

ANTIVIRAL AGENTS



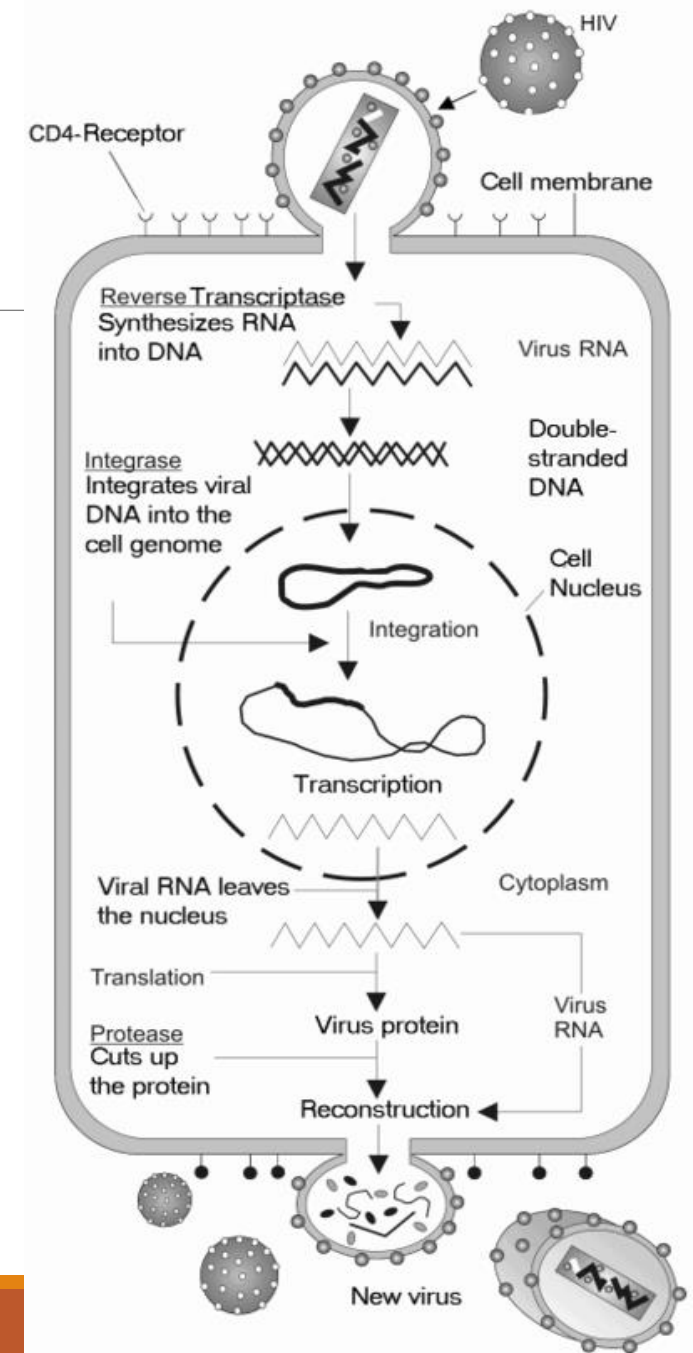
Antiviral drug is an any agent that is used in the treatment of an infectious disease caused by a virus.

Classification of antiviral drugs

Group of preparations	Drugs
Anti-influenza	Rimantadine (Rimantadine) Amantadine Zanamivir (Relenza) Oseltamivir (Tamiflu) Umifenovir (Arbidol)
Drugs acting on the herpes viruses	Acyclovir (Zovirax) Ganciclovir (Cymevene) Idoxuridine Famciclovir (Famvir)
Antiretroviral	Zidovudine (Azidothymidine, AZT) Nevirapine Saquinavir

Stages of viral pathogenesis

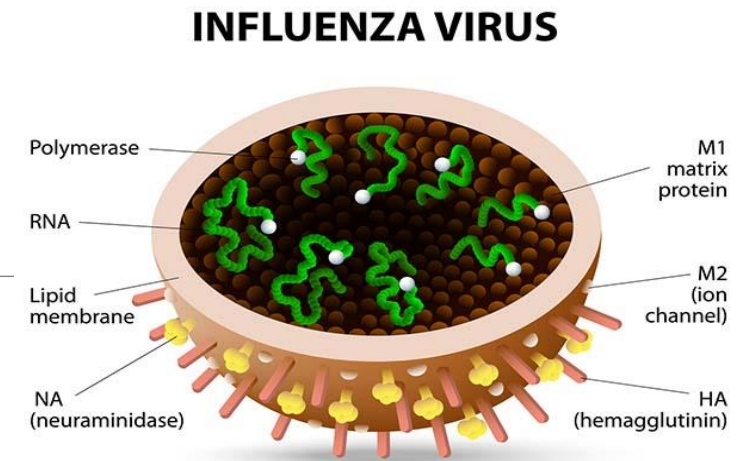
- Adsorption
- Penetration
- Deproteinization
- Transcription
- Translation
- The Assembly of the virus
Exit the cage



