Tikrit University
College of Veterinary Medicine

Pharmacology

Subject name: Antibiotic

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Lecturer name: **Dr. Buthinah Abulhameed**

Email:buthinahamee@tu.du.iq

Antimicrobial

Antimicrobial drugs: are effective in the treatment of infections because of their selective toxicity –th ability to kill an invading microorganism without harming the cells of the host.

Selection of antimicrobial agents :- a- the organisms identity and its sensitivity to a particular agent .

a- the site of the infection
b- the safety of the agent
c- patient factors
d- the cost of therapy.

Antimicrobial drugs are classified

as either bacteriostatic or bactericidal .

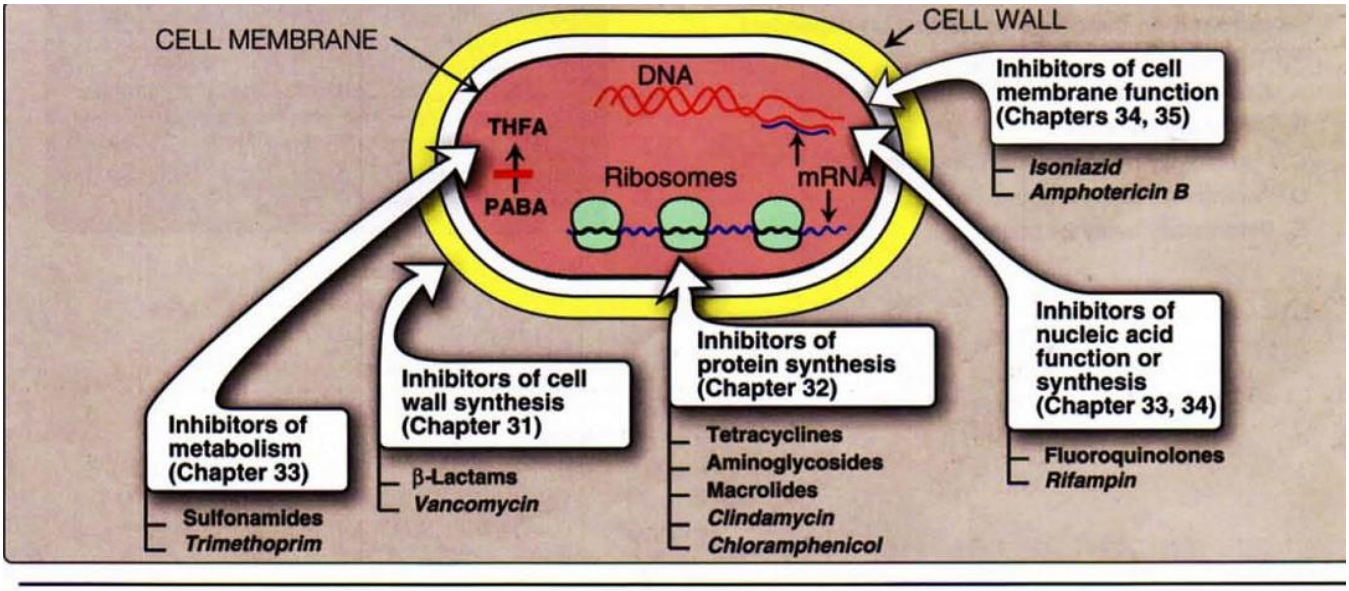
Bacteriostatic drugs :- arrest the growth and replication of bacteria at serum levels achievable in the patient , if the drug is removed before the immune system has scavenged the organism , enough viable organisms may remain to begin a second cycle of infection.

Bacteriocidal agent:- kill bacteria and the total number of viable organisms decreases .

Another classification according to the sit of action:-

1- drug that inhibit cell wall synthesis .(penicillin).
2- Drugs that inhibit cell membrane synthesis (polymixin) this drug is very toxic because there is similarity between the human & bacteria.
3- Drugs that inhibit protein synthesis. many antibiotic act on the protein synthesis especially the protein that is essential for bacteria & different from the human protein.
(tetracycline, aminoglcoside, macrolides..).

4- Drug that inhibit nucleic acid synthesis (refampin , fluroquinolones)
5- Drug that inhibit metabolic pathway.(sulfonamide, trimethoprim).



Chemotherapeutic spectra:-

a- narrow spectrum :- acting only on a single or a limited group of microorganism (isoniazid is active only against Mycobacteria)
b- extended spectrum:- is the term applied to antibiotic that are effective against gram- positive organisms and also against a significant number of gram- negative bacteria. (ampicillin is considered to have an extended spectrum because it acts against gram- positive and some gram – negative bacteria.
c- Broad spectrum :- drugs affect a wide variety of microbial species (tetracycline, chloramphenicol) .

