Sexually transmitted diseases (STD)

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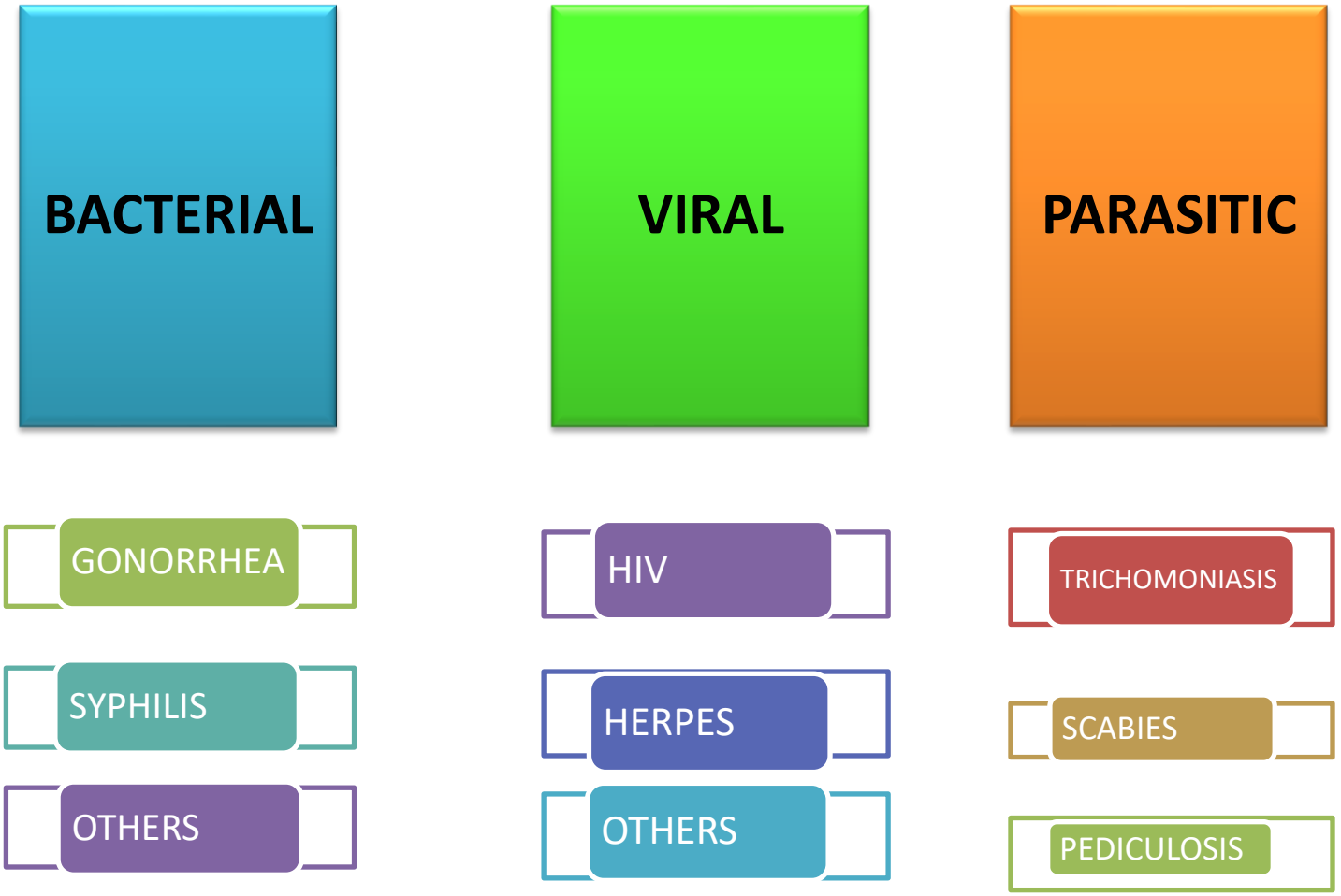
- **Definition and classification:**

Diseases that are transmitted **MAINLY** by sexual contact



▪ Prevention:-

❖ **Education:-**

Patient should be informed :-

A. How diseases spread

B. How can they protect themselves

C. Treatment options

❖ **Abstinence:-**

The most reliable method.

❖ **Vaccination:-**

Some diseases have vaccinations like vaccination against HPV & HBV.

❖ **Condoms:-**

Highly effective in reducing STIs transmission

Gonorrhea and Non-Gonococcal Urethritis

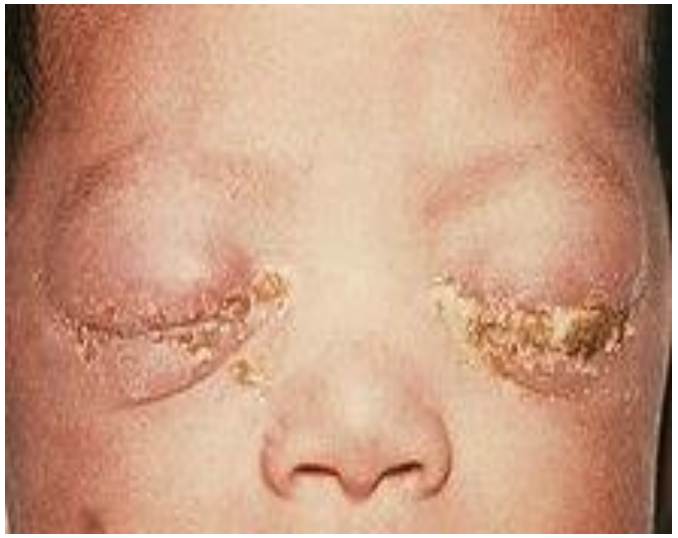
- **Causative agent:-**
  - **Neisseria gonorrhoeae**

Gram-negative diplococcus that occurs only in humans.