Action of antiviral agents at different stages of viral pathogenesis

Interaction stage	Group	Drugs
Adsorption and penetration	Preparations of immunoglobulins	gamma globulin, sandoglobulin
	Adamantane derivatives	amantadine, remantadine
Deproteinization	Adamantane derivatives	amantadine, remantadine
Formation of active proteins	Analogues of nucleosides	acyclovir, ganciclovir, famciclovir, valacyclovir
		ribavirin, idoxuridine, vidarabine
		zidovudine, lamivudine, didanosine, zalcitabine
	Fosfonomuraviina acid derivatives	sodium foscarnet
Synthesis of structural proteins	Derivatives of peptides	saquinavir, indinavir

Amantadine and rimantadine



- Derivatives of adamant
- Suppress the replication of the virus
- Mechanisms of action: the Primary target – the M2 protein of influenza A virus that forms an ion channel in its envelope → blockade of ribonucleic dissociation and entry of the virus into the cytoplasm
- Can act at the stage of Assembly of the virus (some strains of viruses)

Amantadine and rimantadine

Side effects (dose-dependent)

1. nausea
2. decreased appetite
3. Irritability
4. insomnia
5. disturbance of concentration
6. (high doses of amantadine-a significant neurotoxic effect: confusion, hallucinations, epileptic seizures, coma)

Amantadine and rimantadine

Indications:

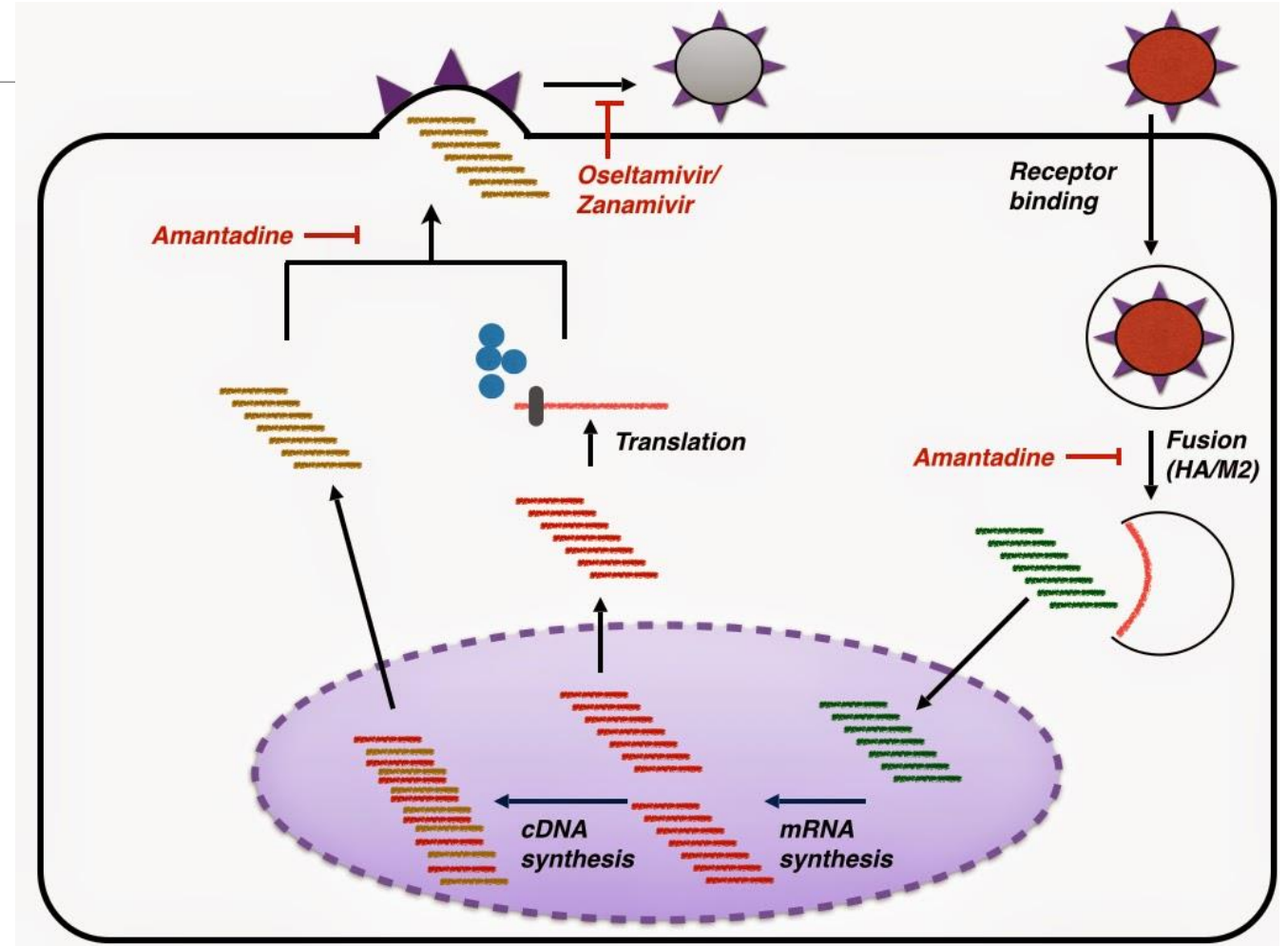
the prevention and treatment of influenza A (safety of use during pregnancy is not established; permitted to use from 7 years of age)

