Introduction to Antibiotics

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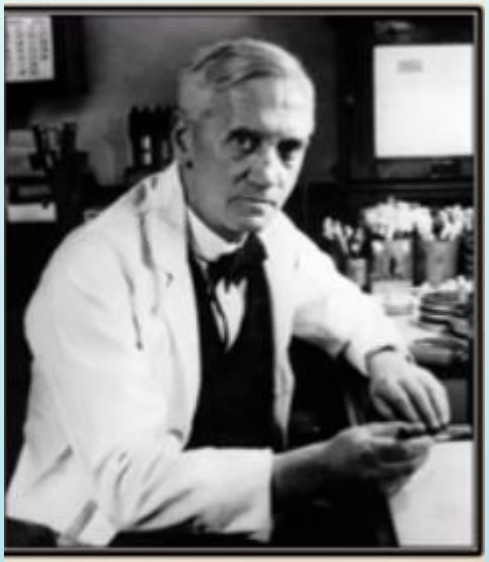
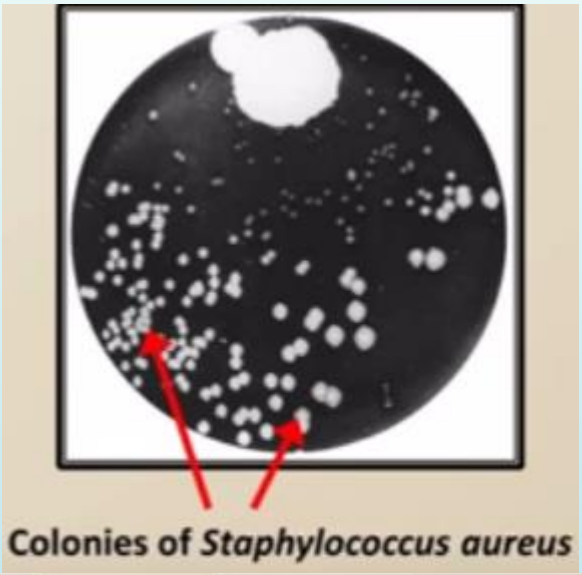
Objectives of the Lecture

- Classification of antibiotics
- Misuses of antibiotics
- Choice of antibiotics
- Bacterial resistance and ways to prevent it
- General principles of antibiotic therapy
- Indications for antibiotics prophylaxis.

What is Antibiotic?



Alexander Fleming
(1881-1955)



Colonies of *Staphylococcus aureus*

Howard Florey
(1898-1968)

Ernst Boris Chain
(1906-1979)