- **Symptoms and Signs:-**

Asymptomatic (10-20%)

1. **Male urethritis**
2. **Female Cervicitis and urethritis**
3. **ophthalmia neonatorum**



Complications

1. Epididymitis and inflammations of other urethral glands:-

- Usually epididymitis cause unilateral scrotal pain, tenderness, swelling.

2. Pelvic inflammatory disease(PID)

- Occur in 10-20% of infected women.

3. Disseminated gonococcal infection (DGI)

Arthritis- dermatitis syndrome

Reflect bacteremia

• Treatment:

1. **Uncomplicated Gonococcal Infections**

Ceftriaxone or cefotaxime (IM) PLUS Azithromycin 1g orally in a single dose

In the case of **azithromycin allergy**:- Doxycycline 100 mg orally twice a day for 7 days

2. **Prophylactic measures to prevent ophthalmia neonatorum:-**

- All newborn given one of these ttt:-

0.5% erythromycin ointment.

, 1% solution of silver nitrate or

1% tetracycline ointment.

C- Treatment of complicated gonorrhea:-

- **Gonococcal Conjunctivitis:-** (Single dose of ceftriaxone 1 g IM. + Azithromycin 1 g PO with saline irrigation+Topical antibiotic solution).
- **Gonococcal Epididymitis:-**

(Single dose of ceftriaxone 250 mg IM.+ Doxycycline 100 mg orally twice daily for 10 days).

- **PID:-**

(Single dose of ceftriaxone 2 g IM+Doxycycline 100 mg orally twice daily for 14 days+With or without Metronidazole 500 mg PO twice daily for 14 days).

- **DGI:-**

(Ceftriaxone 1 g IM/IV every 24 hours+Single dose of azithromycin 1 g PO)

Sex partners:-

- All sex partners with sexual contact with patient within 60 days should be tested for gonorrhea & other STDs and treated if results are positive.
- Sex partners with sexual contact within two weeks should be treated presumptively for gonorrhea.

NON-GONOCOCCAL URETHRITIS (NGU)

- NGU is much more common than gonococcal urethritis.
- The most common causes are:

1. **Bacterial infections:-**

Chlamydia trachomatis (most common).

2. Viral(rare):-

- Herpes simplex virus.

3. Parasitic(rare):-

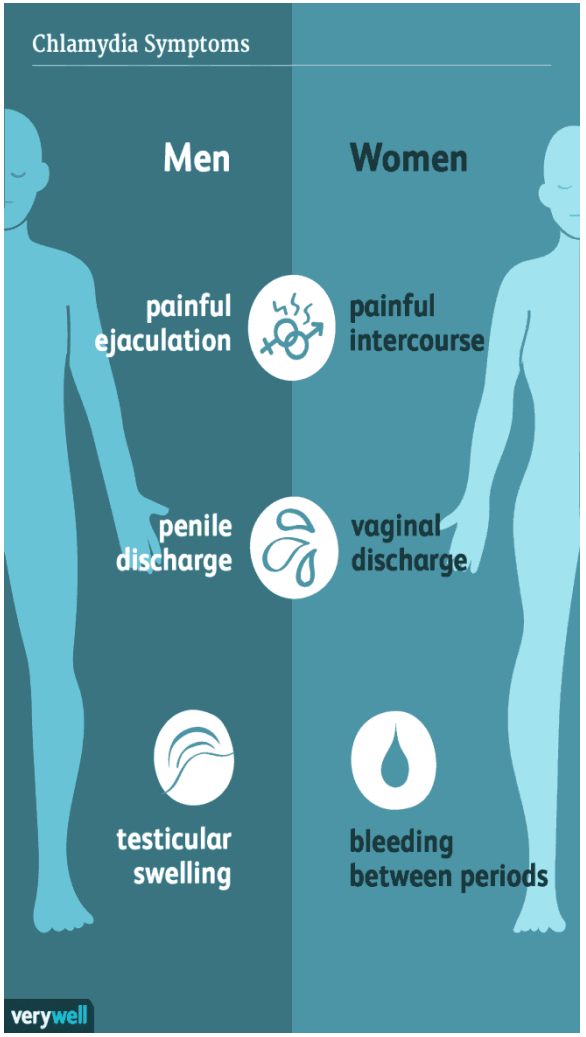
- Trichomonas vaginalis

4. **Non-infectious**

- Mechanical injury (from a urinary catheter or a cystoscope).

Chlamydial URETHRITIS

- **Treatment:-**
- Azithromycin 1 g orally in a single dose OR
- Doxycycline 100 mg orally twice a day for 7 days
- **Alternative Regimens**
- Erythromycin 500 mg orally four times a day for 7 days OR
- Levofloxacin 500 mg orally once daily for 7 days OR
- Ofloxacin 300 mg orally twice a day for 7 days



Syphilis

- **Etiology:-**

Causative agent:- Spirochete Treponema pallidum (T. pallidum).

- **Classification:-**

1- Acquired syphilis

2-Congenital syphilis

- **Treponemes** cross placental barrier and infect fetus

1.Acquired syphilis :

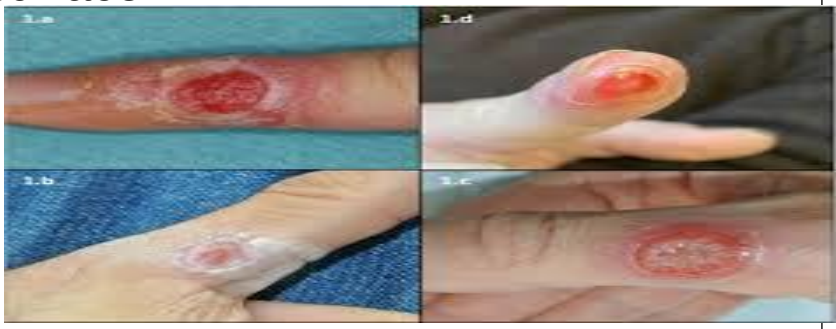
Classified into 4 stages:-

A.Primary B.Secondary C.Tertiary D.Latent

A.Primary Syphilis

The initial lesion is a **papule** which rapidly ulcerates to make a **chancre**.