Currently, the high resistance of influenza virus to these medications

Oseltamivir and zanamivir

Mechanism of action:

Selective inhibitor of neuraminidase (influenza A and B viruses) → slows down of aggregation of viruses on the cell surface and their distribution



Oseltamivir and zanamivir

Indications:

- prevention and treatment of influenza type A and type B
- (in children: oseltamivir is used 1 year and older, zanamivir is used at the age of 5 years)



Oseltamivir

Side effect

- unpleasant sensations in the stomach
- nausea!(!!)

(reduced when taking the drug during meals.

Gastrointestinal disorders usually occur after 1-2 days)



Zanamivir



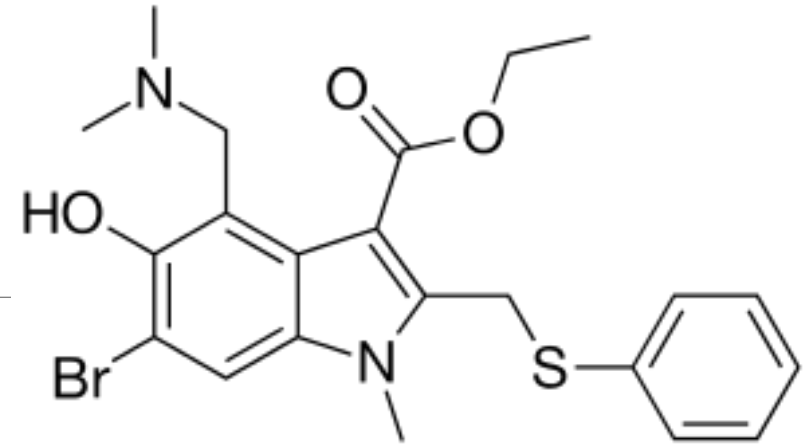
Side effect:

- allergic reactions: face and larynx swelling.
- dermatological reactions: rash, urticaria.
- bronchospasm, dyspnea.

Umifenovir (Arbidol)

Pharmacological action

- Inhibits the fusion of the lipid membrane of the virus with cell membranes
- It has interferon-inducing properties, stimulates the immune system



Umifenovir

Indications

- prevention and treatment of influenza type A and type b
- prevention and treatment of other respiratory
- complex therapy of acute intestinal infections of rotavirus etiology
- normalization of immune status in the postoperative period

Umifenovir

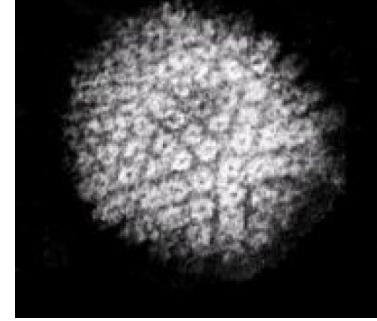
Contraindications:

- Hypersensitivity
- Age to 2 years

Side effects:

