

Unit - II

Chemotherapy



Chemical Treatments

Chemotherapy is a type of treatment which are used in the treatment of Cancer and infectious disease which is caused due to any types of microorganism.

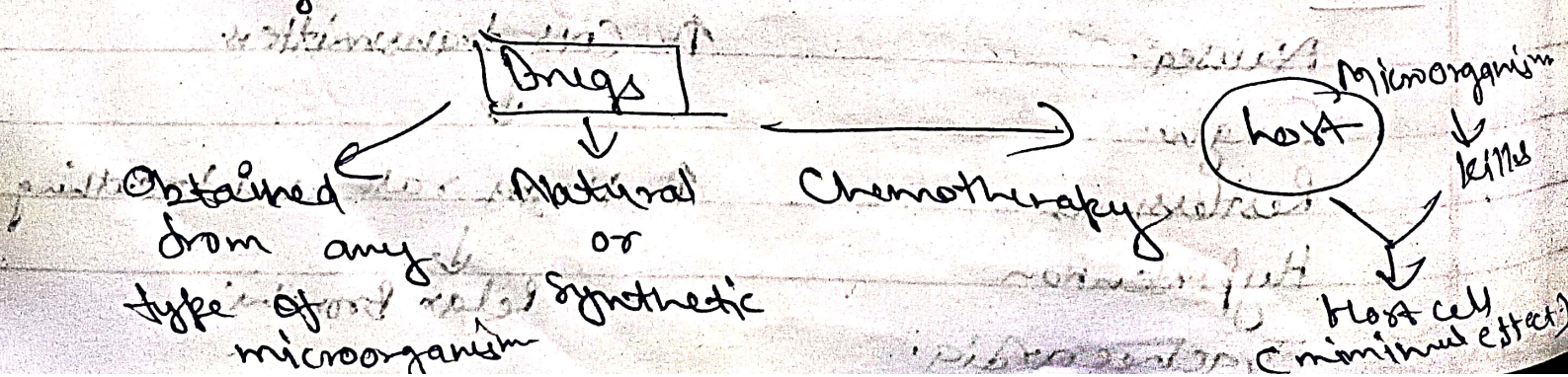
Chemotherapy → Anticancer drug

↓
Anti microbial drugs.

These are those drug which kills or inhibits the growth of microorganism. (Also they obtained from any types of micro organisms).

Principles -

Treatment of infectious disease by destroying microorganism with minimum effect / damage to host cell / Patients.



History -

The term Chemotherapy was first called by Paul Ehrlich.

→ He is known as the father of Chemotherapy.

→ He developed Arsenicals for sleeping sickness
nearsphenamine in 1906 for syphilis.

Classification of Antimicrobial drugs/Chemotherapeutic agents -



Sulfonamides
and related
drugs

Antibiotics

According to chemical structure -

[Sulfonamides] → eg - Sulfadiazine.

Quinolones → eg - Norfloxacin, Ciprofloxacin

B lactam antibiotics → eg - Penicillin, Cephalosporin

Tetracyclines → Oxytetracyclines, Doxycycline

Aminoglycosides → streptomycin, Neomycin

Macrolides → Erythromycin, Azithromycin

Type of organisms against which primarily active -

Antibacterial → Penicillin, Aminoglycosides

Antifungal → Griseofulvin, Amphotericin B

Antiviral → Acyclovir, Zidovudine

Antiprotozoal → Chloroquine, Metronidazole

Anthelmintic → Mebendazole, Diethyl carbamazine

Spectrum of activity -

Narrow spectrum → Penicillin, Streptomycin

Erythromycin

Broad spectrum → Tetracyclines, Chloramphenicol

Type of Action -

Bacteriostatic → Sulfonamides, Tetracyclines,
Chloramphenicol, Erythromycin,
Clindamycin

Bactericidal → Penicillins, Aminoglycosides,
Polypeptides, Rifampin, Isoniazid,
Cephalosporins, Fluoroquinolones, Metronidazole,
Cotrimoxazole.

write quote

Sulfonamides and cotrimoxazole

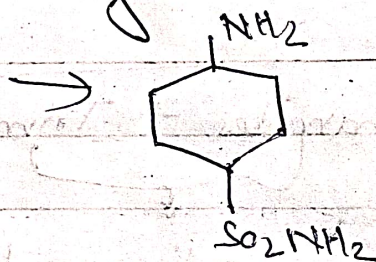
Sulfonamide

It is a first antimicrobial agents which is effective against pyogenic bacterial infections.

