

# Chapter 1: Antibiotics

## 1.1. INTRODUCTION & HISTORICAL DEVELOPMENTS

- 📖 **PC** Chemotherapy is the therapy or treatments of systemic and infective disease by using suitable chemical agents.
- 📖 **PC** These chemicals capable to suppress the growth of microorganism and/or cancer cells without affecting the host cells.
- 📖 **PC** The term **chemotherapy** was coined by **Ehrlich** at the beginning of the 20<sup>th</sup> century to explain the use of synthetic chemicals to destroy infective agents.
- 📖 **PC** These drugs in this class are differing from other drugs including antihypertensive, antianginals, antiulcer etc. The chemotherapeutic drugs are **designed to act on pathogenic microorganism**, due to **analogy between cancerous or malignant cell** with pathogenic microbes therefore the treatment of neoplastic diseases with the drugs is also include in chemotherapy

### Definitions

- 📖 **PC** **Chemotherapy:** is the use of synthetic or natural agents to destroy or inhibit the growth of infective agents (e.g. bacteria, fungi, virus, helminthes and protozoa) and cancerous cells.
- 📖 **PC** **Chemotherapeutic agents:** are chemicals which are designed to inhibit the growth or destroy the infective agents without significantly affecting the host.
- 📖 **PC** **Antibiotics:** are substance produced by microorganism that in suppress the growth or destroy the other microorganism at low concentration.
- 📖 **PC** **Antimicrobial agents (AMA):** are the synthetic or natural substances that are used to treatment of various infections e.g. bacterial, fungal and viral.

### History

#### Phase 1: Emperical phase

- Chaulmoongra oil is used by Hindus in leprosy
- Chenopodium by Aztecs for intestinal worms
- Cinchona bark for fever

## Phase II: Ehrlich phase (1890-1935)- Dyes and Organometalic compounds

- Arsenicals—atoxyl for sleeping sickness
- Arsphenamine (1906) and Neoarsphenamine (1909)—for syphilis
- Ehrlich coined the term “Chemotherapy”

## Phase III: Modern era

- Domagk (1935) – Prontosil (a sulphonamide dye)—for pyogenic infection. And he noticed that p-amino benzene sulphonamide is an active metabolite. Sulfapyridine (M &B 693) is first sulphonamide marketed in 1938.
- Antibiotic phenomenon – by Pasteur (1877) – anthrax bacilli in urine was inhibited by air burn bacteria.
- In 1940s- Waksman and his students research the Actinomycetes as the source of Antibiotics and discovered Streptomycin in 1944.
- Domagk, Fleming , and Waksman--- got NOBEL PRIZE for their discoveries.

\* **commensals**: Many microorganism are not pathogenic in normal condition they share our body spaces (e.g. the gut) these are called **commensals**, even if host is immune compromised they become pathogenic

\*\***Prions**: This is a proteinaceous agent which causes diseases but resist to all attempt to chemotherapeutic agents.