Complication of antibiotic therapy:-

a- hypersensitivity:-hypersensitivity reaction to antimicrobial drugs or their metabolic products frequently occur.(penicillin)
b- direct toxicity :- high serum levels of certain antibiotics may causes toxicity by affecting cellular processes in the host directly. (aminoglycosides can cause ototoxicity by interfering with membrane function.
c- Superinfections :- particularly with broad spectrum antimicrobial or combination of agents, can lead to alteration of normal microbial flora of the upper respiratory , intestinal and urinary tract permitting the overgrowth of organism .

Drug resistance :-

Mechanism of resistance to antibiotics :-

1- production of enzymes that inactivate the drug (b- lactamase which inactivate penicillin).
2- Alteration of the drug binding site , this occurs with amino glycosids, erythromycin & penicillin).
3- Reduction f drug uptake by bacteria (tetracycline).
4- Alteration of enzyme pathways (dihydrrofolate reductase becomes insensitive to trimethoprim.

Combinations of antibiotics:-

This mean the using of two drugs together for:-

1- to get broad spectrum .
2- to prevent drug resistance.
3- To get synergism.

a- bactericidal +bactericidal = synergism (the effect of ampicillin in combined with gentamycin is more great amount than ampicillin alone or gentamycin alon in double.
b- Bacteriostatic + bacteriostatic = additive to reduce the side effect of the drugs by give small dose instead double dose .
c- Bacteriostatic + bactericidal = antagonist except co- trimoxazol

Tri= trimethoprim

Moxazol = sulphamethoxazol

Inhibitors of cell wall synthesis :-

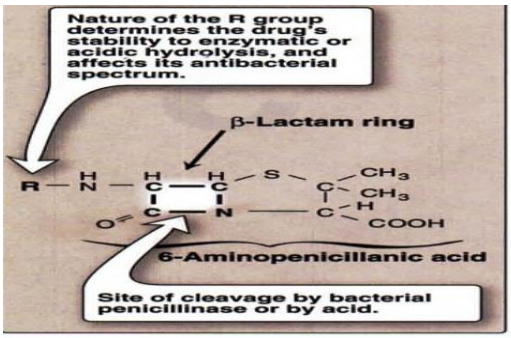
Which include:-

1- B- lactam antibiotics (pencillins , cephalosoporins , carbapenems, monobactams)

2-other drugs (vancomycin, bacitracin ..).

PENICILLIN

All penicillins are derivatives of 6- aminopenicillianic acid and contain a beta lactam ring structure that is essential for antibacterial activity .



mechanism of action :-

B-lactam antibiotics are bactericidal drugs. They act to inhibit cell wall synthesis by the following steps:-

1- binding of the drug to specific receptor (penicillin –binding proteins; PBPs) located in the bacterial cytoplasmic membrane.

2- inhibition of transpeptidas enzymes that act to cross- link linear peptidoglycan chain which form part of the cell wall .

3- activation of autolytic enzyme that cause lesion in the bacterial cell wall

Penicillin are divided into :- group I- natural penicillin.

group II -B- lactamase resistant penicillin .

group III – extended rang penicillin.

Group I : natural penicillin (narrow spectrum):- which include benzylpencillin (G), procaine penicillin , benzathin penicillin, phenoxymethylpenicillin (V).

Benzyl penicillin (G):- it is crystalloid, soluble penicillin . it is effective against streptococci, pneumoccoci, diphtheria, clostridium.the half life of penicillin G is 6 hours,is suscepitable to inactivation by B-lactmase(pecillinase)

Procaine penicillin :- it is penicillin added to it procaine, procaine is added for the following reasons:-

1- crystalline penicillin is painful.

2-to prolong the duration of action so it is given as injection every 12 -24 h.

Benzathin penicillin;- it has long duration of action of about 3-4 weeks because benzathin cause slow release of drug. It is given to patients with rheumatic fever to protect them against infection.

