

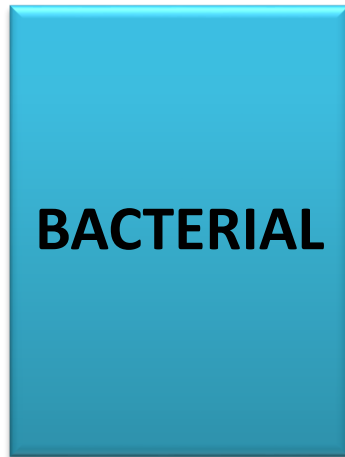
# Sexually transmitted diseases (STD)

**Dr/ Heba Ahmed Hassan**

**Assistant professor of clinical pharmacology  
faculty of medicine, mutah university**

## ■ Definition and classification:

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



# Gonorrhoea 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 gonorrhoea:-

- 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)

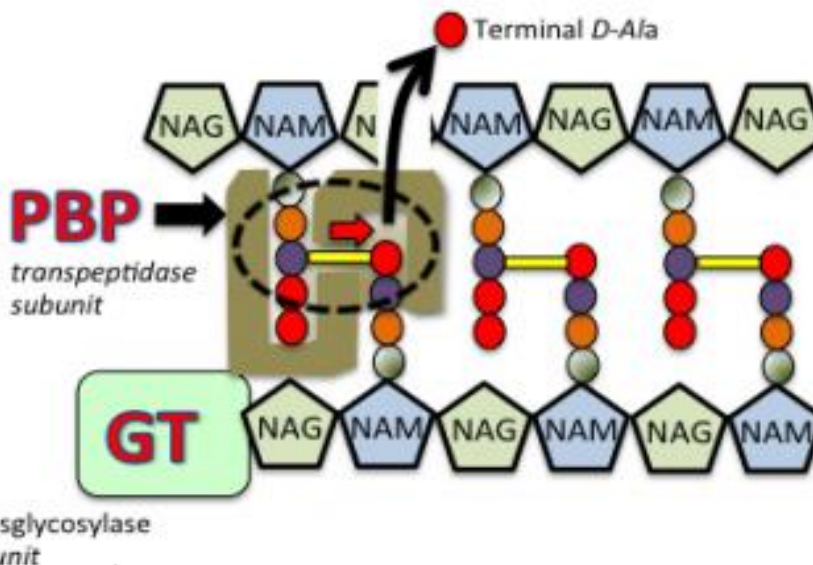
**Sex partners:-**

All sex partners with sexual contact with patient within 60 days should be tested for gonorrhoea & other STDs and treated if results are positive.

Sex partners with sexual contact within two weeks should be treated presumptively for gonorrhoea.