It may occur on any skin or mucous membrane surface.

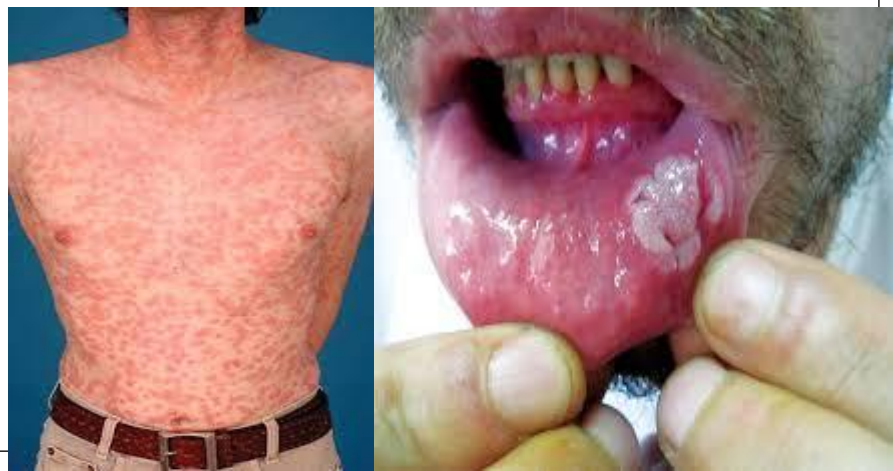


B.Secondary syphilis

Develops 4-10 weeks after appearance of primary lesion.

During this stage, spirochetes multiply and **spread throughout the body**

(general manifestation plus skin manifestations).



C.Latent syphilis

There are no clinical lesions but the disease is detectable by positive serological tests.(early latent and late latent)

D.Tertiary syphilis

tertiary syphilis disease is rare.

It mainly affect CVS (80-85%) & CNS (5-10%)

Cardiovascular syphilis:- Occurs at least 10 years after primary infection.

(Aneurysm in ascending aorta Or Aortic valve insufficiency).

Neurosyphilis:-

Meningiovascular syphilis

Parenchymal neurosyphilis

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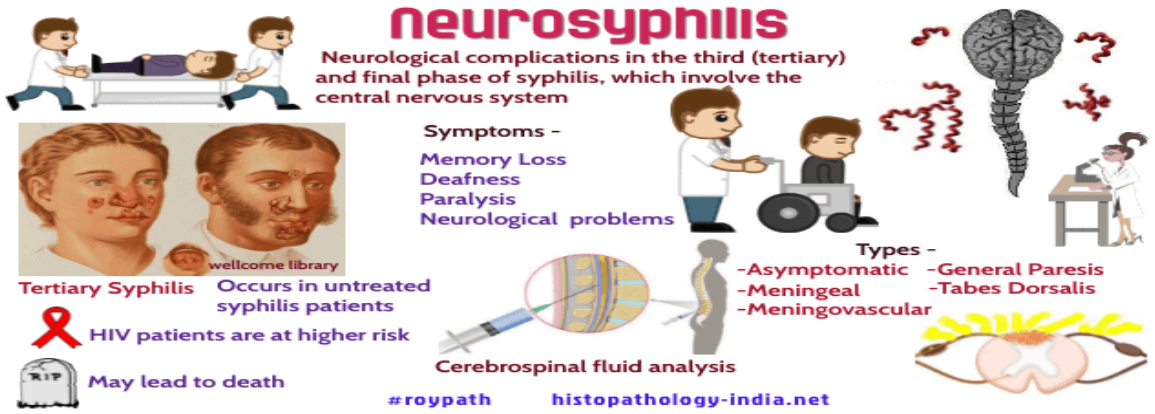


The following regimens are recommended for treatment

1- Primary, secondary or early latent syphilis:-

- Benzathine penicillin G 2.4 million units IM in a single dose.

2- Late latent syphilis or latent syphilis of unknown duration:-

- Benzathine penicillin G 2.4 million units IM weekly for 3 weeks.

1. **In congenital syphilis:-**

- Benzathine penicillin G 50,000 units/kg IM, in a single dose.

1. In patients with a history of penicillin allergy →

- Skin testing is recommended.
- Skin test positive patients should be desensitized in the hospital.

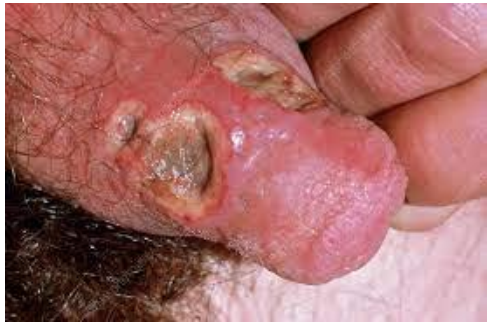
For patients allergic to penicillin:-

1. **Tetracycline:- for 14 0r 28 days**
2. **Erythromycin:- for 14 0r 30 days**
3. **Azythromycin:- for 14 days**
4. **Ceftriaxone: for 10 days**

Neurosyphilis: 2 g i.m or i.v. daily for 10 — 14 days.

Other Bacterial STIs

- **Chancroid (Soft sore)**



Causative agent:- Hemophilus ducreyi → Gram -ve coccobacilli.

Treatment

- The main treatment is erythromycin given for 7 days.
- Ceftriaxone or azithromycin are alternatives given as a single dose.