Phenoxymethylpenicillin (penicillin V)

Its less effective but resistance to gastric acid & so reaches the small instant intact where it is moderately well absorbed. It can be given orally

Pharmacokinetics'-

1- gastric acid inactivates penicillin G, so not given orally .
2- penicillin V is resistance to gastric acid & so reaches the small instant intact where it is moderately well absorbed. It can be given orally.
3- Penicillin G is given either as IM, or IV .
4- The penicillin is not metabolized , they are eliminated unchanged in kidney by the proximal convoluted tubules.
5- Most penicillin's cross the blood –brain barrier only when the meninges are inflamed.
6- Penicillin measured by units , 1 unit = 0.6 μg , million unit = 0.6 g

Group II:- B-lactamase resistant penicillin (anti-staphylococci)

Include :- cloxacillin, flucloxacillin, dicloxacillin, naficillin, oxacillin.

Drugs that resist the action of staphylococcal B- lactamase do by their possession of an acyl side- chain which protects the B – lactam bond by preventing the enzyme getting access to it . they are used in osteomylitis due to staphylococci . these drugs are not metabolized except naficillin which is metabolized in liver& excreted in bile , while the other are excreted by the kidney.

Methicillin its use is now confined to laboratory sensitivity test. It causes interstitial nephritis, identification of methicillin –resistant staphylococcus aureus

Group III :- broad spectrum penicillin.

They have broad antibacterial spectrum and are effective against both gram positive and gram negative organisms. They are hydrolysed by penicillinase. Ampicillin, amoxicillin

AMPICILLIN

-It is a broad spectrum penicillin which is not destroyed by gastric acid but is penicillinase susceptible.
-It is more effective than benzyl penicillin against a variety of gram negative microorganisms.
-After oral administration it is readily but incompletely absorbed and food interferes with its absorption. It is excreted in urine in unchanged form and high amount is also present in the bile.
Adverse effects include skin rash, nausea, , diarrhea, drug fever, urticarial etc.

AMOXYCILLIN

Amoxycillin is a semisynthetic penicillin, active against gram positive and negative organisms. Its absorption is more complete than ampicillin. Food does not interfere with its absorption. Its absorption after oral administration is complete hence less incidence of diarrhea. It is eliminated in urine in unchanged form.

Not\When used in combination with inhibitors of pencillinase (clavulinic acid,etc) their antibacterial activity is enhanced.

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□-LACTAMASE INHIBITORS

CLAVULANIC ACID

. It is used along with **amoxycillin i**n various infections

SULBACTAM

It is another semisynthetic □-lactamase inhibitor used along with **ampicillin**. It is related to clavulanic acid both chemically and in activity.

Known as **Augmentin** in human medicine (Amoxicilin+calvulinic acid)

ANTIPSEUDOMONAL PENICILLINS

These are indicated mainly to treat gram negative bacilli infection by pseudomonas, proteus and enterobacter.

-CARBENICILLIN, PIPERACILLIN, TICARCILLIN

Resistance of bacteria for pencillin:-1-B-lactamase activity.
2-decreased permeability to drug:-decreased penetration of the antibiotic through the outer cell membrane prevent the drug from reaching to target(PBPs).
3-altered penicillin binding protein.
Adverse reaction:-hyprsensitivity:- this is most important adverse effect of the pencillin, cross –allergic reaction do occur among the B-lactmase antibiotic.
-diarrhea, caused by a disruption of the normal balance of intestinal microorganisms.
-nephritis,neurotoxicity,
-cation toxicity:-

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CEPHALOSPORINS

Cephalosporins are important bactericidal broad spectrum □-lactam antibiotics used for the treatment of **septicaemia, pneumonia, meningitis, urinary tract infections, peritonitis and biliary tract infections.**

They are obtained from fungus ***Cephalosporium acremonium*** and are chemically related to penicillin. It consists of beta lactam ring. All cephalosporins act by inhibiting bacterial cell wall synthesis and are bactericidal. Also the autolytic enzymes in cell wall