# $\beta$ -lactam mechanism of action

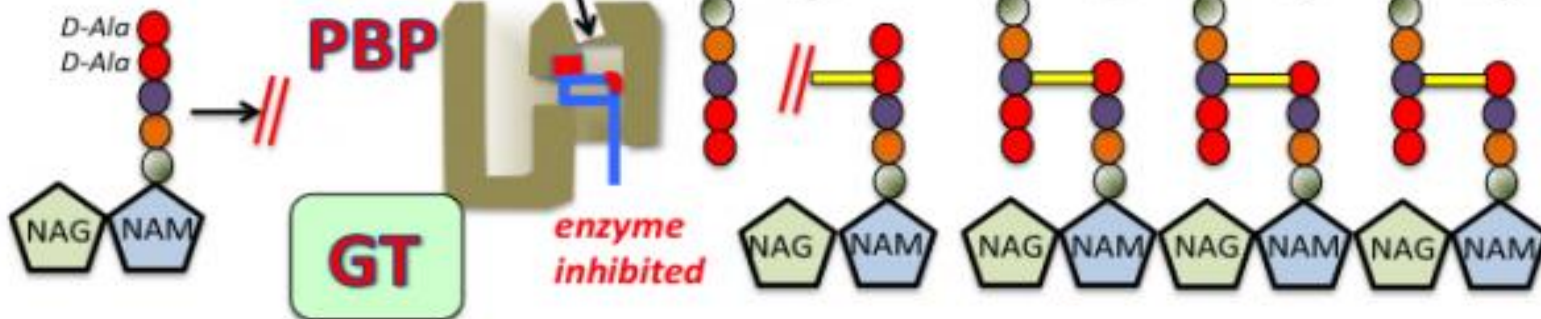
ABX-free  
Cell Wall  
Synthesis



D-Ala-D-Ala structural mimics:  
Pen Ceph Mono Carba

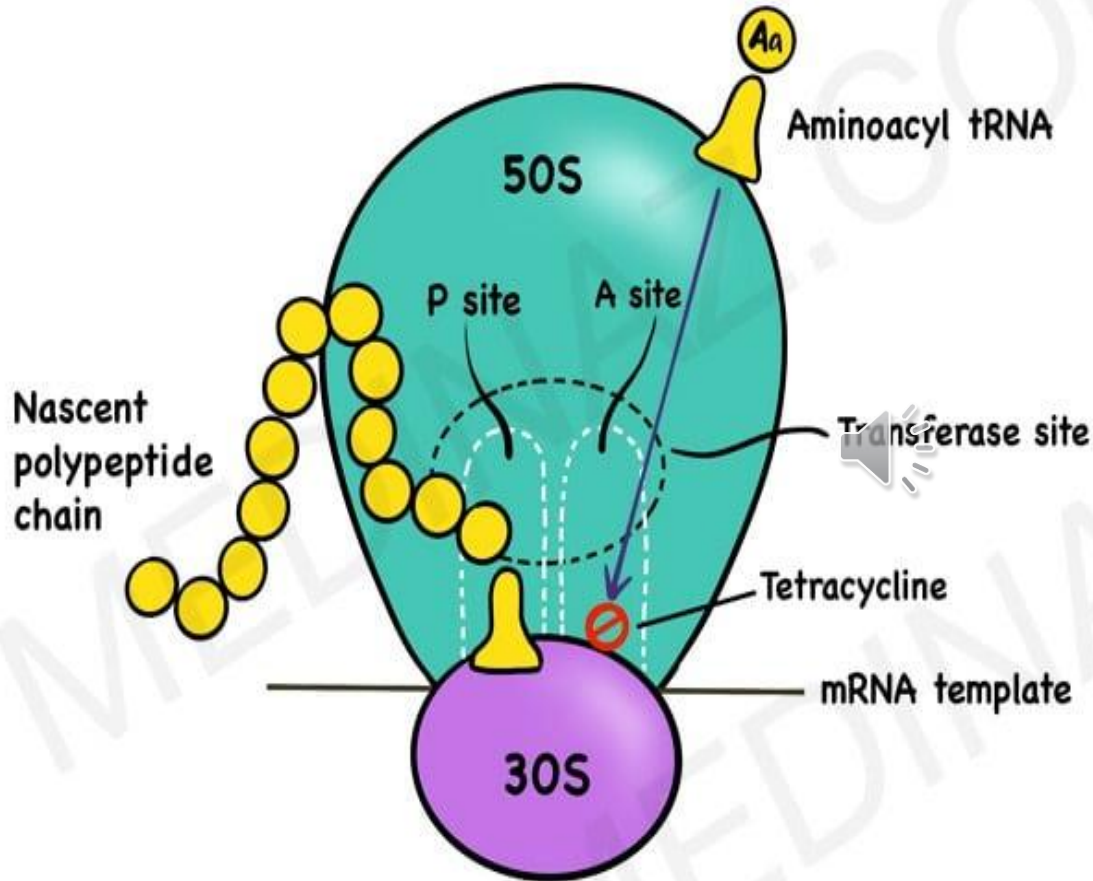
**$\beta$ -lactams** – bind to transpeptidase active site