Nobel prize in 1945

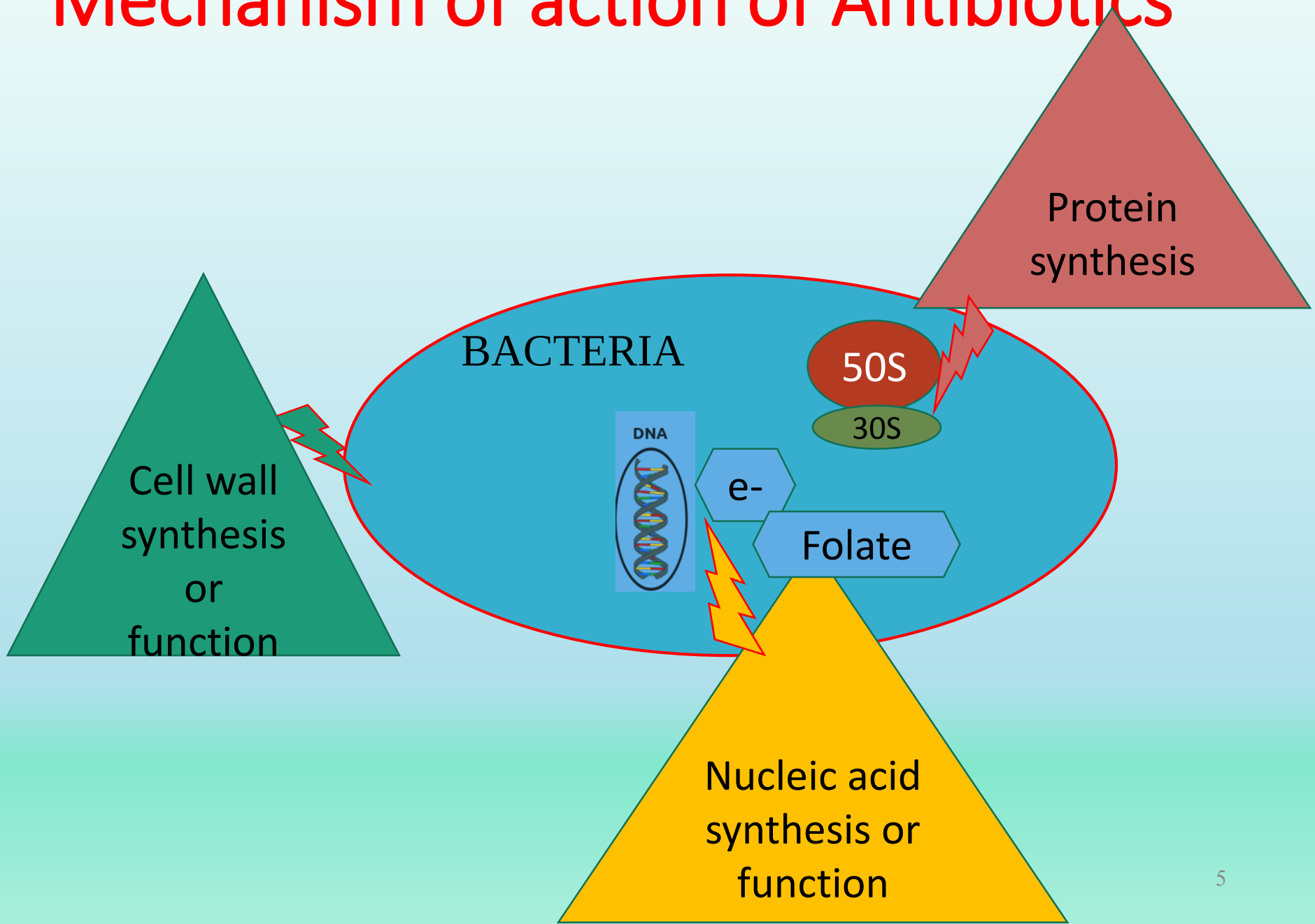
Definition of Antibiotics

Chemical substances produced by various **microorganisms** (bacteria, fungi, actinomycetes) that have the capacity to inhibit the growth or destroy **other microorganisms**.

Nowadays they are chemically synthesized.
They either kill bacteria (bactericidal) or hold bacteria from growing (bacteriostatic)

Antibiotics will not cure infections caused by viruses.

Mechanism of action of Antibiotics



CLASSIFICATION OF ANTIBIOTICS
ACCORDING TO MECHANISM OF ACTION

- **INHIBITION OF bacterial CELL WALL SYNTHESIS e.g. Penicillins, Cephalosporins**

- **INHIBITION OF bacterial PROTEIN SYNTHESIS e.g. Macrolides, Tetracyclines, aminoglycosides**