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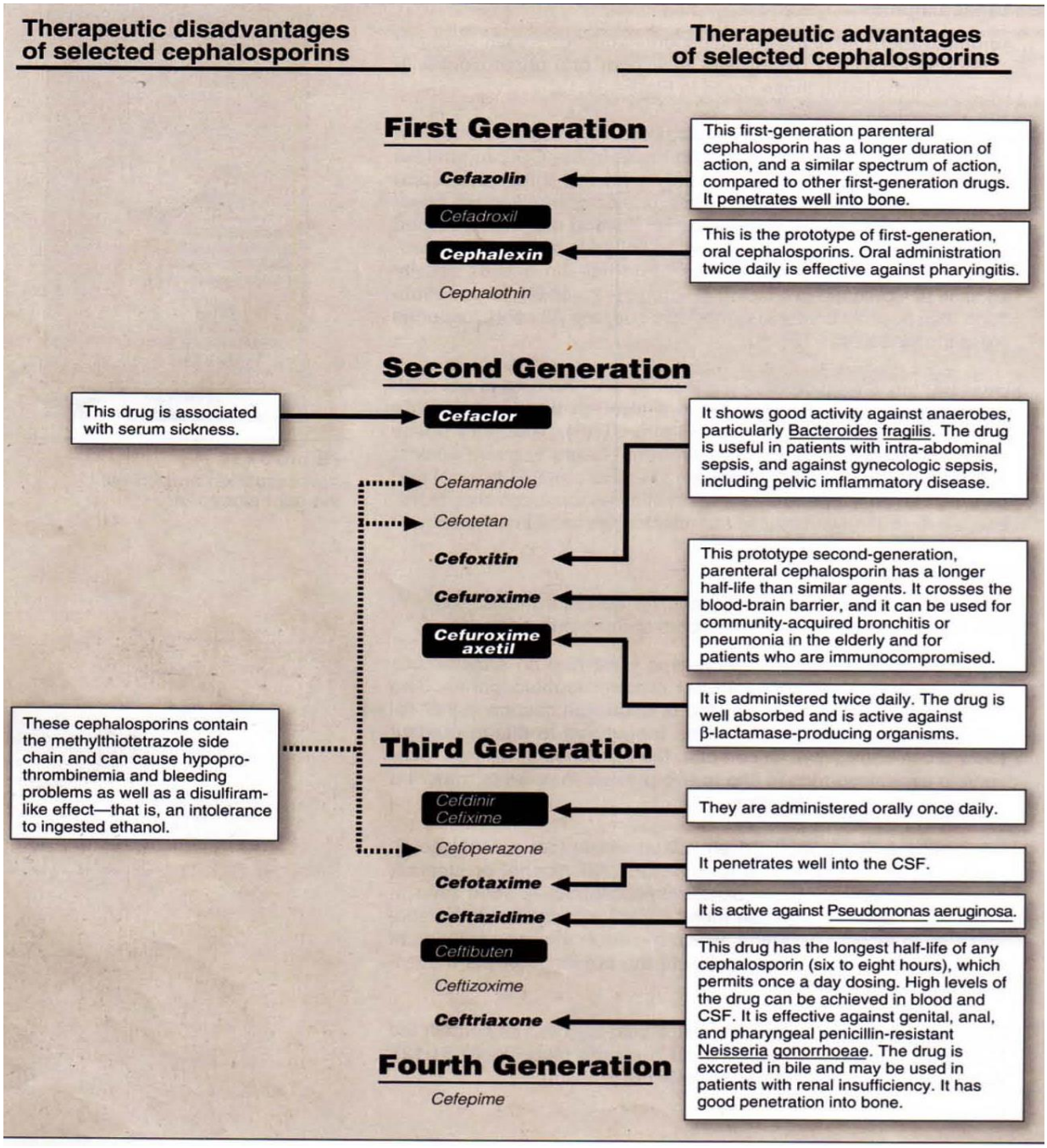
Pharmacokinetics

Cephalosporins are distributed in the body after oral or parenteral administration. the agents that cannot be used orally are too poorly absorbed to provide adequate blood levels. cephalosporins used orally are well absorbed ,after absorbed they are widely distribution through the tissues are excreted by kidney half-lives50-240minutes

Adverse effects: in general cephalosporin have a low of adverse effect
-GIT effects(diarrhea,nausea,vomiting)
-nephrotoxicity
-superinfection
Because cephalosporin are chemically very similar to penicillin a person who has had an allergic reaction to penicillin may have an allergic reaction to a cephalosporin this is referred to as cross sensitivity.

:**There are four generations of cephalosporins**:-
1-**First generation:** Effective against gram-positive bacteria .
2-**Second generation**: Increased activity against gram-negative microorganisms .
3-**Third generation:** More active against gram(); ceftazidime and cefoperazone are . also effective against Pseudomonas aeruginosa (gram–) and β-lactamase–producing microbial strains; less effective against gram () cocci
4. **Fourth generation**: Same as third generation, but is more resistant to β-lactamases