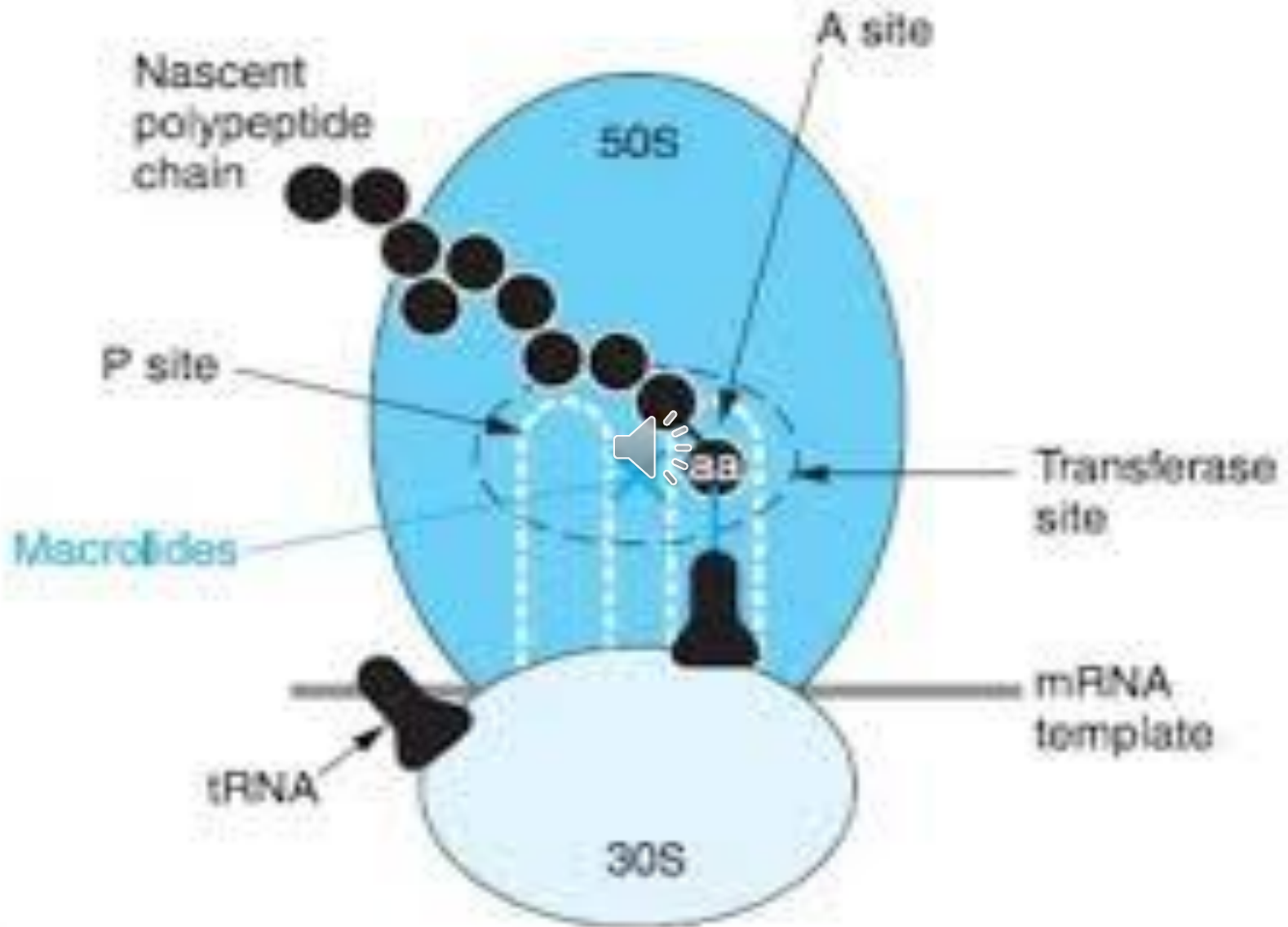
Block of transpeptidase activity interrupts cross-linking & cell wall synthesis