In 1935, Gerhard ~~Domagk~~ Domagk discovered the first sulfonamide - Prontosil

used to treat Experimental spec Streptococcal infections.

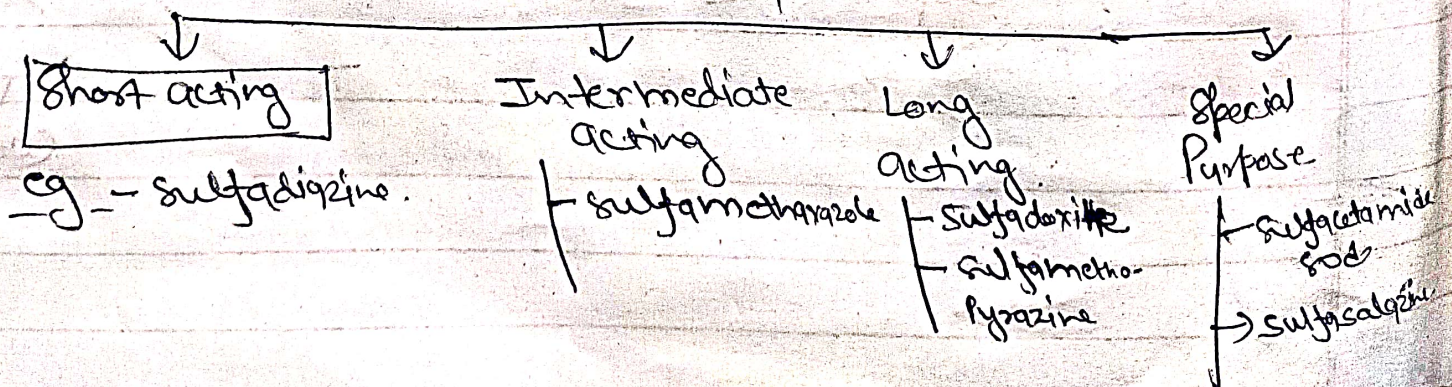
→ Sulfonamides may be considered as derivatives of sulfonamide.



Sulphonamides are primarily bacteriostatic against many gram positive and gram negative bacteria.