Therapeutic disadvantages of selected cephalosporins
Therapeutic advantages of selected cephalosporins
First Generation
Cefazolin
This first-generation parenteral cephalosporin has a longer duration of action, and a similar spectrum of action, compared to other first-generation drugs. It penetrates well into bone.
Cefadroxil
Cephalexin
This is the prototype of first-generation, oral cephalosporins. Oral administration twice daily is effective against pharyingitis.
Cephalothin
Second Generation
This drug is associated with serum sickness.
Cefaclor
It shows good activity against anaerobes, particularly Bacteroides fragilis. The drug is useful in patients with intra-abdominal sepsis, and against gynecologic sepsis, including pelvic imflammatory disease.
Cefamandole
Cefotetan
Cefoxitin
Cefuroxime
This prototype second-generation, parenteral cephalosporin has a longer half-life than similar agents. It crosses the blood-brain barrier, and it can be used for community-acquired bronchitis or pneumonia in the elderly and for patients who are immunocompromised.
Cefuroxime axetil
It is administered twice daily. The drug is well absorbed and is active against β-lactamase-producing organisms.
These cephalosporins contain the methylthiotetrazole side chain and can cause hypoprothrombinemia and bleeding problems as well as a disulfiram-like effect—that is, an intolerance to ingested ethanol.
Third Generation
Cefdinir
Cefixime
They are administered orally once daily.
Cefoperazone
Cefotaxime
It penetrates well into the CSF.
Ceftazidime
It is active against Pseudomonas aeruginosa.
Ceftibuten
Ceftizoxime
Ceftriaxone
This drug has the longest half-life of any cephalosporin (six to eight hours), which permits once a day dosing. High levels of the drug can be achieved in blood and CSF. It is effective against genital, anal, and pharyngeal penicillin-resistant Neisseria gonorrhoeae. The drug is excreted in bile and may be used in patients with renal insufficiency. It has good penetration into bone.
Fourth Generation
Cefepime

Cephalexin(Keflex),cefazolin(Ancef)--------first generation

Cefclor (Ceclor),Cefuroxime(ceftin,kefurox),---------second generation

Cefotaxime (Claforan),Cefixim(suprax) ---------third generation

Cefepime(maxipim)--------fourth generation

OTHER BETA-LACTAM DRUGS

MONOBACTAMS

-Monobactams are drugs with a monocyclic β -lactam ring

-They are relatively resistant to β-lactamases and active against gram-negative rods (including pseudomonas and serratia).

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OTHER CELL WALL OR MEMBRANE-ACTIVE AGENTS

VANCOMYCIN

Vancomycin is an antibiotic produced by *Streptococcus orientalis*.

Vacomycin is bactericidal and has narrow spectrum of activity against many gram – positive cocci (staphylococci,streptococci),its acts by inhibition of bacterial cell wall synthesis

Antifolate drugs(antimetabolitis)

Sulfonamides:-

All sulfonamides in clinical use are synthetic structural analogs of p-aminobenzoic acid (PABA). (sulfadiazine, sulfamethoxazole, sulfisoxazole, sulfaslazine).

Mechanism of action:-

Sulfonamides do not actually destroy bacteria but inhibit their growth. They are considered bacteriostatic antibiotics.

Many bacteria ability to synthesize folate from PABA, pteridine, and glutamate, an essential step in the production of purines and the synthesis of nucleic acides. Sulfonamides are structural analogs of **PABA that competitively inhibit dihydropteroate syntheses**.they inhibit growth by blocking folic acid synthesis.

Sulfonamides inhibit both gram-positive and gram- negative bacterianocardia, Chlamydia trachomatis, and some protozoa.

Some entric bacteria(E coli, klebsilla, salmonella, shigella)

Resistance:- 1- altered enzyme, 2- decreased permeability to sulfa. 3- increased PABA synthesis.

Pharmacokinetics:-

Most sulfa drugs are well absorbed after oral administration.sulfasalazine when administered orally not absorbed therefore used for treatment of chronic inflammatory bowel disease .

Sulfa drugs are distributed throughout body water and cerebrospinal fluid, they can pass the placenta barrier and breast milk.
A portion of absorbed drug is acetylated or glucuronidated in the liver , inactivated metabolites are then excreted into the urine

Clinical uses :-

1-Oral absorbed agents:- sulfisoxazole and sulfamethoxazole are short to medium acting agents that are used to treat urinary tract infections

Sulfadiazine + pyrimthamine treatment of acute toxaplasmosis(block the folate synthetic pathway blockade)

2-Oral nonabsobable agents:- sulfasalazine is widely used in ulcerative colitis, enteritis, and inflammatory bowel disease

3- Topical agents:- sodium sulfacetamide ophthalmic solution or ointment is effective treatment for bacterial conjunctivitis and therapy for trachoma.

