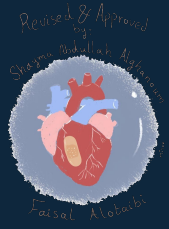


PHARMACOLOGY
TEAM 439

MED439
KING SAUD UNIVERSITY

Introduction to Antibiotics

Objectives:

- 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.

Important

In male and female slides

Only in male slides

Only in female slides

Extra information

Editing file

Antibiotics

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

Note that:

1.Nowadays they are chemically synthesized.

2.Antibiotics will not cure infections caused by viruses.

The **antibiotics** are either

1- Bacteriostatic **hold** bacteria from **growing**.

2- Bactericidal **kill** the bacteria.

Classified according to **Spectrum**:

Narrow spectrum penicillin G, aminoglycosides

works on either gram -ve or +ve bacteria

Broad spectrum ampicillin, amoxicillin

works on both gram -ve and +ve bacteria

Classified according to **Mechanism of action**

1- Inhibition of cell wall synthesis: e.g Penicillins (:Amoxicillin), Cephalosporins

2- Inhibition of DNA synthesis: e.g Quinolones

3- Inhibition of folate metabolism: e.g Sulfonamides, Trimethoprim

*Folate is important for nucleic acid synthesis.

4- Inhibition of RNA synthesis by binding to RNA polymerase: e.g Rifampicin

5- Inhibition of protein synthesis: Macrolides(ex:erythromycin) , Tetracyclines, Aminoglycosides

Choice of Antibiotic:

1 Clinical diagnosis

e.g. syphilis (مرض الزُهريّ ، يقصد انه يحدد المرض وف هالحاله طلع الزُهريّ فيعالج بناءً عليه)

2 Microbiological information

Disadvantages

- The bacteria isolated may <u>not</u> 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.

M=Mycobacterium

Advantages

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

3 Pharmacological consideration

1- Site of infection.

2- Drug Allergy (some patients have penicillin allergy)

4- The cost of therapy

3- Host factors :

- **Immune status** (low immunity) e.g(Alcoholism,diabetes,HIV) malnutrition, advanced age- (requires higher doses or longer courses than usual)
- **Genetic factors** Patients with G-6-PD deficiency with sulfonamides or chloramphenicol could lead to (Hemolysis)
- **Pregnancy and Lactation** <u>Aminoglycosides</u> (hearing loss) <u>Tetracyclines</u> (bone deformity in the child)
- **Age of the patient** :Neonates and elderly e.g. Grey baby Syndrome (chloramphenicol)
- **Renal function:** e.g. Aminoglycosides (renal failure)
- **Liver function:** e.g. Erythromycin (hepatic failure)

5- Potential Side Effects (Drug safety)

- **Chloramphenicol** (plastic anemia)
- **Fluoroquinolones in children & Pregnancy** (tendon damage)

Empiric therapy?

is medical treatment or therapy based on experience, or when absence of complete or perfect information.(شيء مانعرف سببه)

Bacterial resistance:

Definition:

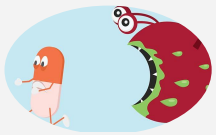
Concentration of antibiotic required to inhibit or kill the bacteria is greater than the concentration that can safely be achieved in the plasma.

تصير البكتريا قوية لدرجة تخلينا لازم نزيد الجرعة ونزيد ونزيد الى ما يصير المضاد بحد ذاته سام للمريض ولا نقدر نستعمله

When does bacterial resistance emerge?

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

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

Prevention of bacterial resistance:

- ★ Use antibiotic only when absolutely required.
- ★ Use antibiotics in adequate dosage for sufficient period of time. Not too brief therapy or too prolonged therapy (exceptions, e.g. TB → 6 months).
- ★ Combination of antibiotics may be required to delay resistance. (e.g. TB)

Misuse of antibiotics

- Treatment of diseases caused by viruses (wrong diagnosis).
- Improper dosage.to keep the effective drug concentration constant.
- Therapy of fever of unknown origin.
- Presence of pus or necrotic tissue , or blood at the surgical site.it's inhibit drug absorption.
- Excessive use of prophylactic antibiotics in travelers.
- Lack of adequate bacteriological information.
- Overuse as growth promoters in animals and agriculture.
- Patients do not take them according to their doctor's instructions.
- Some patients save unused antibiotics for another illness, or pass to others.

Reasons for Misuse of Antibiotics

- Availability of a very wide selection.
- Limitation of physician's time.
- Physician shortage and expenses.
- Availability without prescriptions in pharmacies.
- Public demand (pressure to prescribe).