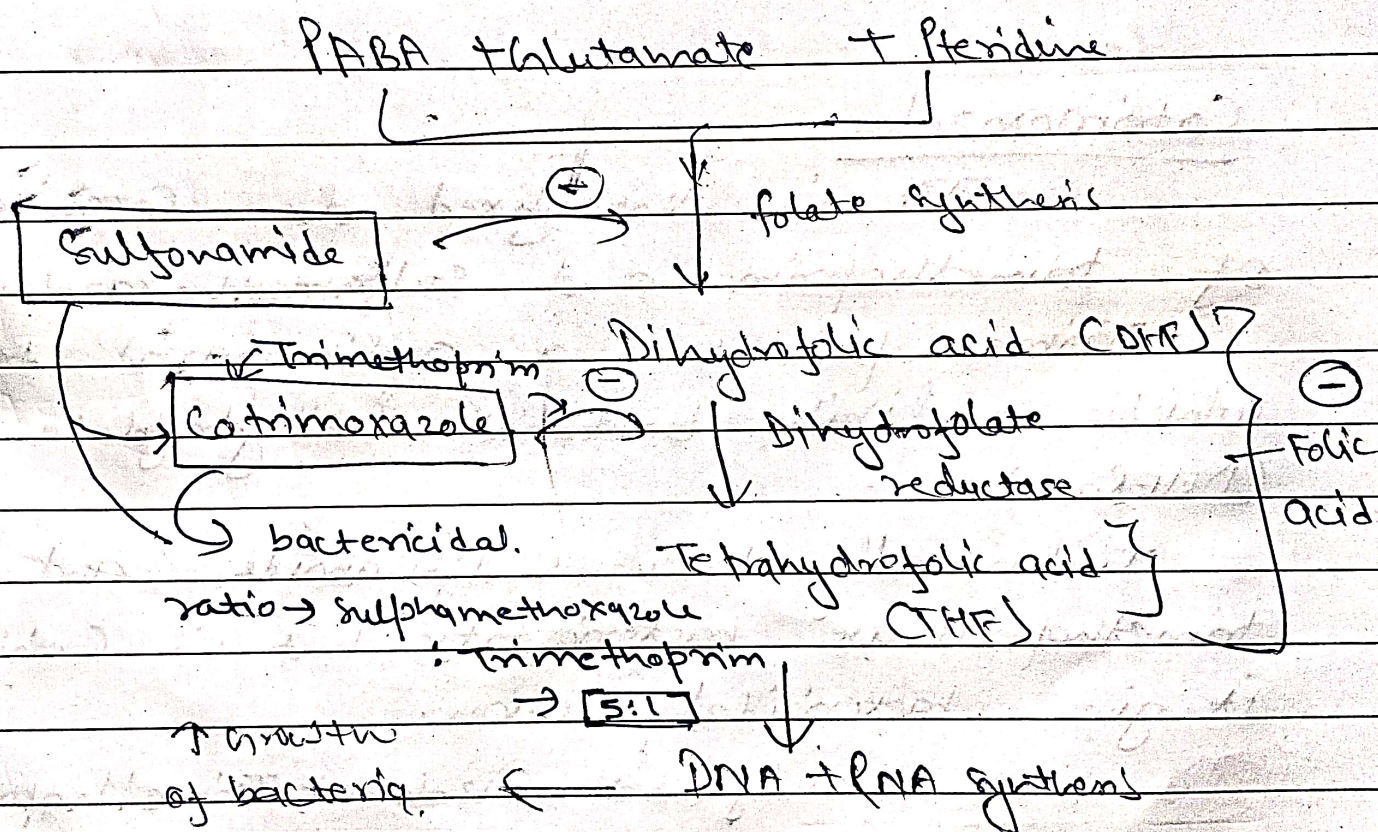
Classification

Sulphonamides



MOA →

They are basically bacteriostatic in nature which gives their action by inhibiting folic acid synthesis which are responsible for the synthesis of DNA & RNA and helps in the growth of bacteria.



Pharmacokinetics →

- Rapidly and slowly nearly completely absorbed from GIT.
- Distribution (widely - also in CHF & placenta)
- Metabolism in liver by non-microbial enzymes
- Excretion by kidney $t_{1/2} \rightarrow 10\text{hrs}$

Adverse Reaction →

- Nausea, vomiting and epigastric pain
- Hypersensitivity reaction occurs in 2-5% Patients
- Rashes.

Uses → Meningitis
UTI.
Malaria, (Burns - ocular infection)

Cotrimoxazole -

It is the fixed dose combination of trimethoprim and sulfamethoxazole. Trimethoprim is an antimalarial drug which inhibits bacterial dihydroplate reductase (DHFRase).

Individually both sulfonamide and trimethoprim are bacteriostatic but in combination it gives bactericidal action.

(Sulfamethoxazole + Trimethoprim)

P^r kinetics -

- It is more rapidly absorbed than Sulfamethoxazole.
- Trimethoprim (40%) & Sulfamethoxazole (65%) Plasma protein bound.

- Partly metabolized in liver.
- Excreted in urine $t_{1/2} \rightarrow 10$ hrs.

Adverse Effects

- Nausea, Vomiting, Stomatitis, headache & rashes.
- Folate deficiency (Megaloblastic anemia).
- * Should not be given during pregnancy.

Uses → Bacterial diarrhoea — Typhoid — GIT
→ UTIs (Urinary tract infections) —
Respiratory tract infections.

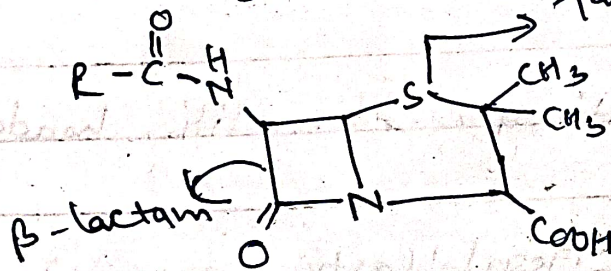
Antibiotics →

These are those chemotherapeutic agents which are used to kill or inhibit the growth of bacteria and they also obtained from any type of microorganism.