# Tetracycline Mechanism of Action





# 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).

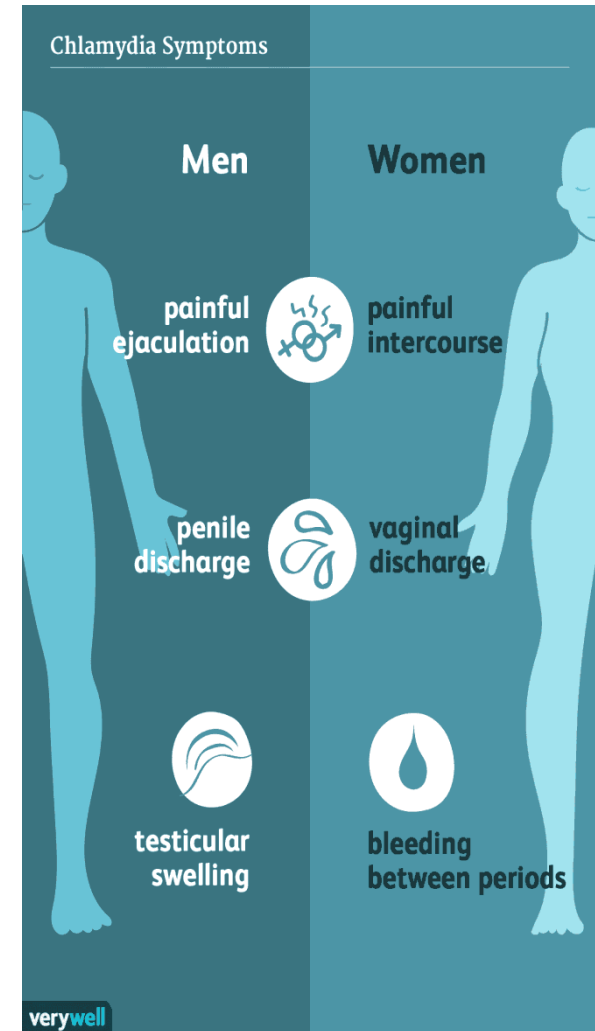
# Chlamydial URETHRITIS

## ■ 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



# Levofloxacin (fluoroquinolone)

## Mechanism of action

- Bactericidal against susceptible organisms.
  - It interferes with bacterial DNA synthesis by inhibiting 2 important bacterial enzymes:
    1. Topoisomerase II.
      - Topoisomerase II (DNA gyrase) is responsible for relaxing supercoiled DNA during normal transcription.
    2. Topoisomerase IV.
      - Topoisomerase IV interferes with separation of chromosomal DNA during cell division.

# 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%)

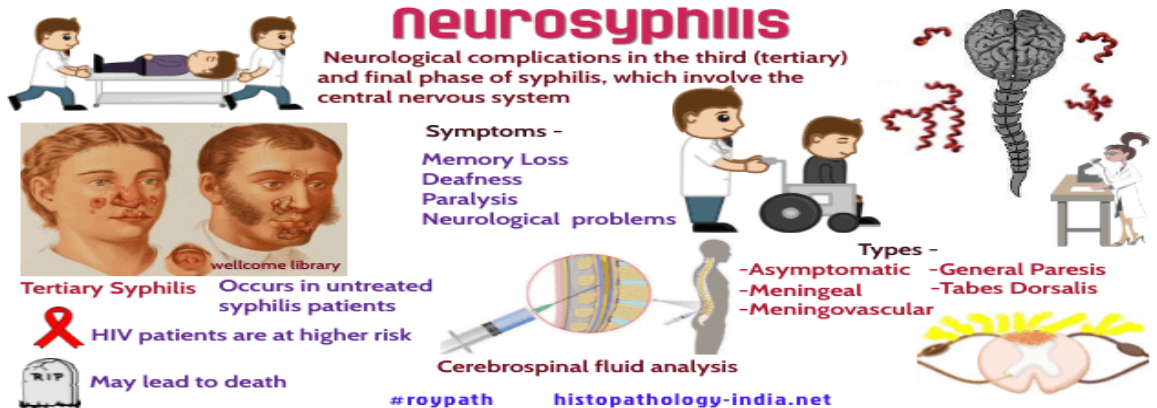
**Cardiovascular syphilis:-** Occurs at least 10 years after primary infection.

(Aneurysm in ascending aorta Or Aortic valve insufficiency).

**Neurosyphilis:-**

Meningiovascular syphilis

Parenchymal neurosyphilis



**neurosyphilis**  
Neurological complications in the third (tertiary) and final phase of syphilis, which involve the central nervous system

**Symptoms -**  
Memory Loss  
Deafness  
Paralysis  
Neurological problems

**Types -**  
-Asymptomatic  
-Meningeal  
-Meningovascular  
-General Paresis  
-Tabes Dorsalis

**Tertiary Syphilis** Occurs in untreated syphilis patients  
HIV patients are at higher risk  
May lead to death

**Cerebrospinal fluid analysis**

#roypath histopathology-india.net

The infographic includes several illustrations: a doctor examining a patient in a hospital bed, a person in a wheelchair, a brain with red worms representing the parasite, a microscope, a syringe, and a person at a desk. It also features a red ribbon symbol and a tombstone icon.