- **Lymphogranuloma venereum**

- **Causative agent**: It is caused by Chlamydia trachomatis types L1, L2, L3

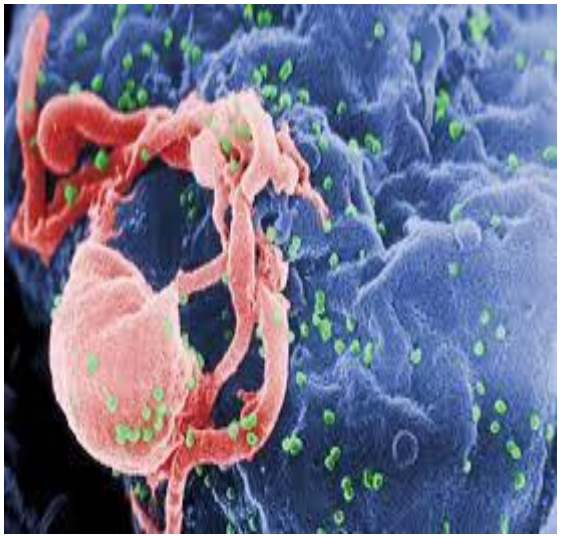
- **Treatment**

- Tetracycline:- 500 mg 4 times daily for 14 days.
- Erythromycin or doxycycline or azithromycin are effectiv
- Most cases require repeated courses.

Human Immunodeficiency Disease

- **Etiology:-**

Causative agent:- Caused by infection with HIV-1 or HIV-2, which is a single-stranded RNA virus.



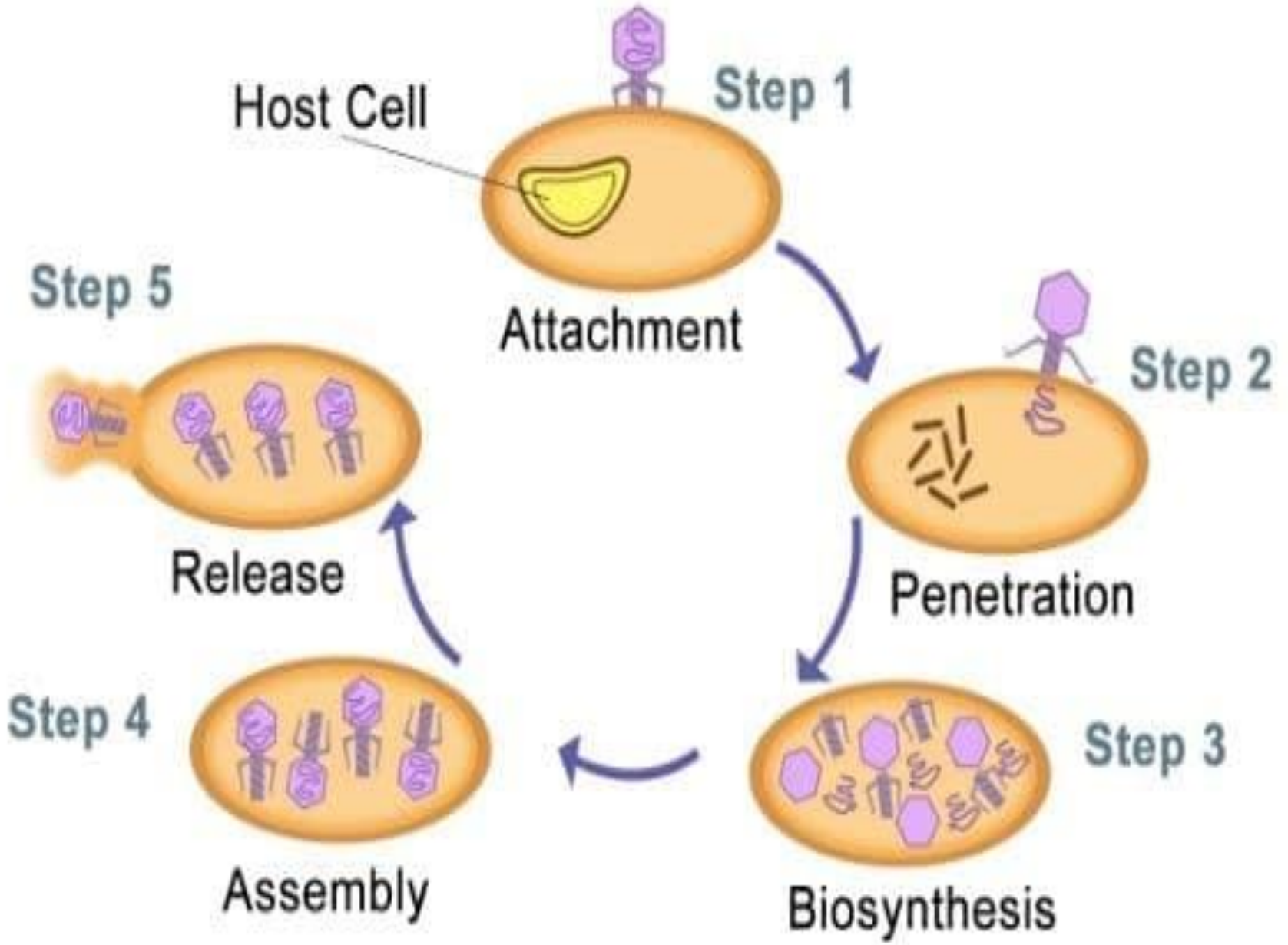
- -It was identified as the cause of AIDS in 1983.

Mode of transmission:-

- HIV is blood-borne virus transmitted via:-
- 1.Sexual intercourse including anal intercourse.
- 2.Use of contaminated injecting equipment.
- 3. Mother-to-child transmission, during birth process or during breastfeeding

Treatment of HIV

- **Highly active antiretroviral therapy (HAART)** is often initiated on the time of diagnosis. Strongest indication is for patients with AIDS-defining illness, low CD4+ (< 500 cells/mm^3), or high viral load.
- Regimen consists of 3 drugs (to prevent resistence):
- 2 NRTIs &1 of the following (NNRTIs, protease inhibitors, or integrase inhibitors)


Host Cell
Step 1
Attachment
Step 2
Penetration
Step 3
Biosynthesis
Step 4
Assembly
Step 5
Release

• Nucleoside reverse transcriptase inhibitors (NRTIs)

- zidovudine, didanosine, lamivudine
- **Mechanism**

Phosphorylated by host kinases

competitive inhibition of reverse transcriptase and chain termination of DNA.

