polymerase, leading to chain termination following its incorporation into viral DNA .

resistance of (HSV):- can involve changes in viral DNA polymerase.

Pharmacokinetics:- acyclovir can be administered by the topical, oral and intravenous routes. Renal excretion is the major route of elimination of acyclovir and dosage should be reduced in patients with renal impairment.

Adverse effect:- gastrointestinal distress, headache.

-delirium, tremor, seizures , hypotension, nephrotoxicity.

In veterinary medicine my be used in birds &cats

Acyclovir congeners :- several new antiviral agents have characteristics similar to acyclovir include :- **famciclovir, penciclovir, valacyclovir.**

2-foscarnet:-

4- **ganciclovir:-**

Anti- HIV AGENTS

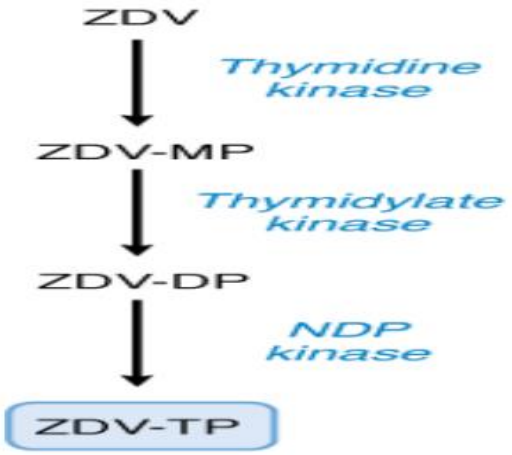
A-Anti-HIV agents :-

A- nucleoside reverse transcriptase inhibitors (NRTIs)

a- zidovudine (ZDV):

mechanism:- Like other nucleoside analogs, intracellular zidovudine is phosphorylated by thymidine kinase to zidovudine 5'- monophosphate, which is then phosphorylated by thymidylate kinase to the diphosphate and by nucleoside diphosphate kinase to zidovudine 5'-triphosphate.

2.Zidovudine 5'-triphosphate terminates the elongation of proviral DNA because it is incorporated by reverse transcriptase into nascent DNA



Resistance mutation at several sites on the gene which encodes for several proteins , include reverse transcriptase.

Pharmacokinetics :- its active orally , and is distributed to most tissues, including the CNS. Elimination of the drug involves both hepatic and renal excretion.

Toxicity:- bone marrow suppression leading to anemia and neutropenia. Gastroinsetinal distress, thrombocytopenia, headaches.

Drug interaction:- acetaminophen , bendzodizepines, cimetidine, may increase plasma levels of zidovudine. Rifampin

b- didanosine (ddi):-c- lamivudine :d- **zalcitabine (ddc**

e- **stavudine**

b-Anti- HIV : nonnucleoside reverse transcriptase inhibitors(NNRTIs)

Mechanisms:-NNRTIs bind to a site on reverse transcriptase different from the binding site of NRTIs.
-Nonnucleoside drugs do not require phosphorylation to be active and do not compete with nucleoside triphosphate.
-There is no cross- resistance with NRTIs.
- that greatly reduces its activity, and thus they act as noncompetitive inhibitors.

a- **nevirapine:-**
b- delavirdine
c- efavirenz:

c-a**nti- HIV agents : protease inhibitors:-**

a- **indinavir:** inhibits HI-1 protase,(an enzyme that cleaves viral precursor proteins and is critical to the production of mature infection virions.)
Oral bioavailabilty is good except in the food. Clearance is mainly via the liver, with 10% renal excretion.
They bind to protease molecule, interfere with its cleaving function. They act at a late step of viral cycle , they are effective in both newly and chronically infected cells.

Toxicity: nausea, diarrhea, thrombocytopenia

interferones:- are glycoproteins produce in human lukocytes(alpha-beta-gamma).they exert multiple actions that affect viral RNA and DNA synthesis. Interferons induce the formation of enzyme, including a protein kinase that phosphorylates which blocks peptide chain .
clinical: interferon alpha is approved for use chronic hepatitis A, B infection, papillomatosis.
In veterinary medicine is administration orally to treat cats (Reforen-A)

Intreferon α

1.IFN- α is a cytokine that acts through host cell surface receptors increasing the activity of Janus kinases (JAKS).
2. These enzymes phosphorylate signal transducers and activators of transcription (STATS) to increase the formation of antiviral proteins.
3. The selective antiviral action of IFN- α is primarily due to activation of a host cell ribonuclease that preferentially degrades viral mRNA.

IFN- α also promotes formation of natural killer cells that destroy infected liver cells.