# 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 Or 28 days
2. Erythromycin:- for 14 Or 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 effective
- Most cases require repeated courses.



# Human Immunodeficiency Disease

- **Etiology:-**

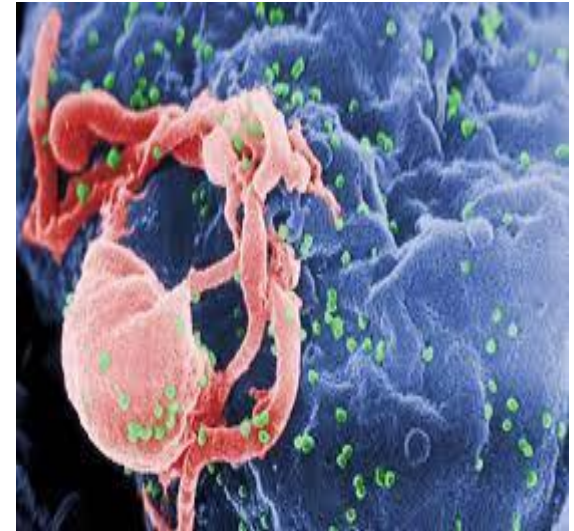
Causative agent:- Caused by infection with HIV-1 or HIV-2, which is a single-stranded RNA virus.