- **Clinical use**

Main component of HAART.

Zidovudine is used for general prophylaxis and for prevention of vertical transmission in pregnancy.

• Non-nucleoside reverse transcriptase inhibitors (NNRTIs);

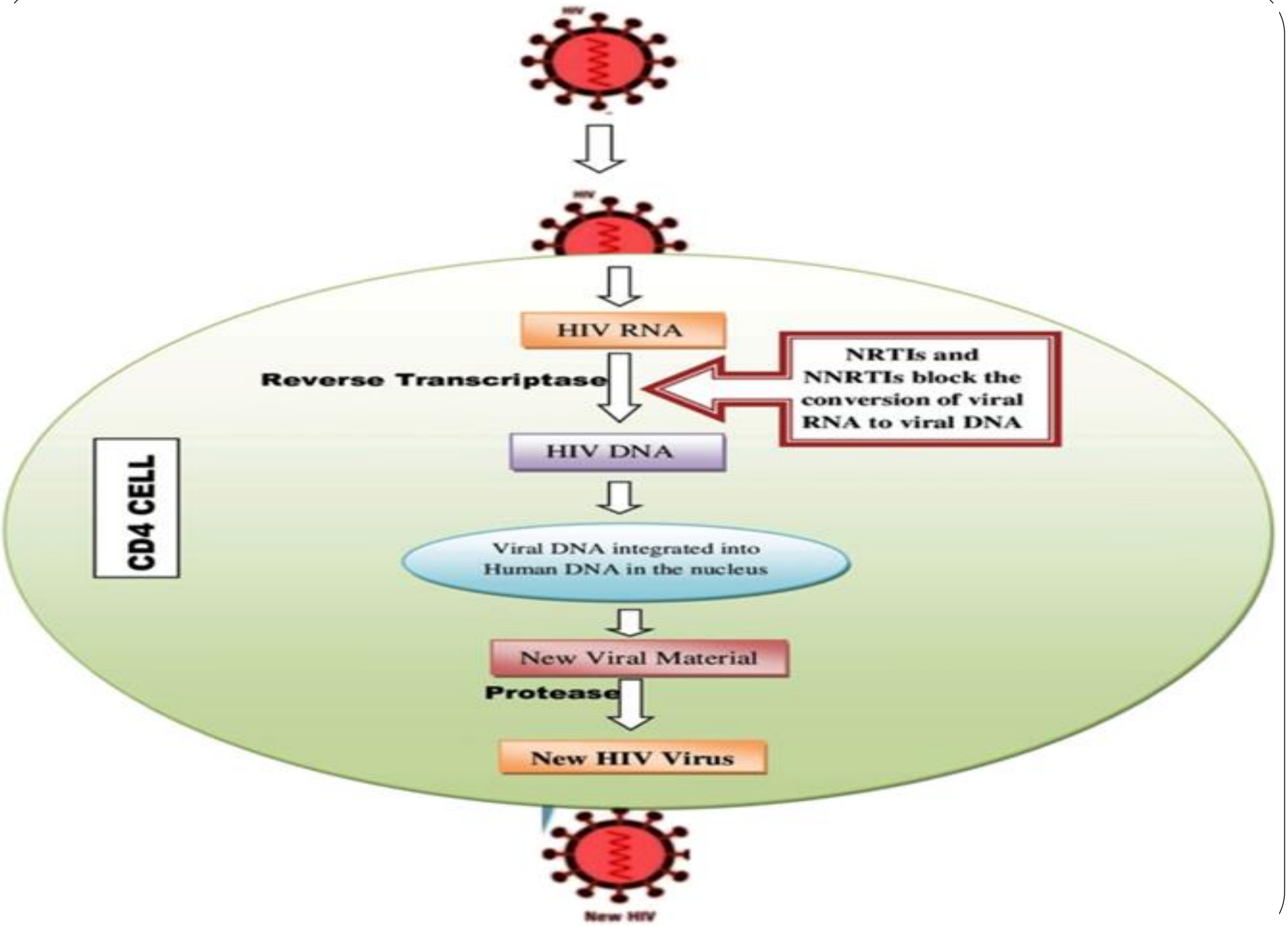
- efavirenz
- **Mechanism**

Bind to and inhibit reverse transcriptase inhibiting DNA synthesis.

No need for phosphorylation

Not competitive (bind to a site other than site of NRTIs).

- **Protease inhibitors (PIs); atazanavir, lopinavir, ritonavir**
- **Mechanism**
- HIV-1 protease cleaves the polypeptide products of the viral mRNA into functional parts → assembly & maturation of new viruses.
- PIs act by inhibiting this enzyme.