INHIBITION OF FOLATE METABOLISM e.g. Sulfonamides, Trimethoprim

- **INHIBITION OF bacterial DNA SYNTHESIS e.g. Quinolones**

- **INHIBITION OF RNA synthesis by binding to RNA polymerase e.g. Rifampicin.**

According to spectrum

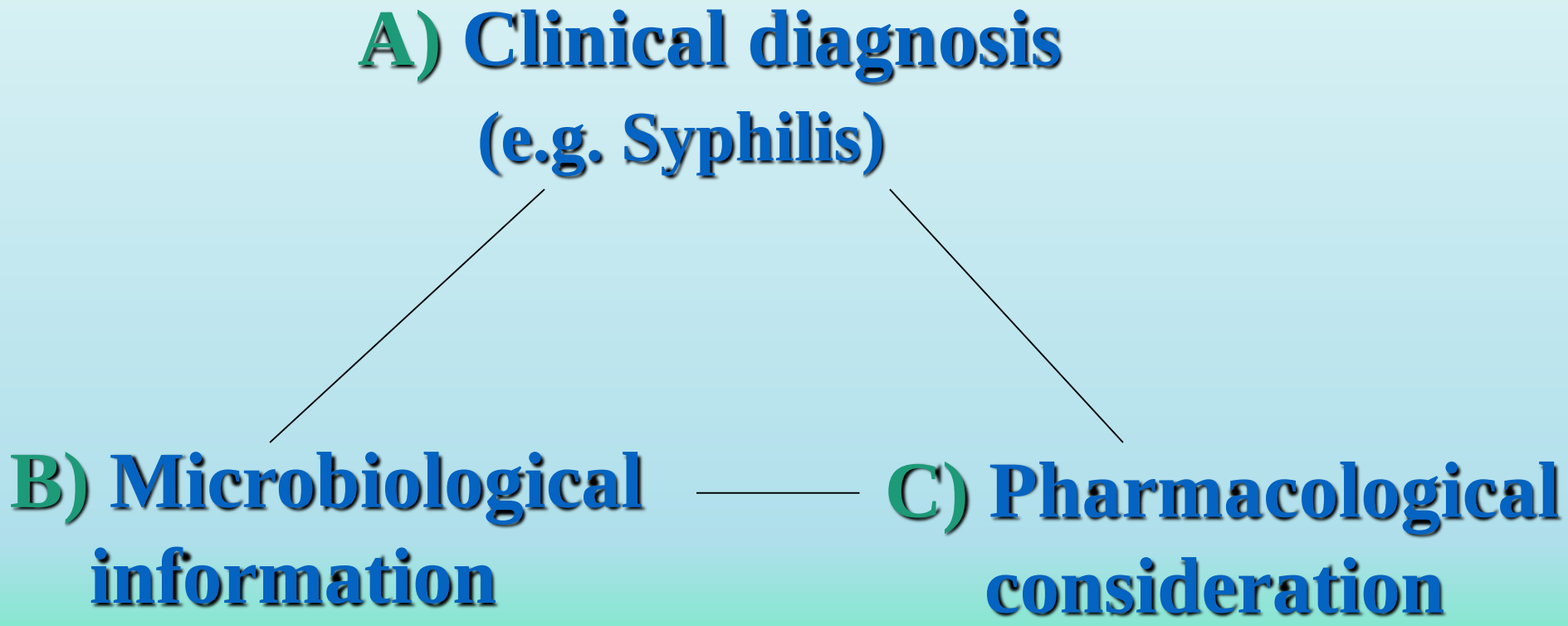
- **Narrow spectrum , e.g.:**

  penicillin G, aminoglycosides

- **Broad spectrum , e.g.:**

  ampicillin, amoxicillin

Choice of Antibiotic



B) Bacteriological informations

Advantages

- **The exact antibiotic to be used**
- **The most effective and reject the one with little or no activity**
- **The least toxic**
- **The cheapest.**

B) Bacteriological informations (Cont')

Disadvantages

- The bacteria isolated may not be the prime cause of the disease
- do not take in consideration site of infection
- some bacteria cannot be cultivated or take time to grow (e.g. M. Leprae, M. Tuberculosis)
- Bacteriological services are not available at all hospitals.

Choice of Antibiotics (cont')

C) Pharmacological consideration

1. Site of infection

2. Host factors

a) Immune system e.g. Alcoholism, diabetes, HIV, malnutrition, anticancer drugs, advanced age- (higher than usual doses or longer courses are required)

b) Genetic factors

e.g. Patients with G-6-PD deficiency treated with sulfonamides (Hemolysis).

Choice of Antibiotics (Cont')

c) Pregnancy and Lactation

Aminoglycosides **(hearing loss)**

Tetracyclines **(bone deformity)**

d) Extreme Age

Neonates and elderly

e) Renal function

e.g. Aminoglycosides **(renal failure)**

f) Liver function

e.g. Erythromycin **(hepatic failure)**

3. Drug Allergy.

MISUSES OF ANTIBIOTICS

- Treatment of diseases caused by viruses
- Improper dosage
- Therapy of fever of unknown origin
- Presence of pus or necrotic tissues, or blood at the surgical site
- Excessive use of prophylactic antibiotics in travelers
- Lack of adequate bacteriological information
- Overuse as growth promoters in animals & agriculture
- Pts do not take them according to their doctor's instructions
- Some pts save unused antibiotics for another illness, or pass to others.

Reasons for MISUSES of ANTIBIOTICS

A consequence of many factors:

1- Availability of a very wide selection

2- Limitation of physician's time

3- Physician shortage and expenses

4- Availability without Rx in pharmacies

3- Public demand (pressure to prescribe).

Bacterial Resistance

- **One result of the widespread use of antibiotics has been the emergence of resistant pathogens that have been sensitive in the past**

Definition

Conc of antibiotic required to inhibit or kill the bacteria is greater than the conc that can safely be achieved in the plasma.

Mechanisms of Acquired Antibiotic Resistance

1. Inactivation by enzyme produced by bacteria

Bacterial β-lactamase inactivates penicillins & cephalosporins by cleaving the β-lactam ring of the drug

2. Bacteria develops an altered receptor for the drug
3. Bacteria develops an altered metabolic pathway
4. Reduced bacterial permeability to antibiotic
5. Actively transporting the drug out of the cell.

Prevention of Resistance

***Use antibiotics only when absolutely required**

***Use antibiotics in adequate dosage for sufficient period of time**

Not too brief therapy

Not too prolonged therapy

(exceptions, e.g. TB)

***Combination of antibiotics may be required to delay resistance (e.g. TB).**

General Principles of antibacterial therapy

- Administer drug in *full dose*, at *proper interval* and by the b*est route*
- When apparent cure achieved, continue antibiotic for about 3 days further to avoid relapse
- Skipping doses may decrease effectiveness of antibiotic & increase the incidence of bacterial resistance.
- In some infections, bacteriological proof of cure is desirable (e.g. TB, UTI)
- Measurement of plasma conc. of antibiotics is seldom needed, except for systemic aminoglycosides (e.g., streptomycin, gentamicin).

General Principles of antibacterial therapy (cont')

❖ 2 or > antimicrobial drugs should not be used without good reason, e.g.:
- Mixed bacterial (polymicrobial) infections
- Desperately ill patient of unknown etiology
- To prevent emergence of resistance (e.g. TB)
- To achieve synergism

e.g. piperacillin + gentamicin (p. aeruginosae)

Disadvantages of multiple antibiotics

- Increased risk of sensitivity or toxicity
- Increased risk of colonization and infection with a resistant bacteria
- Possibility of antagonism
- Higher cost.

Indications for antibiotics prophylaxis

Surgical prophylaxis, e.g.:

bowel surgery, joint replacement, etc. to prevent postoperative infections

Immunosuppressed Patients, e.g.:

Very old, Very young, Diabetics, Anaemics, AIDS, Cancer pts

Dental extractions, e.g.:

Pts with total joint replacements

Pts with cardiac abnormalities.