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

- **Mode of transmission:-**

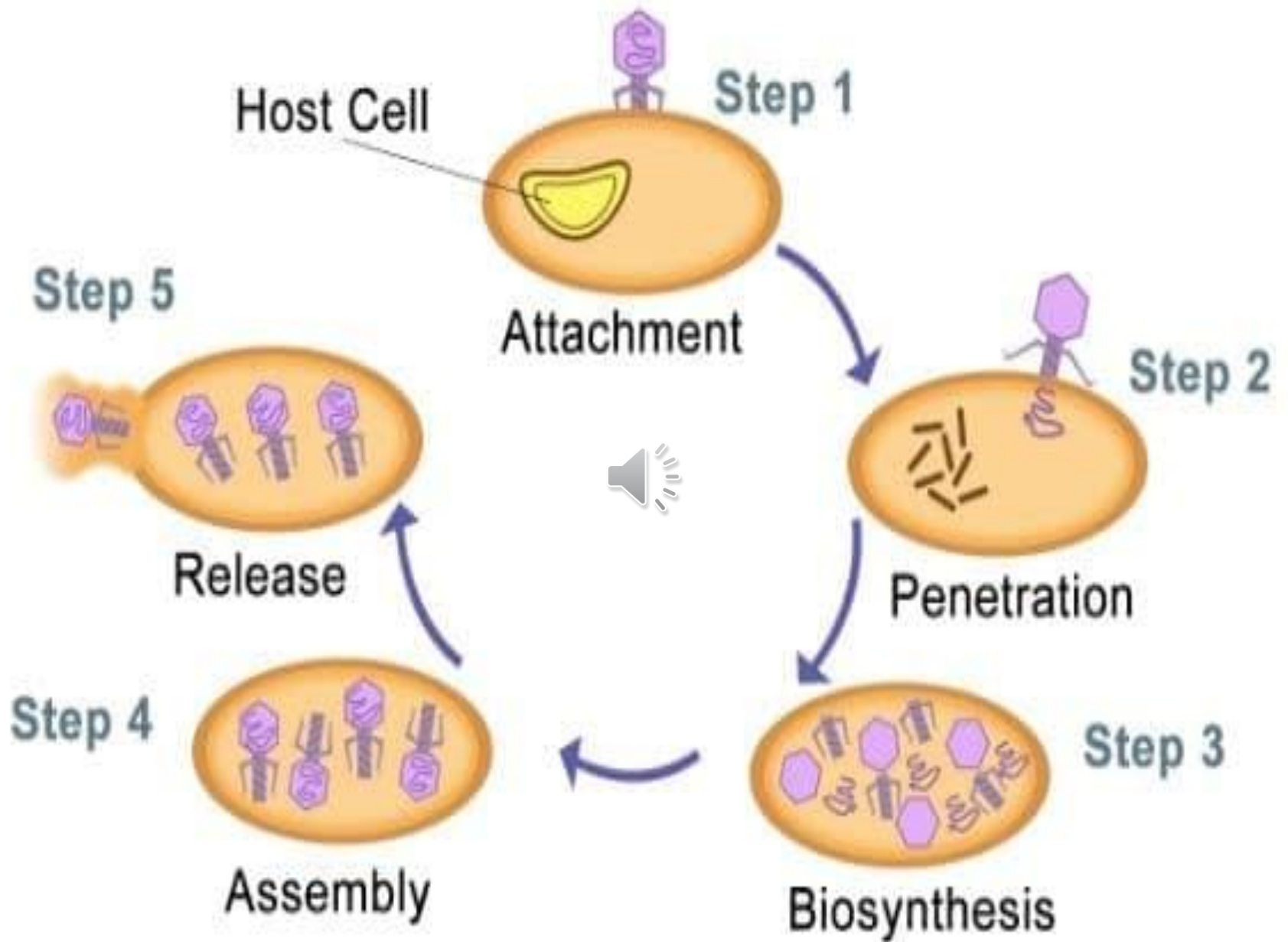


- HIV is blood-borne virus transmitted via:-
  - 1. Sexual intercourse including anal intercourse.
  - 2. Use of contaminated injecting equipment.
  - 3. Mother-to-child transmission, during birth process or during breastfeeding



# 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<sup>3</sup>), or high viral load.
- Regimen consists of 3 drugs (to prevent resistance):
- 2 NRTIs & 1 of the following (NNRTIs, protease inhibitors, or integrase inhibitors)



- **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, Etravirin.*

- ***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).

- ***Toxicity:***

- Rash & hepatotoxicity (common with all members).
- Efavirenz causes vivid dreams and is contraindicated with pregnancy.




## *Integrase inhibitors.*

### ► Raltegravir and Elvitegravir

- Inhibit **integration** of viral genome in host cell DNA.

## *Protease inhibitors (PIs)*

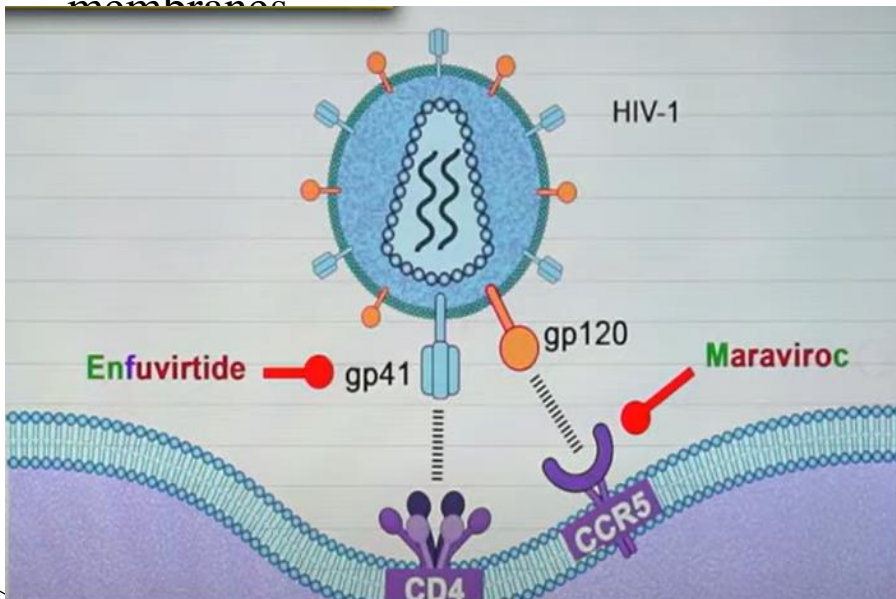
- *atazanavir, lopinavir, ritonavir* 
- **Mechanism**
- HIV-1 protease cleaves the polypeptide products of the viral mRNA into functional parts → assembly & maturation of new viruses.
- PIs act by inhibiting this enzyme.