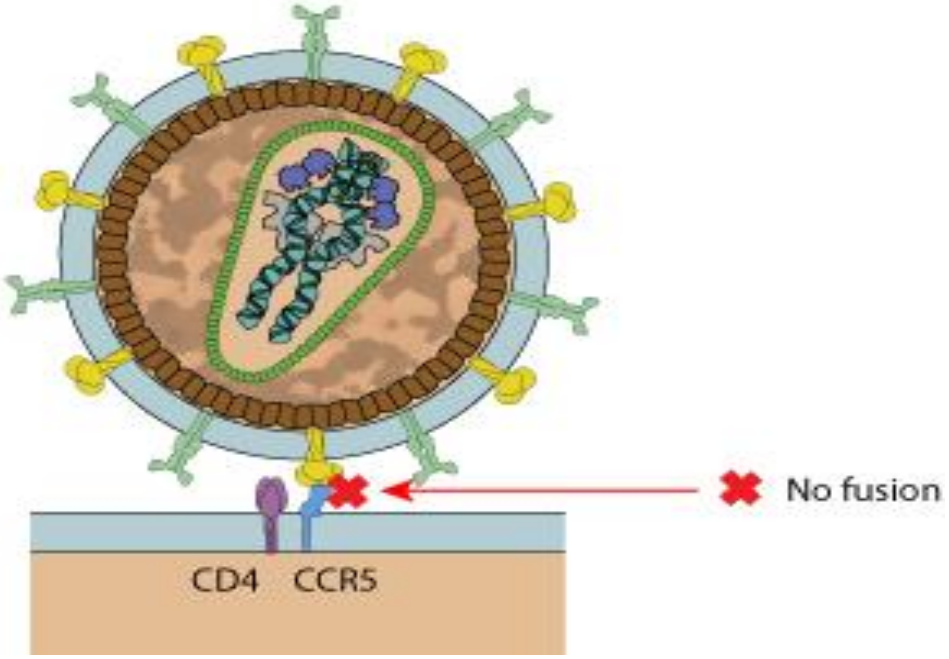

HIV
HIV
HIV RNA
Reverse Transcriptase
NRTIs and NNRTIs block the conversion of viral RNA to viral DNA
HIV DNA
CD4 CELL
Viral DNA integrated into Human DNA in the nucleus
New Viral Material
Protease
New HIV Virus
New HIV

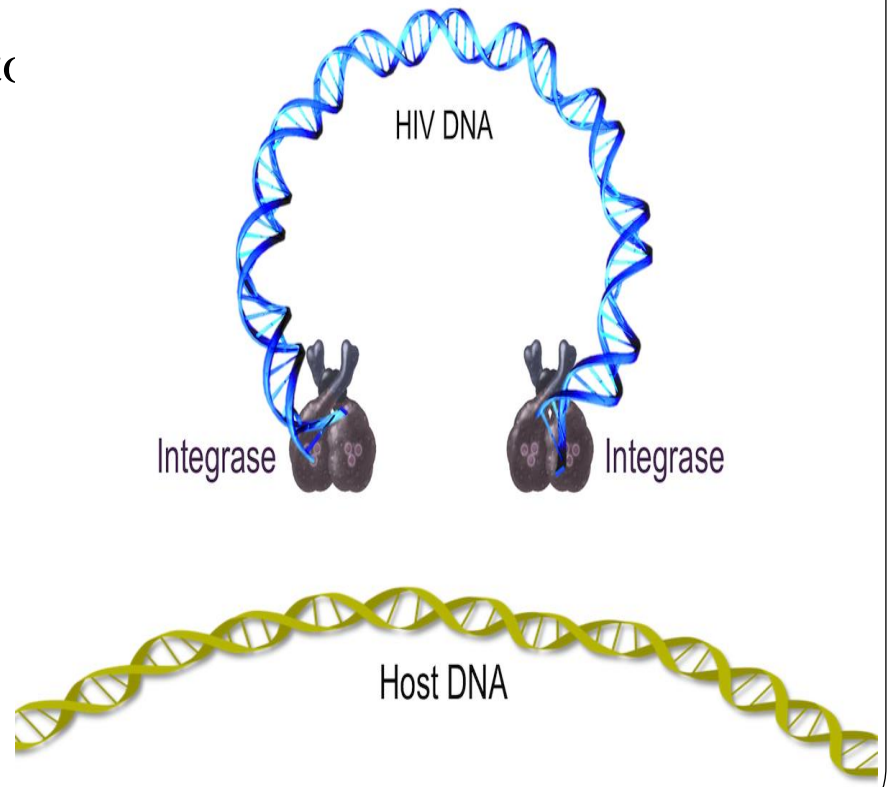
- **Integrase inhibitors; raltegravir**
- Mechanism

Inhibit integration of viral genome in host cell DNA.

- **Fusion inhibitors; maraviroc**
- Mechanism

Inhibit binding and entry of the virus int



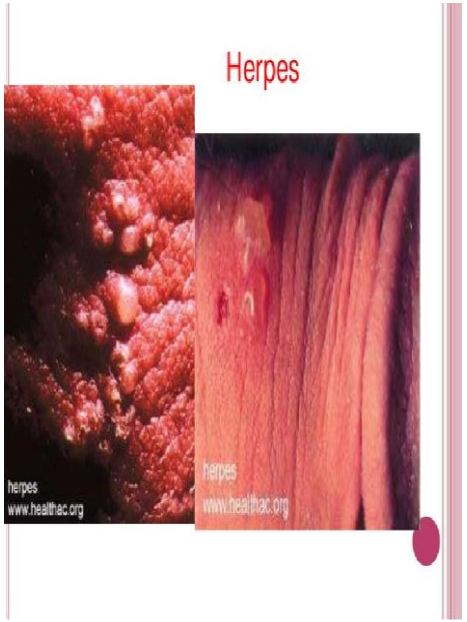


Genital Herpes

Etiology:-

Causative agent: Herpes simplex virus (HSV)

- It is a DNA virus.
- HSV has been classified into two types HSV-1 & HSV-2.