Silver sulfadiazine ---- prevention of infection of burn wound.

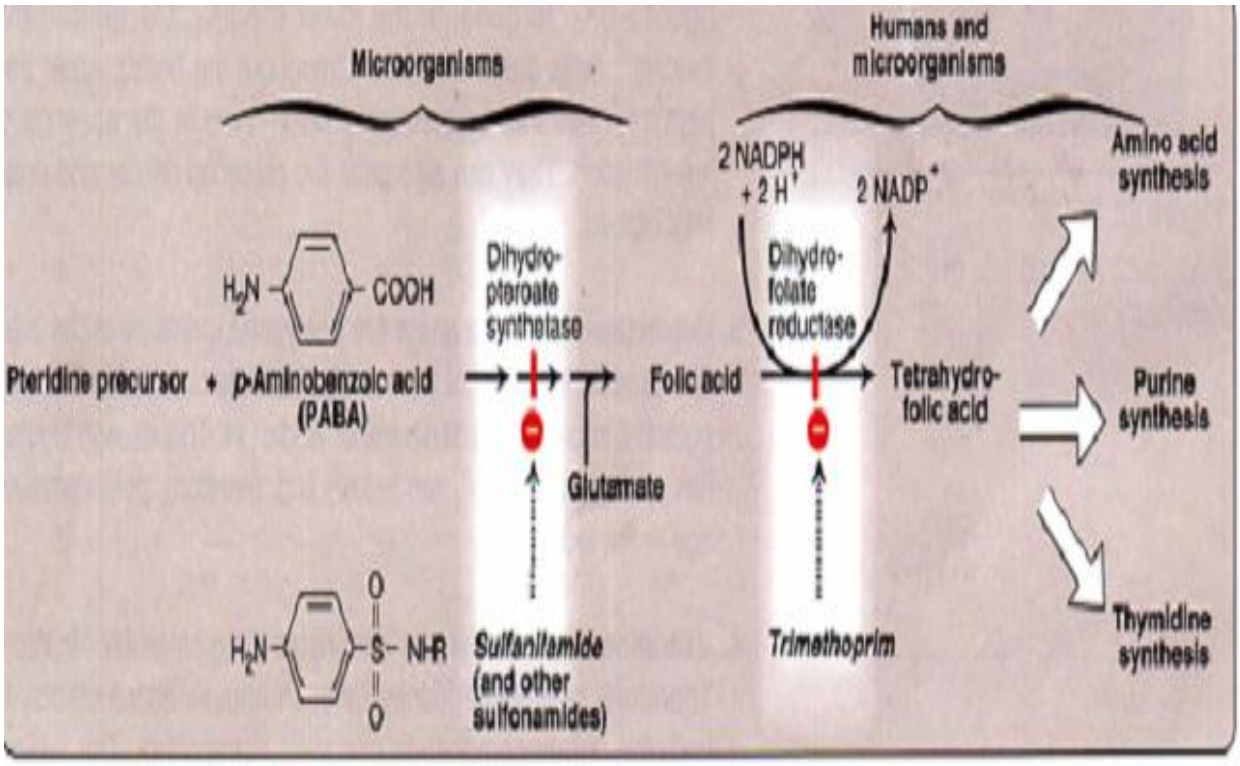
Adverse effects:-

1-**Crystalluria:** sulfonamides may precipitate in urine, especially at neutral or acid ph producing crystalluria , hematuria.

2- hypersensitivity:

3- hematopoitic disturbances: can cause hemolytic or aplastic anemia, granulocytopenia, thrompocytopenia. Sulfonamides may provoke hemolytic reaction in patients whose red cells are deficient in G-6-P D

Contraindications: sulfas should be avoided in newborns and infants less than 2 months old , pregnant women



Trimethoprim:-

A potent inhibitor of bacterial dihydrofolate reductase.

Mechanism of action :- the active form of folate is the tetrahydro derivative that is formed through reduction by dihydrofolatea. This enzymatic reaction is inhibited by trimethoprim, leading to a decrease in the folate coenzymes for pyrimidin, purine and amino acide synthesis. Bacterial reductase has a much stronger affinity for trimethoprim than dose the mammalian enzyme (selective toxicity).

Not| other folate redactase inhibitors:- pyrimethamine used with sulfonamides in parasitic

Methotrexate used in cancer chemotherapy.

Clinical uses: the antibacterial spectrum of trimethoprim is similar to that of sulfamethoxazole, trimethoprim is 20- 50 times more potent than the sulf.