## 1.2. CLASSIFICATION OF ANTIMICROBIAL AGENTS

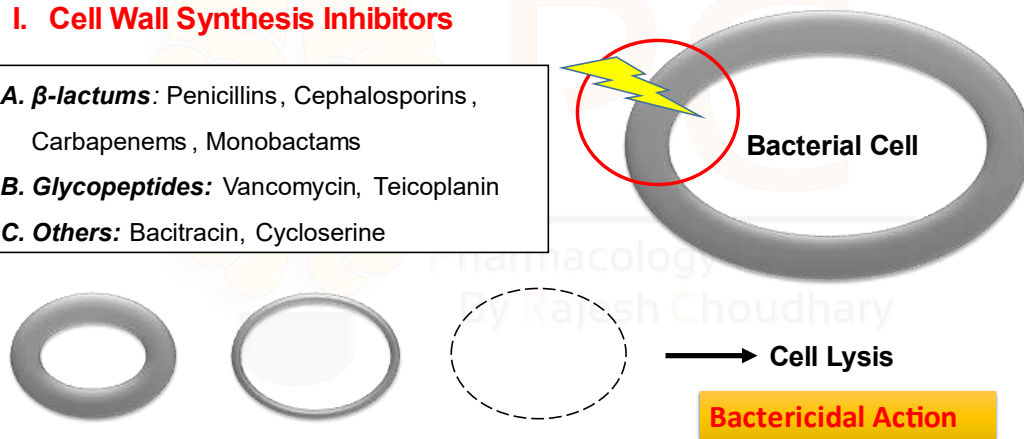
### BASED ON MECHANISM OF ACTION

#### (1) Inhibition of cell wall synthesis

- (a)  **$\beta$ -lactams**: Penicillins, Cephalosporins, Carbapenems, Monobactams
- (b) **Glycopeptides**: Vancomycin, Teicoplanin
- (c) **Others**: Bacitracin, Cycloserine

## I. Cell Wall Synthesis Inhibitors

- A.  $\beta$ -lactams:** Penicillins, Cephalosporins, Carbapenems, Monobactams  
**B. Glycopeptides:** Vancomycin, Teicoplanin  
**C. Others:** Bacitracin, Cycloserine



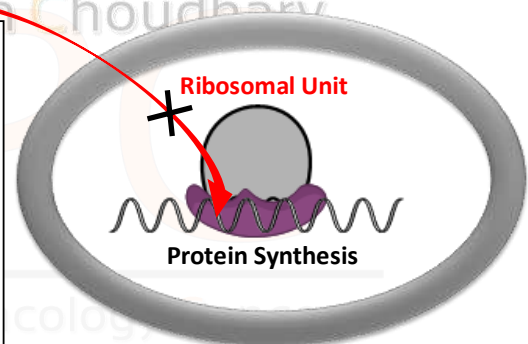
### (2) Cell membrane function inhibitors

- (a) **Polypeptides:** Polymyxins, Bacitracin, Colistin  
(b) **Polyenes:** Amphoterecin B, Hamycin, Nystatin

### (3) Inhibition of protein synthesis

- (a) **Aminoglycoside:** Streptomycin, Kanamycin, Amikacin, Neomycin, Gentamicin  
(b) **Tetracyclines:** Tetracycline, Oxytetracycline, Demeclocycline, Doxycycline  
(c) **Macrolides:** Erythromycin, Roxithromycin, Clarithromycin, Azithromycin  
(d) **Lincosamides:** Lincomycin, Clindamycin  
(e) **Oxazolidione:** Linezolid  
(f) **Others:** Chloramphenicol

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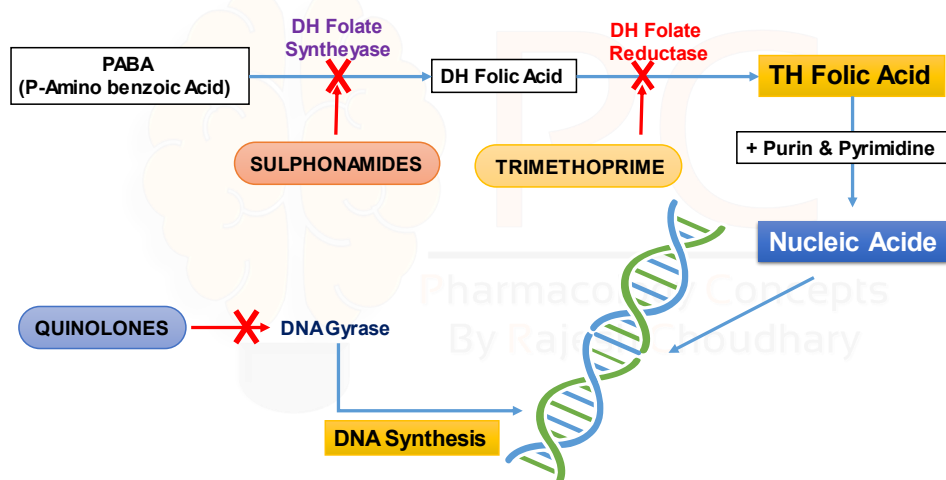
**Bacteriostatic Action**

