PHARMACOLOGY

Lecture: introduction to antibiotics

OBJECTIVES:

PHARMACOLOGY
435

- Important.
- Extra notes.

Definition of Antibiotics

Antibiotics (also known as antibacterial, chemotherapeutic drugs) are Chemical substances produced by various microorganisms (bacteria, fungi, actinomycetes) that have the capacity to inhibit or destroy other microorganisms.
Nowaday they are chemically synthesized drugs, not naturally occurring, yet still called "anti-biotics". A better naming would be: anti bacterial / chemotherapeutics

They either kill bacteria (bactericidal) or keep them from growing(bacteriostatic).

Antibiotics will not cure infections caused by viruses. They are only antibacterial.

CLASSIFICATION OF ANTIBIOTICS ACCORDING TO:

Spectrum of action

NARROW SPECTRUM
e.g.: penicillin G , aminoglycosides

BROAD SPECTRUM
e.g.: ampicillin, amoxicillin

What is empiric therapy?

It is giving the drug before identification of the organism & its drug susceptibility in extremely ill patients with unknown etiology. In this case, a combination of antibiotic should be used, where one of them is broad spectrum. This decision is influenced by experience, site of infection and the patient's history.

Mechanism of action

INHIBITION OF CELL WALL SYNTHESIS
e.g. β-lactam :Penicillins , cephalosporins.
They are bactericidal, as the cell can't live without a wall

INHIBITION OF PROTEIN SYNTHESIS
e.g. Macrolides, Tetracyclines

INHIBITION OF DNA SYNTHESIS
e.g. Quinolones

INHIBITION OF FOLATE METABOLISM
e.g. : Trimethoprim, sulfonamides

Inhibition of RNA synthesis by inhibiting RNA polymerase
e.g. : Rifampin (used for TB)

YouTube Microbiology - Antibiotics Mechanisms of Action

Choice of Antibiotics

1- Clinical diagnosis

e.g. syphilis . The symptoms of syphilis are known, the causing agent is also known "*Treponema pallidum*" , the best antimicrobial agent is usually penicillin . In this case, you can go ahead and prescribe.

2- Microbiological information

Advantages

Microbiology helps in choosing:

- **The exact antibiotic to be used, through studying the sensitivity of the infecting organisms to antibiotics**
- **The most effective & reject the one with little or no activity**
- **The least toxic**
- **The cheapest**

Disadvantages

- **The bacteria isolated** (and cultured in microbiology lab) **may not be the prime cause of the disease.**
- **Do not take in consideration the site of infection.** in vitro, they choose the concentration of the antibiotic as it is proper in plasma, this doesn't apply to infections in other sites in the body e.g. bone, urinary tract.
- **Some bacteria can not be cultivated or take time to grow (M. leprae, M. tuberculosis)**
- **Bacteriological services are not available at all hospitals,** due to the high expenses.

3- Pharmacological consideration

Patient factors

- **Immune status,** as in **patients with alcoholism, diabetes, HIV, malnutrition, advanced age**. They need higher doses than usual, or courses longer than those required for otherwise healthy individuals.
- **Genetic factors** e.g. Patients with G-6-PD deficiency treated with sulfonamides or chloramphenicol
  (G-6-PD enzyme functions in protecting RBCs, oxidizing drugs will interfere with its function and result in **Hemolysis**)
- **Pregnancy and Lactation.**
  - **Aminoglycosides may cause hearing loss**
  - **Tetracyclines cause bone deformity**
- **Age e.g. Grey baby Syndrome (chloramphenicol)**
  This phenomenon occurs in newborn infants because they don't yet have fully functional liver enzymes, so chloramphenicol remains unmetabolized in the body. Characterized by hypotension & cyanosis.
- **Renal function** e.g. **Aminoglycosides. They** have low margin of safety and **are excreted** unchanged in urine. So In patients with renal failure, elderly, and fetus-where the kidney is not fully matured- its concentration will increase and cause ototoxicity. (loss of hearing)
- **Liver function** e.g. Erythromycin (hepatic failure)

Drug Factors

- **Site of infection.**
  Important to choose the proper drug depending on its lipid solubility (penetration of BBB) and protein binding
- **Drug Allergy**
  Skin testing for allergy is very important before administering drugs

- **Potential Side Effects (Drug safety)**
  - Chloramphenicol (aplastic anemia)
  - Fluoroquinolones **in children & Pregnancy** (tendon damage)
- **The cost of therapy**

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.