- **Treatment**

- **Aim of treatment:-**

- With the first episode ⟶ to reduce duration and severity of symptoms.
- With recurrent infections ⟶ to reduce duration and severity of symptoms, and the likelihood of further recurrences

Antiviral drugs:-
1-Acyclovir- famciclovir- valacyclovir

Mechanism of action:-

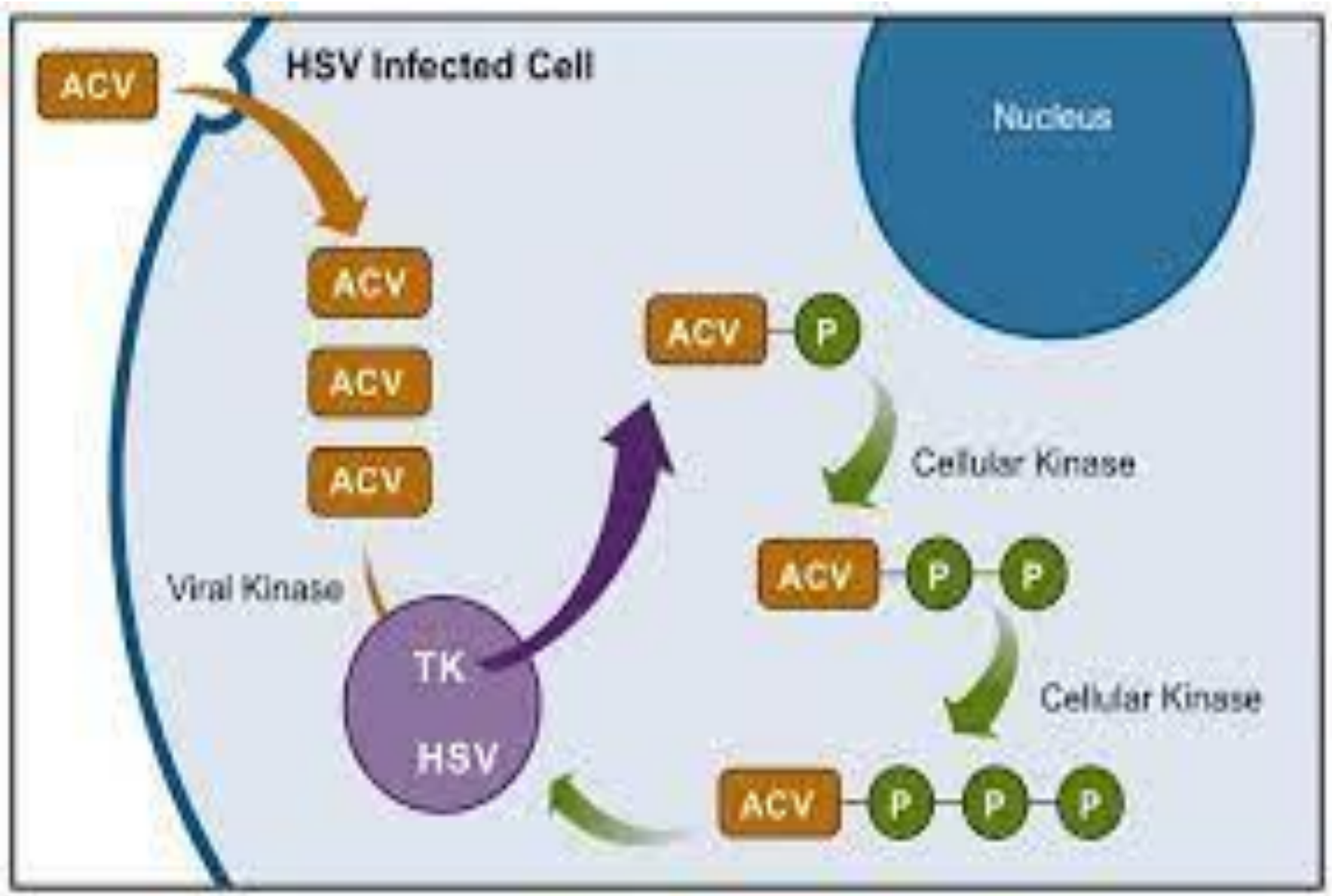
- -**Activation:** **Guanosine analogs**.

- Mono-phosphorylated by HSV thymidine kinase (TK) (not phosphorylated in uninfected cells → few adverse effects).

- They are further activated by host-cell kinases to the triphosphates

Valaciclovir

- Valaciclovir is the pro-drug of acyclovir.
- Valaciclovir is converted into acyclovir by intestinal & liver enzymes resulting in improved bioavailability of acyclovir.


ACV
HSV Infected Cell
Nucleus
ACV
ACV
ACV
ACV
P
Cellular Kinase
Viral Kinase
ACV
P
P
TK
HSV
Cellular Kinase
ACV
P
P
P

•Triphosphates are substrates for viral DNA polymerase → incorporated into the DNA molecule → chain terminations