**\*Except Aminoglycosides**

### (4) Inhibition of nucleic acid synthesis

- (a) **Sulphonamides:** Sulfadiazine, Sulfamethoxazole, Sulfadoxine,

- (b) **Quinolones:** Nalidixic acid, Ciprofloxacin, Ofloxacin, Lomefloxacin, Gatifloxacin
- (c) **Others:** Metronidazole, Rifampicin, Idoxorudine, Acyclovir, Zydovudine, Bleomycine



### BASED ON SUSEPTIBLE MICROORGANISM

- (1) **Antibacterial:**  $\beta$ -lactum antibiotics, Aminoglycosides, Tetracyclines, Sulfonamides etc.
- (2) **Antifungal:** Amphotericin B, Ketoconazole, Clotrimazole, Griseofulvin, Terbinafine
- (3) **Antivirals:** Acyclovir, Idoxuridine, Amantadine, Zidovudine, Nevirapine, Indinavir
- (4) **Antiprotozoal:** Metronidazole, Chloroquine, Pyrimethamine, Diloxanide, Pentamidine
- (5) **Antitubercular:** Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, Streptomycin
- (6) **Antileprotic:** Depsone, Rifampicin, Ethionamide, Minocycline
- (7) **Anthelmintic:** Mebendazole, Albendazole, Pyrantel, Levamisole, Praziquantel

### BASED ON SPECTRUM

- (1) **Narrow spectrum:** Penicillin G, Streptomycin, Erythromycin
- (2) **Broad spectrum:** Tetracyclines, Chloramphenicol, Ampicillin, Amoxicillin

### BASED ON ACTION


- (1) **Bacterostatics:** Sulfonamides, Tetracyclines, Erythromycin, Chloramphenicol
- (2) **Bacterocidal:** Aminoglycosides, Penicillins, Co-trimazole, Cephalosporins


## Pharmacology Lectures:


1. Introduction & History: <https://youtu.be/83CLHo-sz9E>
2. Molecular Basis of Chemotherapy: <https://youtu.be/5CDOMqSCGew>
3. Classifications: <https://youtu.be/DcVF8Ru1rcY>
4. MOA (most important): <https://youtu.be/QDvIEzR8HmQ>
5. Problems during Chemotherapy: [https://youtu.be/\\_dKREiyvl\\_I](https://youtu.be/_dKREiyvl_I)
6. Drug Resistance: <https://youtu.be/xILsEqYCeVw>
7. General Choice & Selection of AMA: <https://youtu.be/pMmwrSKepU0>

### 1.3. ANTIBIOTICS


 The term antibiotic has its origin in the word anti-biosis that means against life.


 **Antibiotics** are substance produced by microorganism (bacteria, fungi, actinomycetes) that in suppress the growth or destroy the other microorganism at low concentration.

 The term “Antibiotic” was introduced by Waksman in 1942 (during the discovery of Streptomycin)

 Antibiotics differ in their antimicrobial profile. According to their spectra these are termed as:

- **1. Narrow Spectrum Antibiotics:** These antibiotics are effective against a single or a limited group of microorganisms. e.g. streptomycin, Penicillin G, Erythromcin.
- **2. Extended Spectrum Antibiotics:** Extended spectrum antibiotics are effective against gram positive and also against gram negative organisms. e.g. Ampicillin, Amoxycillin
- **3. Broad Spectrum Antibiotic:** These antibiotics are effective against gram positive organism, gram negative organism, rickettsia’s and protozoa. e.g. Tetracycline and Chloramphenicol.

 Majority of antibiotics are obtained from fungi but some are obtained from bacteria (e.g. bacitracin, colistin and polymyxin B).

 Based on their chemical structure it can be classified as

1.  $\beta$ -lactam antibiotics
2. Aminoglycoside antibiotics
3. Tetracycline antibiotics
4. Polypeptide antibiotics
5. Macrolide antibiotics
6. Lincomycins