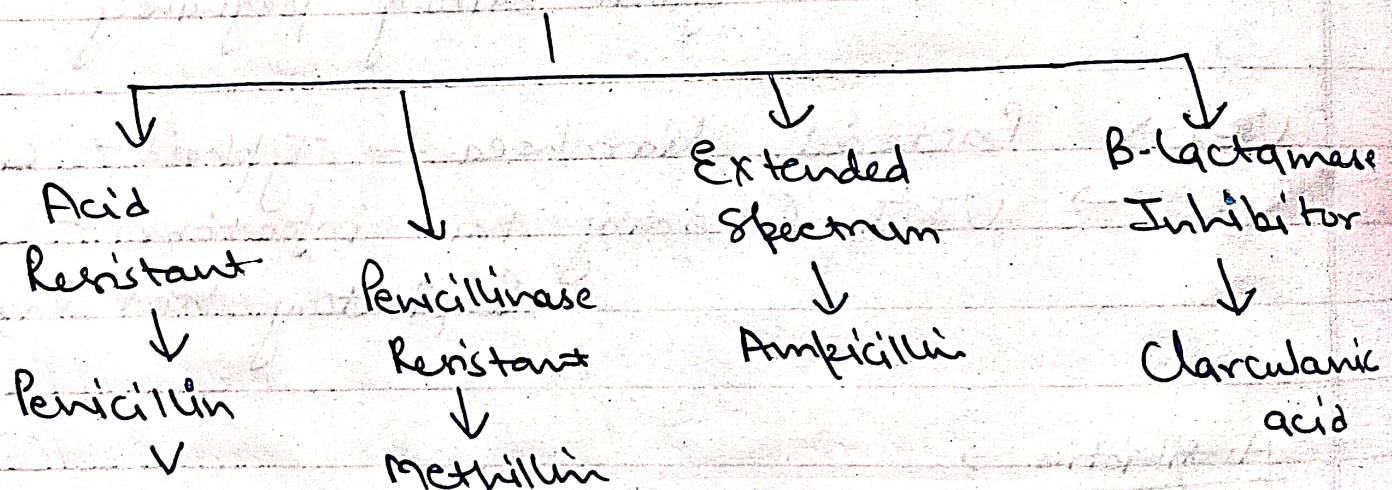
Penicillins

First antibiotic discovered by Alexander Fleming
obtained from fungus *penicillium notatum*.

Have two fused Rings



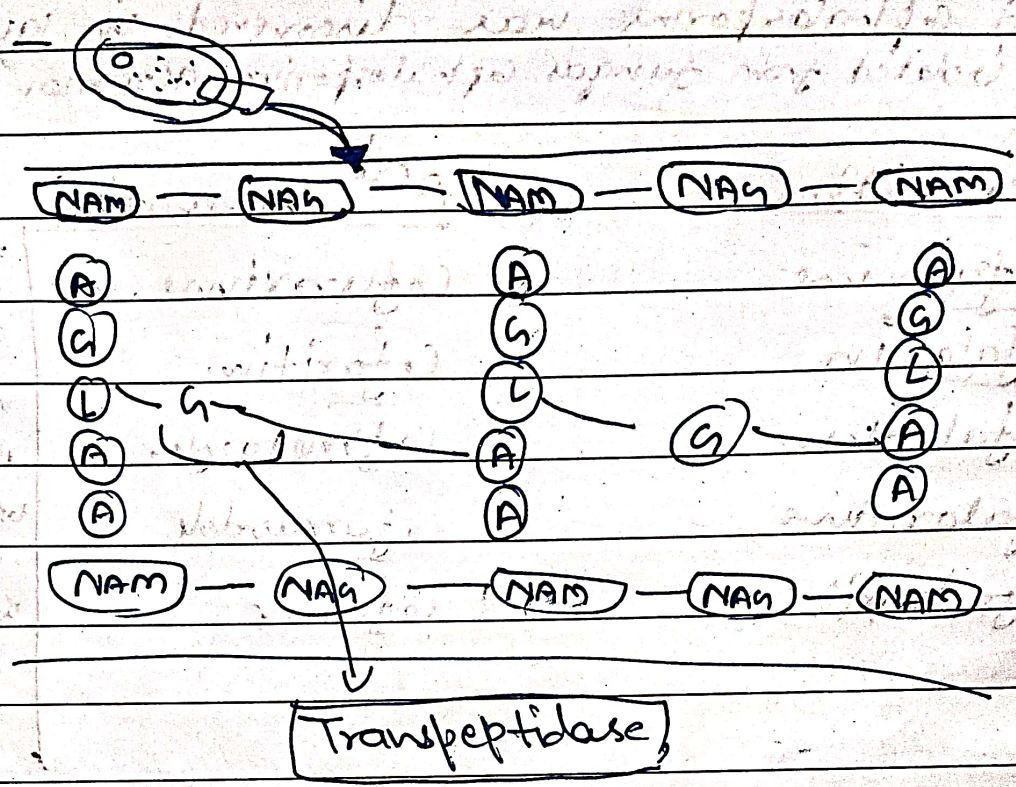
Classification of Semisynthetic Penicillins