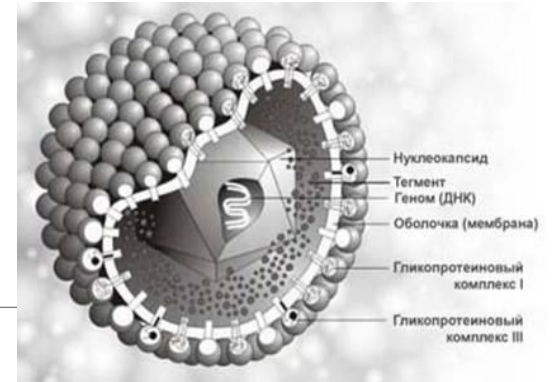
- Allergic reactions (rare)

The herpes viruses of man (by A. N. Boyum, 2006)



Subfamily	Kind	Official name	Common use name
Alpha-herpes-viruses	Simplex virus	Human herpesvirus 1	Herpes simplex virus, type 1
		Human herpesvirus 2	Herpes simplex virus, type 2
		Human herpesvirus 3	Varicella–Zoster-virus (varicella/herpes zoster)
Beta-herpes-viruses	Cytome-galovirus	Human herpesvirus 5	Cytomegalovirus
	Roseolo-virus	Human herpesvirus 6	Human herpesvirus 6 type's
		Human herpesvirus 7	Human herpesvirus 7 type's
Gamma-herpes-viruses	Lympho-crypto-virus	Human herpesvirus 4	Epstein-Barr Virus
		Human herpesvirus 8	Human herpesvirus 8 type's

Acyclovir



The acyclic analogue of guanosine

Mechanism of action:

suppression of viral DNA synthesis

(acyclovirtriphosphate is embedded in the DNA chain → the cessation of the growth of the viral DNA chain → binds to DNA polymerase → irreversibly inactivating it).

Acyclovir

Side effect:

- Irritation of mucous membranes (local)
- Headache
- Dizziness
- Rash
- Diarrhea
- Renal failure and lesions of the Central nervous system (i/v)

Acyclovir

Indications:

- Genital herpes
- Herpes of the skin and mucous membranes
- Herpetic encephalitis
- Varicella
- Shingles
- Prevention cytomegaloviral infection

Famcyclovir



❖ The mechanism of action is similar to acyclovir

Famciclovir

Side effect:

- Headache
- Nausea
- Diarrhea
- Urticaria
- Hallucinations and confusion (in the elderly)
- Contact dermatitis and ulceration (preparations for topical use)

Famciclovir

Indications:

- genital herpes
- herpes of the skin
- herpes zoster
- postherpetic neuralgia

Gancyclovir



❖ The mechanism of action is similar to acyclovir.

Ganciclovir

Side effect:

- suppression of hematopoiesis
- CNS lesions of varying severity – 5-15% of patients
- phlebitis, azotemia, anemia, rash, fever, hepatotoxicity, nausea, vomiting, eosinophilia (i/v)

(In laboratory animals, the drug had a teratogenic and embryotoxic effect, irreversibly violated reproductive function)

Ganciclovir

❖ Interaction: Cytostatic drugs increase the side effects of ganciclovir on the bone marrow.

❖ Indications:

➤ Cytomegaloviral infection

➤ Herpetic keratitis

➤ Malignant neoplasm

Idoxuridine



Mechanism of action:

➤ phosphorylated derivatives are embedded in viral and cellular DNA, but inhibit replication of viral DNA only.

the DNA is destroyed → errors of transcription

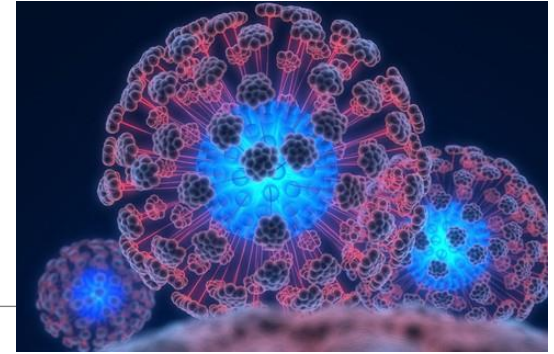
Idoxuridine



- ❖ The drug is allowed only for topical use.
- ❖ Side effects:
 - Pain
 - Itching
 - Inflammation and swelling of eyes
 - Allergic reactions

- ❖ Indications: Herpetic keratitis and conjunctivitis

Zidovudine



Mechanism of action:

- Inhibits reverse transcriptase of HIV
- Sequentially phosphorylated and embedded in the growing DNA and stops replication
- Suppression of cellular and mitochondrial DNA polymerase and cellular thymidylate kinase