General principles of Antibacterial therapy:

01

Administer drug in full dose, at proper interval and by the best route

02

When apparent cure achieved, continue for about 3 days further to avoid relapse

03

Skipping doses may decrease effectiveness of antibiotics & increase the incidence of bacterial resistance

04

Measurement of plasma conc. of antibiotics is seldom (rarely) needed, except for systemic Aminoglycosides e.g. streptomycin, gentamicin or streptomycin in renal TB; I.M gentamicin

05

In some infections, bacteriological proof of cure is desirable (e.g. TB ,UTI)

Usage of multiple antimicrobial agents

disadvantages:

- Higher cost
- Increased risk of sensitivity or toxicity

- Possibility of antagonism
- Increased risk of colonization and infection with a resistant bacteria

Exceptions where combining antibiotics is a good option:

- 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 (pseudomonas aeruginosa)

Indications for Antibiotics Prophylaxis:*

1

Surgical prophylaxis:

- bowel surgery, joint replacement, and some gynecological interventions to prevent postoperative infections.

2

Immunosuppressed Patients:

-Very old
-Very young
-Diabetics
- Anaemics
- AIDS
-Cancer patients

3

Dental extractions: blood may get infection after dental extraction and then spread to the body especially in :

-Patients with total joint replacements
- Patients with cardiac abnormalities

slides notes just to read

- **Altered permeability of the antimicrobial agent:** Altered permeability may be due to the inability of the antimicrobial agent to enter the bacterial cell or alternatively to the active export of the agent from the cell. **Inactivation of the antimicrobial agent :** Resistance is often the result of the production of an enzyme that can inactivate the antimicrobial agent. **Altered target site:** Resistance can arise due to alteration of the target site for the antimicrobial agent. **Replacement of a sensitive pathway:** Resistance can result from the acquisition of a new enzyme to replace the sensitive one.
- Narrow spectrum : primarily effective against 1 type of organism or vs narrow range of bacteria. Penicillin G & V activity is limited to gm+ve organisms mainly anaerobic. **Penicillin** is a group of antibiotics which include penicillin G (IV use), penicillin V (used po), procaine penicillin, and benzathine penicillin (IM use).
- Broad spectrum : effective against both gm+ & -ve organisms. **Ampicillin** is used to treat infections by many Gm+ive & Gm-ive bacteria.. Its spectrum of activity is enhanced by co-administration of sulbactam, a drug that inhibits beta lactamase, an enzyme produced by bacteria to inactivate ampicillin. **Amoxicillin** is active against gm+ive & gm-ve bacteria.
- Location of the infection like some bacteria located in poorly vascularized tissues & TF -> difficult to treat . it is very important to reach the site of the infection
- The AB (antibiotics) should reach the site of infection. & we should choose the best route to attack bacteria in certain area of the body.
- ABs vary in their ability to be absorbed orally or to cross the BBB & these factors will affect their routes of administration. The ability of the AB to achieve therapeutic concentrations at the site of infection is another important consideration thus ABs used for treating urinary infections should ideally be concentrated in urine. Some ABs have very severe toxic effects & are best avoided in certain conditions.

MCQ

1-Which of the following antibiotics inhibit protein synthesis?			
A- Penicillins	B- Rifampicin	C-Tetracyclines	D-Quinolones

2-Which of the following is considered Narrow spectrum antibiotic?			
A-amoxicillin	B-aminoglycosides	C-ampicillin	D-Rifampicin

3-Which of the following destroy the bacteria?			
A-Bactericidal	B-Bacteriostatic	C-A & B	D-None

4-It is beneficial to prescribe prophylactic antibiotics in these conditions,except ?			
A-very young age	B-for diabetic patients	C-Patients with kidney failure	D-after surgery

5-when combination of antibiotics isn't a good option?			
A-to achieve synergism	B-mixed bacterial infection	C-patient of known etiology	D-to prevent resistance

6-what are they disadvantages of multiple antimicrobial agents usage ?			
A-high cost	B-increased risk of sensitivity	C-possibility of antagonism	D-all

Answers

1	2	3	4	5	6
C	B	A	C	C	D

SAQ

Q1) What are the mechanisms of action of antibiotics ?

Q2) Define Antibiotics?

Q3) Enumerate Advantages of Bacteriological information in Choice of Antibiotic ?

Q4) bacterial resistance can be prevented by?

Q5)Enumerate 3 mechanisms of acquired antibiotic resistance:

Q6)mention three indications to use antibiotics as prophylaxis?

Answers

A1) Inhibition of cell wall synthesis, Inhibition of DNA synthesis, Inhibition of folate metabolism, Inhibition of RNA synthesis by binding to RNA polymerase, Inhibition of protein synthesi

A2) Antibiotics are chemical substances produced by various microorganisms (bacteria, fungi, actinomycetes) that have the capacity to inhibit the growth or destroy other microorganisms

A3) The exact antibiotic to be used, the most effective and reject the one with little or no activity, the least toxic and the cheapest.

A4) use antibiotic:when absolutely required ,in adequate dosage for sufficient period of time

A5) Bacteria develops an altered metabolic pathway, Actively transporting the drug out of the bacterial cell,Reduced bacterial permeability to antibiotic

A6)Pts with total joint replacements ,Pts with cardiac abnormalities,Diabetic patients

GOOD LUCK!

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