Indication

- Streptococcal Infection.
- Meningococcal Infection
- Syphilis
- Tetanus
- Pneumococcal Infection.
- Gonorrhoea.
- Diphtheria.
- Pseudophyllactic uses

MOA →



↑ ⊖

Penicillins

~~They inhibit the~~

• Gram $\oplus$ ~~bacteria~~ cell

They inhibit the cell wall synthesis of Gram $\oplus$ bacteria by targeting Transpeptidase enzyme, which can not be cross by peptidoglycans.

ADR →

- Local irritancy
- Hypersensitivity
- Superinfection.

→ It is an antibiotic drug.

Cephalosporin → It is a bactericidal drug.

→ The first cephalosporin was discovered in 1948 & named cephalosporin C.

→ It was isolated from fungus *Cephalosporium acremonium* by Prof. Z. Newton & Abraham (1954).

1st Generation

Cefazolin

Cefalexin

Cefalothin

Cefalonidine

Cefadroxil

2nd Generation

Cefuroxime

Cefoxitin

Cefmetazole

Cefamandole

Cefaclor

→ The molecular modification in cephalosporin C.
→ They are also β lactam antibiotics with the same structural differences with penicillins.

3rd Generation

Cefoperazone

Ceftriaxone

Cefotaxime

Ceftizoxime

Cefepodoxime

Ceftazidime

Ceftibuten

Cefexime

Moxalactam

4th Generation

Cefepime

Cefpiroxime

5th Generation

~~Cef~~ Ceftibiprole

Ceftaroline

A

Bind with the Enzyme present in bacteria and inhibit the ^{growth} synthesis of cell wall and ~~inhibit~~ kill the bacteria.

Classification

① First generation cephalosporins

→ Broad spectrum introduced b/w 1960-1970

→ Low ability to penetrate cerebrospinal fluid.

→ Some compounds ~~are~~ are orally & others are given parentally.

② 2nd generation

→ Introduced late 1970 to present

→ It is more active against gram - ve bacteria

& resistant to extracellular β lactamases.

→ Generally used parentally & More penetration power in to cerebrospinal fluid.

③ 3rd generation

→ Broad spectrum active against gram - ve

& stable against β lactamases.

→ Poor ability to penetrate cerebrospinal fluid.

④ 4th generation -

similar to 3rd generation but are

zwitter ionic

Active against Gram -ve & against *B. Paenugense*.

⑤ Miscellaneous 5th generation

MOA →

It also have a me. MOA is similar to penicillins

They mainly inhibit the cross linking of the peptidoglycan units in bacterial cell walls by inhibiting transpeptidase enzyme.

However they bind in the target proteins other than penicillins binding proteins.

β lactam Antibiotics

↓
Binds with Penicillin binding proteins (PBP) on the cell wall of susceptible bacteria & inactivates them / Target proteins (cephalosporins)