Resistance: in gram bacteria -------- altered dihydrofolate reductase lower affinity for the drug

Adverse effects:- trimethoprim can produce the effects of folate deficiency, that is megaloblastic anemia, lukopenia and granulocytopenia.

Co- trimoxazole :- trimethoprim is most often compounded with the sulfa drug (sulfamethoxazole the resulting combination called co-trimoxazole greater antimicrobial activity than equivalent quantities of either drug used alone. Its effective treatment for(*P carinii pneumonia. Shigellosis, salmonella* infections, complicated urinary tract infections, prostitis.

Adverse effects:- dermatologic , GIT irritation, hematologic(megaloplastic anemia, lukopenia, thrombocytopenia)

Drug interaction: prolonged prothrombin times in patients receiving warfarin.

Inhibitors of nucleic acid function and synthesis

Fluoroquinolones:-

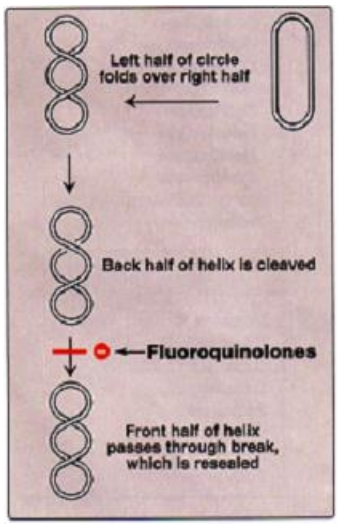
Consist of a carboxyl group, fluorine atom and piprazine ring to quinilone ring.

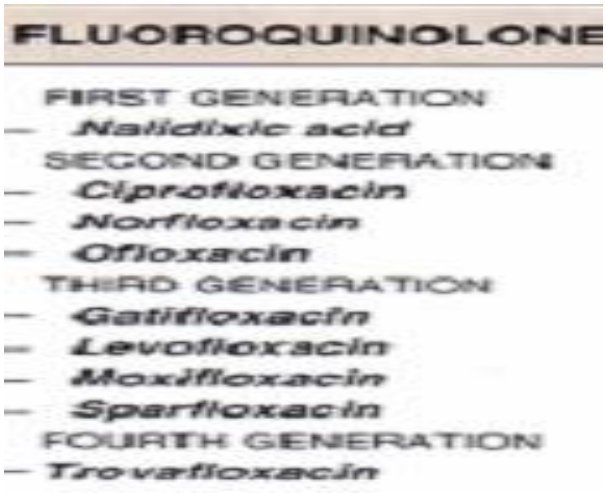
-its weak acids and are lipophilic .

Mechanism of action:-

Inhibit bacterial DNAgyrase an enzyme that control DNA supercoling as the replicating strand separate,

fluoroquinolones are bacteriocidal.broad spectrum





Pharmacokinetics:-

-absorption:-oral absorption rapidly achieve peak plasma concentration 1 hour after administration.

-wide distribution (CNS,Prosta).

-metablites are excreted in urine and bile.

Adverse effects:-erosion of articular cartilage.

-nephrotoxicity

-phototoxicity

Resistance:-

-alterd target

-decrease accumulation .

Drug interaction:-

-the effect of antacid,cations on absorption

-ciprofloxacin can increase the level of warfarin,caffeine,thyophyllin by inhibiting its metabolism

-cimetidine interfers with elimination of fluoroquinilole.

Protein synthesis inhibitors:-

A number of antibiotic exert their antimicrobial effect by targeting the bacterial ribosome, which has components that differ structurally from those of the mammalian cytoplasmic ribosome .(tertracyclines, aminoglycosides, macrolides, chloramphnicol,clindamycin).

Tetracyclines:-

Introduction

All of the tetracyclines have the basic structure:

Classification of tetracyclines.

Tetracycline (SUBAMYCIN) 250-500 mg/day, 1-3% topical (eye/ear drop, skin oint)
Oxytetracycline (TERRAMYCIN) 250-500 mg/day, 1-3% topical (skin, eye ointment)
Chlortetracycline (AUREOMYCIN) 250-500 mg/day, 1-3% topical (skin, eye ointment)
Demeclocycline (LEDERMYCIN) 300 mg BD, 0.5% skin oint.
Doxycycline (BIODOXI) 200 mg OD
Minocycline (CANOMYCIN) 100 mg BD

Are polycyclic compounds that are amphotric and that fluoresce when exposed to UV light .they form insoluble chelate with cations such as (calcium, magnesium,iron, and aluminum).

