\*lack both a cell wall and a cell membrane/ Viruses are obligate intracellular parasites / do not carry out metabolic processes / use host’s metabolic machinery

\*clinical symptoms appear late > most of the virus particles have replicated > block viral replication has limited effectiveness/some useful as prophylactic agents

Antiviral drugs TREATMENT OF RESPIRATORY ( only existed for influenza A and B and respiratory syncytial virus (RSV) / antiviral agents are used

VIRAL INFECTIONS when patients are allergic to the vaccine or outbreaks occur / influenza A > Immunization )

Neuraminidase inhibitors : (Zan , Oselt ) - amivir

\* against both type A and type B influenza viruses / prevent infection

\* do not interfere with the immune response to influenza vaccine. / bot are eliminated unchanged in the urine

\* when administered within 24 to 48 hours after the onset of symptoms > decrease the intensity and duration of symptoms.

\* inhibit neuraminidase > preventing the release of new virions and their spread from cell to cell

\* *Oseltamivir* is an orally active prodrug > hydrolyzed by the liver to its active form / *Zanamivir - administered* *via inhalation*

\* adveerse ( 1- Irritation of the respiratory tract ( Zanamivir) )

(2- GI distress with (Oseltamivir) which can be alleviated by taking the drug with food)

\* used with caution in individuals with asthma or chronic obstructive pulmonary disease, because bronchospasm may occur.

\* resistance ( 1-Mutations of the neuraminidase enzyme > but these mutants are less infective and virulent )

Adamantane antivirals : ( a ,ri ) - mantadine

\* limited to influenza A infections

\* widespread resistance > not recommended for treatment and prophylaxis of influenza A

\*interfere with the function of viral M2 protein>block uncoating of the virus particle> preventing viral release in infected cells

\* Orall / *Amantadine- cross the blood–brain barrier(CNS) / rimantadine-does not cross the blood–brain barrier to the same extent.*

\**Amantadine-unchanged in urine / Rimantadine- metabolized by liver, ( metabolites and Rimantadine) are eliminated by the kidney*

\*adverse (1- CNS effects (diziness,ataxia..) and hallucinations and seizures ((*Amantadine))*

2- fewer CNS reactions ((*Rimantadine))*

3- GI intolerance (( both))

\* with caution in pregnant and nursing mothers.

\* *Amantadine* > cautiously in patients with psychiatric problems, cerebral atherosclerosis, renal impairment, or epilepsy.

\* resistance (change in one amino acid of the M2 protein ) / Cross-resistance occurs between the two drugs

Ribavirin (synthetic guanosine analog / against a broad spectrum of RNA and DNA viruses )

\* treating immunosuppressed infants and young children with severe RSV infections

\* when combined with interferon-*α >* treats chronic hepatitis C infections

\* inhibits replication of RNA and DNA viruses.

\* ribavirin triphosphate > inhibit GTP formation > preventing viral(mRNA) capping and blocking RNA-dependent RNA polymerase

\* orall or inhalation / aerosol > treatment of RSV infection / Absorption is increased when taken with a fatty meal

\* drug and metabolites > eliminated in urine ///\* contraindicated in pregnancy

\* adverse (1- dose-dependent transient anemia / 2- Elevated bilirubin / 3- aerosol may be safer)

TREATMENT OF HERPESVIRUS (Herpes viruses are associated with (1-cold sores / 2-viral encephalitis / 3- genital infections)

INFECTIONS (exert their actions during acute phase of viral infections and are without effect during latent phase)

Acyclovir ((guanosine analog))

\*treatment of Herpes simplex virus (HSV) types 1 and 2, varicella-zoster virus (VZV), and some Epstein-Barr virus–mediated infections

\*treatment of choice in HSV encephalitis / therapy for genital herpes infections / (IV), oral, or topical

\*given prophylactically to seropositive patients before bone marrow transplant and post–heart transplant

\*monophosphorylated by the herpesvirus-encoded enzyme thymidine kinase(this is why virus infected cells are most susceptible) then

converted to the di- and triphosphate forms by thehost cell kinases >> \*Acyclovir triphosphate competes with deoxyguanosine

triphosphate as substrate for viral DNA polymerase and itself incorporate into the viral DNA, causing premature DNA chain termination

\* distirbutes well including CSF / \* partially metabolized > Excretion into the urine occurs by glomerular filtration and tubular secretion

\* valyl ester, *valacyclovir*, has greater oral bioavailability than *acyclovir >> this ester rapidly hydrolyzed to acyclovir and achieves levels*

*comparable to those of acyclovir following IV administration*

\*adverse (-Transient renal dysfunction may occur at high doses or in a dehydrated patient receiving the drug intravenously)

\*resistance (Altered or deficient thymidine kinase and DNA polymerases / Cross-resistance occurs(if its resistance to one its to all)

Cidofovir ((nucleotide analog of cytosine))

\* treatment of cytomegalovirus (CMV) retinitis in patients with AIDS //\* inhibits viral DNA synthesis // \* IV

\* Slow elimination > prolonged dosage intervals and eliminates the permanent venous access needed for *ganciclovir* therapy

\* Intravitreal injection(vitreous humor between lens and retina) > hypotony and uveitis (((only for extraordinary cases)))

\* contraindicated in patients with renal impairment and patients taking nephrotoxic drugs .

\*adverse (1- renal toxicity/2- Neutropenia/3- metabolic acidosis)

\* to reduce the risk of nephrotoxicity >> Oral *probenecid* and IV normal saline are coadministered with *cidofovir*

Foscarnet ((is not a purine or pyrimidine analog , it is a phosphonoformate > does not require activation by kinases))

\* treatment of CMV retinitis in immunocompromised hosts and for *acyclovir*-resistant HSV infections.

\* reversibly inhibiting viral DNA and RNA polymerases > interfering with viral DNA and RNA synthesis.

\* resistant(Mutation of the polymerase) / \* IV / \* given frequently to avoid relapse when plasma levels fall

\* greater than 10% enters the bone matrix, from which it slowly leaves /

\* eliminated by glomerular filtration and tubular secretion /

\*adverse (nephrotoxicity/ anemia,/ hypocalcemia and hypomagnesemia > Due to chelation with divalent cations/ hypokalemia, hypo-

and hyperphosphatemia, seizures, and arrhythmias

Ganciclovir ((analogue of *acyclovir)) //\*(* *carcinogenic,* *embryotoxic,* *teratogenic)//\*resistance(lower ganciclovir triphosphate)*

\* analogue of *acyclovir* that has greater activity against CMV(treatment of CMV retinitis and CMV prophylaxis in transplant patients)

\*like acyclovir // \* IV // \* Excretion into the urine occurs through glomerular filtration and tubular secretion // \*

\* *alganciclovir*, an oral drug, is the valyl ester of *ganciclovir //\*adverse(severe, dose-dependent neutropenia.) // \**