↓
Inhibit Transpeptidase enzyme

↓
Inhibit cross linking of peptidoglycans

↓
Cell wall deficient forms

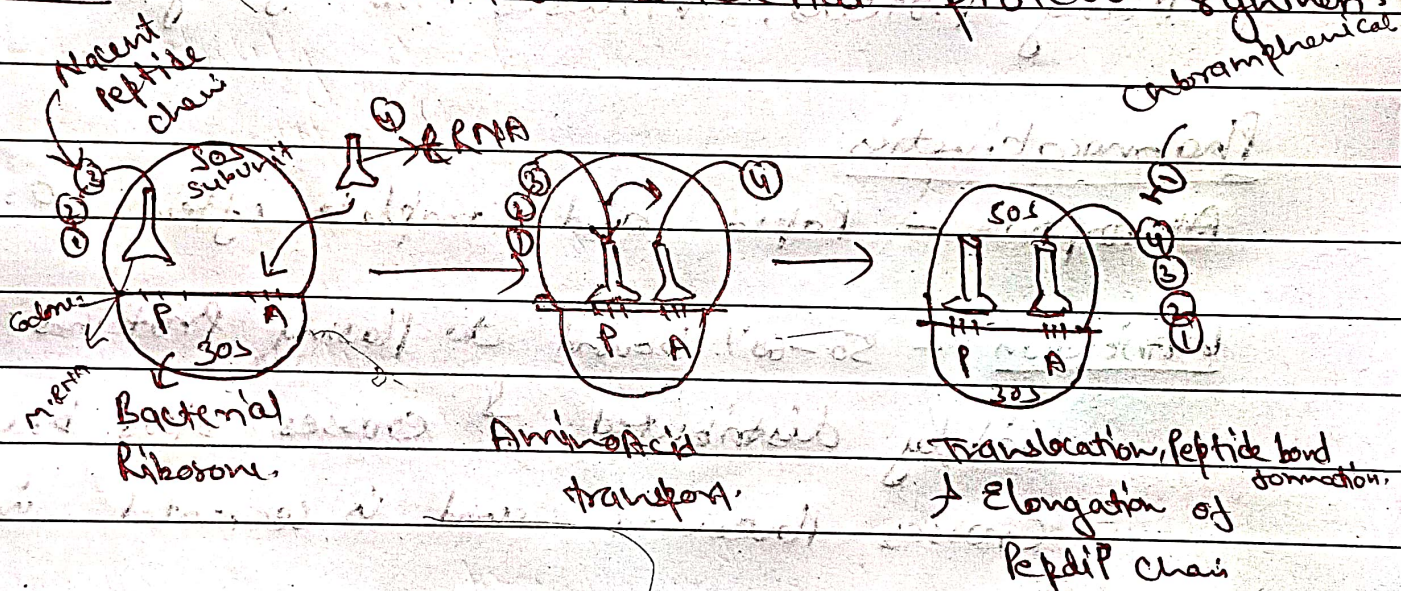
↓
Undergo Autolysis

↓
Cell death

Chloramphenicol

Chloramphenicol is a broad spectrum Antibiotic with highly restricted clinical use. Initially obtained from bacterium *Streptomyces venezuelae*. Now it's synthesized chemically.

MOA - Inhibits bacterial protein synthesis.



- Chloramphenicol reversibly binds to bacterial 50S ribosomal subunit.
- It inhibits peptidyl transferase enzyme required for transpeptidation.
- This inhibits elongation of peptide chain inhibiting protein synthesis.
- Inhibits bacterial growth $\rightarrow$ Bacteriostatic.
- In high doses it can produce Bactericidal effect.

Antimicrobial Spectrum

- a) Primarily bacteriostatic, high concentrations exert bactericidal effect on some bacteria.
- b) It is a broad spectrum antibiotic, active against Gram positive and negative cocci and bacilli, rickettsiae, mycoplasma. High incidence of resistance has developed among many bacteria.
- c) It is ineffective against mycobacteria, Pseudomonas, many protozoa, viruses and fungi.

Pharmacokinetics

Absorption - Rapid and complete after oral administration.

Distribution - 50-60% bound to plasma proteins.

Widely distributed & crosses blood brain barrier.

Crosses placenta and is secreted in milk.

Metabolism -

Conjugated with glucuronic acid & excreted in urine.

Plasma $t_{1/2}$ is 3-5 hours in Adults.

Also administered topically as ear drop or eye drop ointment & parentally.

Indications

Used is limited to severe infections not treated by other safer antimicrobials.

- ① Topically: Superficial Eye infection.
- ② Intraocular Infections.
- ③ Pyogenic/Bacterial meningitis.
- ④ Anaerobic Infections.
- ⑤ Enteric fever / Typhoid.
- ⑥ Brucellosis and Rickettsial Infections.
- ⑦ Whooping cough.

ADR -

- ① Bone marrow Depression.
- ② Optic Neuritis.
- ③ Imitative Effects.
- ④ Super infection.
- ⑤ Hypersensitivity.