Zidovudine



Side effect:

early

- Decreased appetite
- fatigue
- Headache
- Myalgia
- nausea
- Insomnia
- Neutropenia

Side effect:

after 4 weeks

- Anemia

Late

- Hyperpigmentation of nails
- Myopathy
- lactic acidosis
- Lypodystrophy of liver

Zidovudine

Indications:

- Treatment of HIV-1-and HIV-2-infections (including in children)
- Prevention of HIV infection in newborns (mother is HIV-infected)
- Prevention HIV infection
- The drug is more effective in combination therapy

Nevirapine



Mechanism of action:

- Binds to the active site of reverse transcriptase and inactivates its

Nevirapine

Side effect:

- Rash, itching
- Fever
- Fatigability
- Headache
- Drowsiness
- Nausea
- Increased activity of liver enzymes
- Drug-induced hepatitis (1%)
- The Stevens-Johnson Syndrome (0,3%)

Nevirapine

Indications:

- Treatment of HIV-1 infections (for combination therapy)
- Prevention of HIV in newborns

Saquinavir



Mechanism of action:

inhibits the maturation of the virus protease, preventing polyprotein degradation and maturation of the virus

Saquinavir

Side effect:

- Nausea, vomiting, diarrhea
- Hemolytic collapse (obesity of the upper type, hyperglycemia, etc.)
- Headache
- Confusion, convulsions
- Neuropathy
- Osteoporosis

Saquinavir

❖ Indications:

➤ Combination therapy of HIV infections

❖ be careful when

➤ Severe liver damage

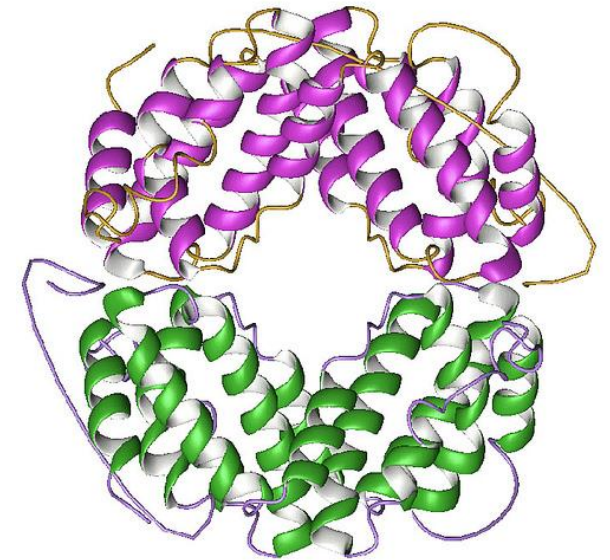
➤ Severe renal failure

➤ Up to 16 years and over 65 years

Interferons

Mechanism of action:

Bind to specific receptors → activation of the synthesis of antiviral proteins → inhibition of virus multiplication



Interferons

Side effect:

- Influenza-like syndrome
- supression of hematopoiesis
- Violations by the CNS
- Autoimmune disorders
- inhibit the activity of microsomal liver enzymes.

Interferons

Indications:

- Hepatitis B
- Hepatitis C
- Infection caused by the human papillomavirus
- Herpes infections (including herpes skin, genital, shingles, cytomegalovirus infection)
- HIV infection
- Malignant neoplasms
- Prevention of rhinovirus infection



Lamivudine



❖ Mechanism of action:

- inhibits HIV reverse transcriptase and
- hepatitis b virus DNA polymerase

❖ Indications:

- HIV infection
- Hepatitis B

Lamivudine

Side effect:

- Headache, Dizziness, Sleep disturbance
- Hypothermia
- Neuropathy
- Cough
- Flu-like syndrome
- Necrotic pancreatitis
- Myalgia
- Suppression of hematopoiesis
- Allergic reaction

Ribavirin



Mechanism of action:

- inhibits the reproduction of many RNA - and DNA-containing viruses
- prevents the synthesis of guanine nucleotides and viral mRNA.

Ribavirin

Side effect:

- Rash, conjunctivitis, transient bronchospasm,
- Arterial hypotension,
- disturbance of thyroid function,

Suppression of hematopoiesis

- Allergic reactions (when the system introduction)

The drug has a teratogenic, embryotoxic, carcinogenic effect (!!!)

It is absolutely contraindicated in pregnancy.

Ribavirin

Indications:

- Herpetic infection
- Flu type A and B
- Measles
- Hepatitis A, B, chronic C
- Infections caused by respiratory syncytial virus