## Fusion inhibitors:

### Enfuvirtide

#### ⊗ Mechanism of action:

- It binds to the gp41 subunit of the viral envelope glycoprotein, preventing the fusion of the viral and cellular membranes



### Maraviroc

#### ⊗ Mechanism of action:

- binds specifically and selectively to the membrane host protein **CCR5**, one of two chemokine receptors necessary for entry of HIV into CD4+ cells
- So, it inhibits binding and entry of the virus into immune cells

# 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:-

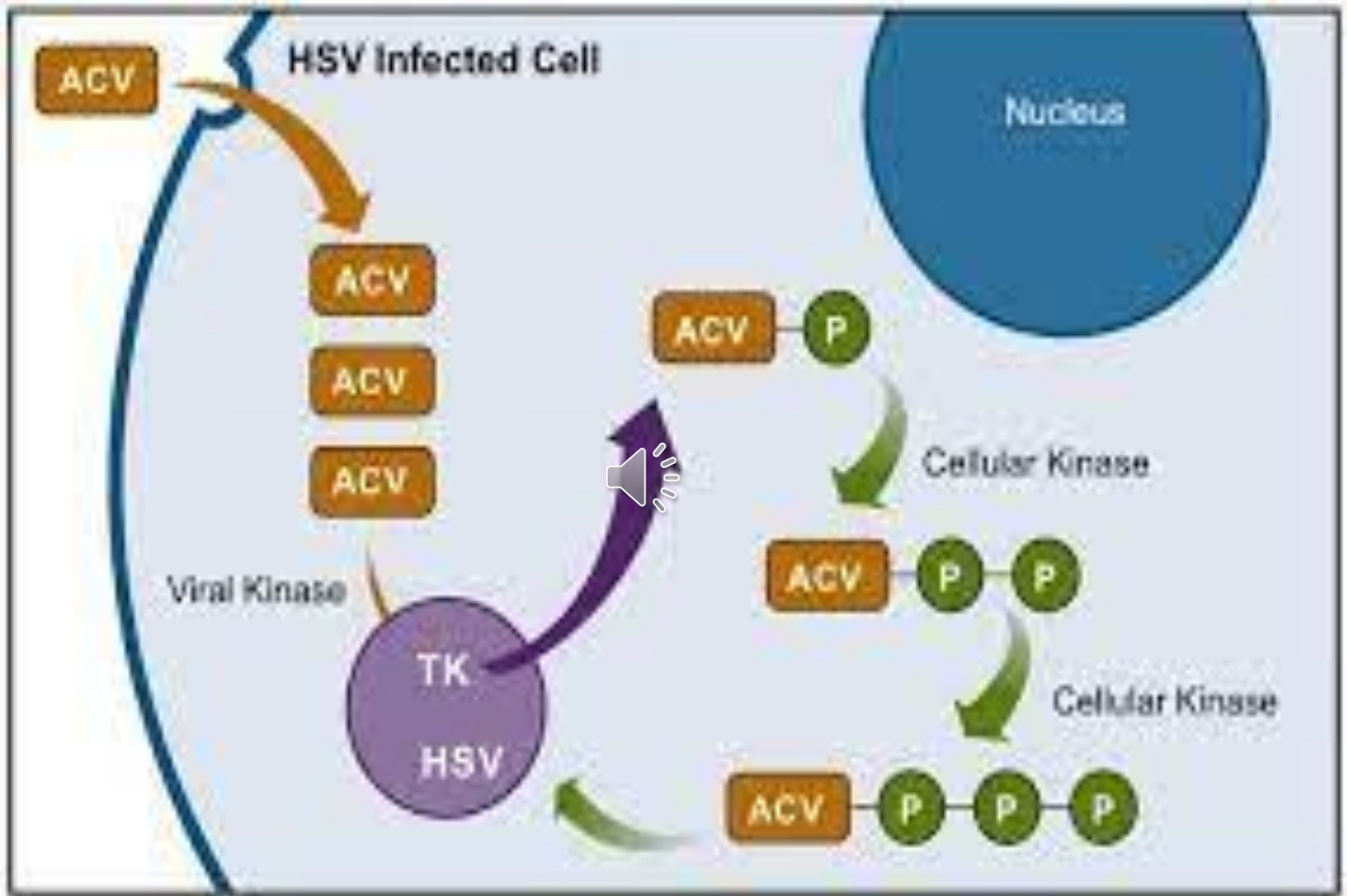
### 1-Acyclovir- famciclovir- valacyclovir