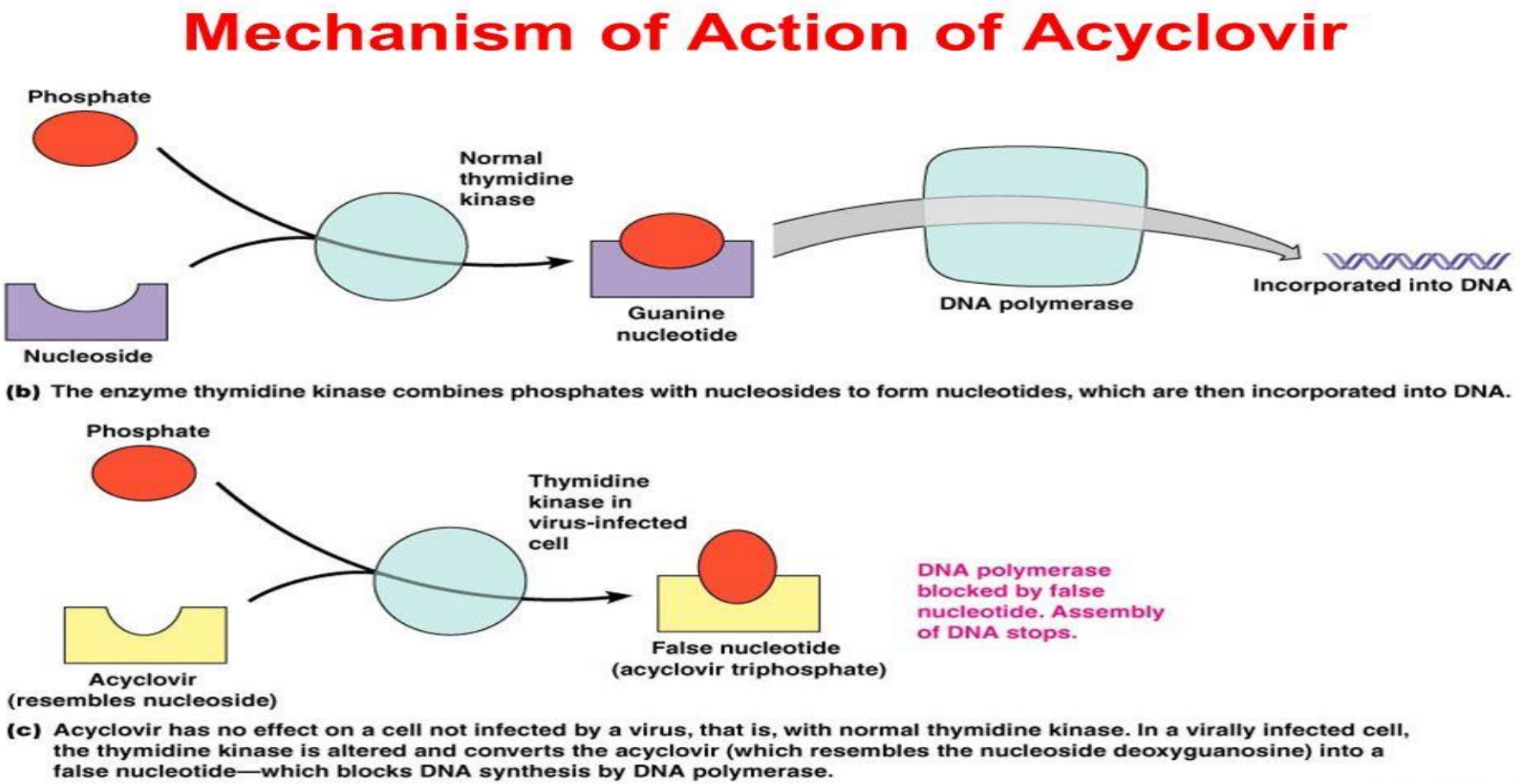


Fig 20.16

2-Foscarnet

- Doesn't require activation by viral or human kinases
- **Mechanism of action:**
- Inhibition(-) of Viral DNA polymerase
- (-) RNA polymerase
- (-) HIV reverse transcriptase
- **clinical uses:**
- Acyclovir-resistant **HSV infection**
- **Toxicity:**
- Nephrotoxicity
- Electrolyte disturbances that may cause seizures (hypocalcemia & hypomagnesemia)

Hepatitis B

Causative organism:-Hepatitis B virus (HBV) is a double stranded DNA virus.

Treatments:-

Currently there are seven approved drugs for treating HBV :-

- Interferon2b&2a.
- Lamivudine
- Adefovir
- Entecavir
- Telbivudine
- Tenofovir

Interferon2b&2a

Glycoproteins normally synthesized by virally infected cells.

They have wide range of antiviral and antitumor effects.

The exact mechanism is unclear, but possibly they may act through:

- Inhibition of viral penetration, translation, transcription, protein processing, maturation, and release.
- Enhanced phagocytic activity.
- ↑↑ proliferation and survival of cytotoxic T cells.

- **Lamivudine :** This cytosine analog is an inhibitor (HBV) DNA polymerase. Lamivudine must be phosphorylated by host cellular enzymes to the triphosphate (active) form.
- **Adefovir:** Adefovir dipivoxil is a nucleotide analog that is phosphorylated to adefovir diphosphate, which is then incorporated into viral DNA. This leads to termination of further DNA synthesis and prevents viral replication.
- **Entecavir:** is a guanosine analog . Following intracellular phosphorylation to the triphosphate, it competes with the natural substrate, deoxyguanosine triphosphate, for viral reverse transcriptase.

Entecavir is effective against lamivudine-resistant strains of HBV

- **Telbivudine** is a thymidine analog. The drug is phosphorylated intracellularly to the triphosphate, which can either compete with endogenous thymidine triphosphate for incorporation into DNA or else be incorporated into viral DNA, where it serves to terminate further elongation of the DNA chain.

Hepatitis C

Causative organism:- Hepatitis C virus which is a single stranded RNA virus.

Mode of transmission:-

- The main form of transmission is parenteral.
- However vertical transmission, sexual contact, and other forms have been reported.

Treatments:- a combination of antivirals that can be used according to liver condition and type of hepatitis C virus e.g.:-

- **Ribavirin** : Competitive inhibition of IMP (inositol monophosphate) dehydrogenase → inhibition of guanine nucleotides synthesis. Inhibition of viral RNA polymerase.

HCV protease inhibitor → ↓↓ viral replication. **Toxicity:** photosensitivity & rash.	***NS3/4A Protease inhibitors*** **e.g. simeprevir**
Inhibition of HCV RNA-dependent polymerase. **Toxicity:** sofosbuvir (Sovaldi) → headache & fatigue.	***NS5B polymerase inhibitors*** a. Nucleoside (sofosbuvir) b. Non-nucleoside (dasabuvir)
Inhibition of HCV NS5A replication complex (replicase) → ↓↓ viral replication.	***NS5A (replicase)inhibitors*** e.g. daclatasvir & ledipasvir

Parasitic STIs

• Trichomoniasis

Causative agent:- It is caused by Trichomonas vaginalis.

Treatment

1. Oral metronidazole (Flagyl 250 & 500 mg tab):-

-Cure rates are >95%.

-Treatment should include infected persons & their partners due to:-

High rates of infection in asymptomatic partners.

High rates of re-infection

2. Oral Tinidazole (Fasygen, 500 mg tab)

-Single-dose therapy consists of 2 g taken with food.

-Cure rates range from 86-100%.

-For resistant infections → 2 g twice daily for 14 days.

-When metronidazole fails tinidazole may be used.


Thank
you