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. It could develop due to misuse.

Misuse of Antibiotics:

- Treatment of untreatable infections, e.g. viral infections
- Improper dosage. (doses smaller or larger than required)
- Therapy of fever of unknown origin. Fever is a natural defense mechanism, in viral infections, antibiotics are not effective. The proper treatment of fever in viral infections is by resting and administration of fluids & antipyretics.
- Presence of pus or necrotic tissues, or blood at the surgical site, because antibiotics can't then penetrate the site of infection and produce their effects. Thus the area should be surgically cleaned before administration.
- Excessive use of prophylactic antibiotics in travelers.(prophylaxis therapy is not recommended, exceptions are mentioned later on)
- Lack of adequate bacteriological information. Using the wrong/ unnecessary antibiotic may cause emergence of bacterial resistance

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 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. Even after symptoms disappear, bacteria mayn't have eradicated completely. Thus, patient should continue the course of treatment to avoid relapse & resistance.

Not too prolonged therapy (exceptions, e.g. TB is 6 months).

Prolonged therapy may cause eradication of healthy bacteria or opportunistic infection by C. difficile (Pseudomembranous colitis)

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

Video: **What causes antibiotic resistance? - Kevin Wu**

General Principles of Chemotherapy

General Principles of Chemotherapy

- Administer drug in full dose, at proper interval and by the best route
- When apparent cure achieved, continue for about 3 days further to avoid relapse
- Skipping doses may decrease effectiveness of antibiotics & increase the incidence of bacterial resistance.
- Measurement of plasma conc. Of antibiotics is seldom (rarely) needed, except in some conditions such as streptomycin in renal TB. I.M gentamicin
- In some infections, bacteriological proof of cure is desirable **(e.g. TB, UTI)**
- Usage of multiple antimicrobials has many disadvantages :
  - Increased risk of sensitivity, toxicity or colonization with a resistant bacteria
  - Possibility of antagonism. E.g. bactericidal drugs shouldn't be used with bacteriostatic, because they need rapidly multiplying organisms to be effective.
  - Higher cost.

Exceptions where combining antibiotics is a good reason:

- 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 (psudomonos aeruginosae)

Indications for antibiotics prophylaxis

Prophylactic therapy by antibiotics is not recommended except with patients undergoing procedures that may cause bacteremia, in which the benefits outweigh the potential risks.

Surgical prophylaxis

bowel surgery, joint replacement, and some gynecological intervention **to prevent postoperative infections.**

Immunosuppressed patients

very old, very young, diabetic, **Anaemics, AIDS and** cancer patients

Dental extraction

In patient with total joint replacement

And patients with cardiac abnormalities

Drugs Summary + extra information

Antibiotic	Mechanism	Contraindications	Side effects
chloramphenicol	Inhibition of protein synthesis	Patients with G-6-PD deficiency	Hemolysis
		Pregnancy newborn infants	aplastic anemia Grey baby Syndrome
Aminoglycosides	Inhibition of protein synthesis	Pregnancy Renal failure	hearing loss
Tetracyclines	Inhibition of protein synthesis	Pregnancy	bone deformity
Erythromycin (Macrolide)	Inhibition of protein synthesis	Hepatic failure	
Fluoroquinolones	Inhibition of DNA synthesis	Children & Pregnancy	tendon damage
sulfonamides	Inhibition of folate metabolism	Patients with G-6-PD deficiency	Hemolysis
Piperacillin (Penicillin) + gentamicin (Aminoglycoside)	**Penicillin:** Inhibition of cell wall synthesis **Aminoglycoside:** Inhibition of protein synthesis	**Use**	
		Used together to achieve synergism, for psudomonos aeruginosae	