#### Mechanism of action:-

- -Activation:Guanosine analogs.
- Mono-phosphorylated by HSV/VZV thymidine kinase (TK) (not phosphorylated in uninfected cells → few adverse effects).
- They are further activated by host-cell kinases to the triphosphates

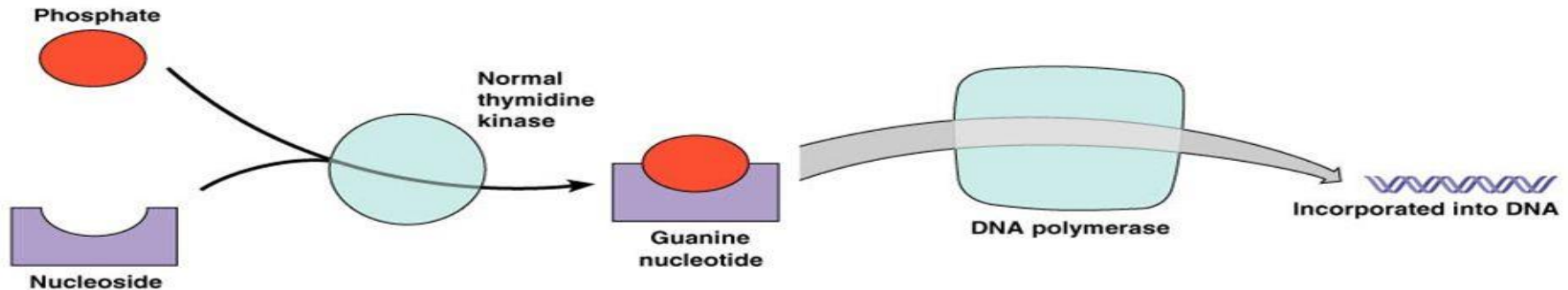
#### 2- Valaciclovir

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

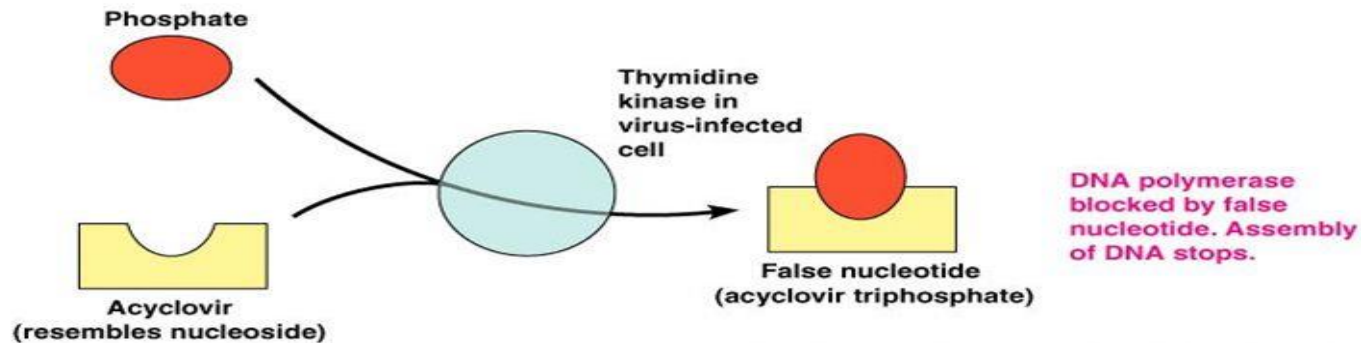


- Triphosphates are substrates for viral DNA polymerase → incorporated into the DNA molecule → chain terminations

## Mechanism of Action of Acyclovir




**(b)** The enzyme thymidine kinase combines phosphates with nucleosides to form nucleotides, which are then incorporated into DNA.



**(c)** Acyclovir has no effect on a cell not infected by a virus, that is, with normal thymidine kinase. In a virally infected cell, the thymidine kinase is altered and converts the acyclovir (which resembles the nucleoside deoxyguanosine) into a false nucleotide—which blocks DNA synthesis by DNA polymerase.

# 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





# Interferon 2b & 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.