Antibiotics contraindicated during pregnancy: FACT

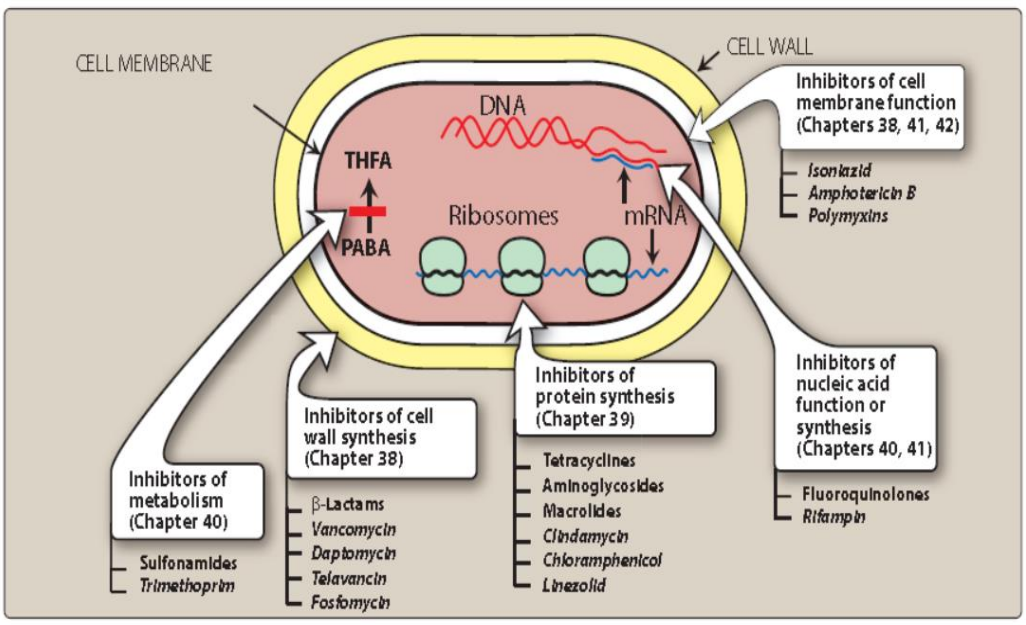

Figure 37.10
Classification of some antimicrobial agents by their sites of action. (THFA = tetrahydrofolic acid; PABA = *p*-aminobenzoic acid.)

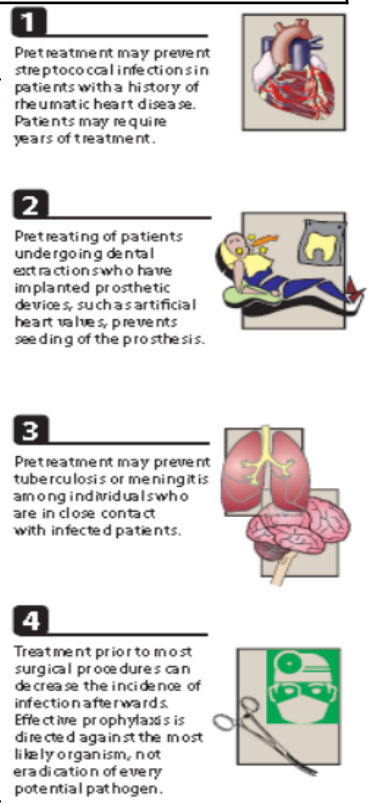

Figure 37.9
Some clinical situations in which prophylactic antibiotics are indicated.

[Link: Antimicrobial mnemonics]

QUIZ

THANK YOU FOR CHECKING OUR WORK

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