Mechanism of action:-

Tetracycline's which are bacteriostatic,inhibit bacterial protein synthesis by binding to the 30S ribosome and preventing attachment of aminoacyl transfer ribonucleic acid (tRNA)to the mRNA-ribosome complex they block the addition of amino acid to the growing peptide chain.

Pharmacokinetics:-

Absorbtion:-oral absorption tetracycline, range from 60-90% except for chlortetracycline is only 35% absorbed divalent,rtivlent cation impair absorption (milk,antacid,iron salt should be avoided 3h before and after oral administration.

Distribution is wide all tissues except CNS,deoxycycline is more lipid soluble than tetracycline it penetration the CNS ,eye,and prostate at therapeutic Conce.

Excretion:-renal excretion by gluemrular filtration is the major rout of elimination for tetracycline but small amount excreted into feces via bile

Spectrum of activity:-include Grame –positive,Gram negative and anerobes(broad spectrum)

Bacterial resistance :- decreased drug up-take or active transport of the tetracyclines out the bacterial cell.

Therapeutic Use

1. Respiratory tract infection:
2. Urinary tract infection:

4. Dermatological infections: Acne vulgaris, when antibiotic therapy is considered necessary.
5. Ophthalmic infections:
6. Prophylaxis and treatment of Traveller's diarrhoea.
7. Miscellaneous infections caused by susceptible strains of bacteria causing psittacosis, cholera, melioidosis, leptospirosis, brucellosiss

Adverse effects:--tetracyclines except doxycycline are potentially nephrotoxic and should be avoided if renal function is impaired.

-gastroinstinal disturbances:- nausea,diarrhea

-bony structure and teeth :-may lead to tooth enamel dysplasia and irregular in bone growth ,contraindication in pregnancy .

-hepatic toxicity lead necrosis

-photosensitivity:-cause enhanced skin sensitivity to ultraviolet light

-vestibular toxicity :-dizziness, nausea, vomiting.

Chloramphenicol:-

It is a broad spectrum antibiotic originally derived from ***Streptomyces venezuelae*** and later on became the first completely synthetic antibiotic.

Palmitate salts are water insoluble orally

-chloramphenicol sodium succinate is water soluble for parenteraluse, It is soluble in alcohol but poorly soluble in water. Chloramphenicol succinate, which is used for parenteral administration, is highly water-soluble.

Mechanism of action :-bacteriostatic agent,bind to the bacterial 50S ribosom unit to inhibit peptide bond formation and protein synthesis.

Pharmacokinetics:-absorption is rapidly absorbed from GIT tract

Distribution:-is widely distributed to all tissue include CNS,eye

Metabolism:-gluronide conjugation

Excretion:-the elimination t1\2 1-1.5h in dog and horses 4-5h in cat

Spectrum :-is a broad spectrum

Bacterial resistances:-resistant bacteria inactivate chloramphenicol by producing actyltransferase and other metabolizing enzyme.
--change in perambility,

Clinical Uses

-Because of potential toxicity, bacterial resistance, and the availability of many other effective alternatives, chloramphenicol is rarely used.

-Chloramphenicol is used topically in the treatment of eye infections because of its broad spectrum and its penetration of ocular tissues and the aqueous humor. It is ineffective for chlamydial infections.

Adverse Reactions

A. GASTROINTESTINAL DISTURBANCES

Adults occasionally develop nausea, vomiting, and diarrhea. This is rare in children. Oral or vaginal candidiasis may occur as a result of alteration of normal microbial flora.

B. BONE MARROW DISTURBANCES

Chloramphenicol commonly causes a dose-related reversible suppression of red cell

C. TOXICITY FOR NEWBORN INFANTS

Newborn infants lack an effective glucuronic acid conjugation, when infants are given dosages above 50 mg/kg/d, the drug may accumulate, resulting in the **gray baby syndrome**, with vomiting, flaccidity, hypothermia, gray color, shock, and collapse. To avoid this toxic effect, chloramphenicol should be used with caution in infants and the dosage limited to 50 mg/kg/d or less (during the first week of life) in full-term infants more than 1 week old and 25 mg/kg/d in premature infants.

D. INTERACTION WITH OTHER DRUGS

Chloramphenicol inhibits hepatic microsomal enzymes that metabolize several drugs.

Half-lives are prolonged, and the serum concentrations of phenytoin, tolbutamide, chlorpropamide, and warfarin are increased.

MACROLIDES

INTRODUCTION

The macrolides are a group of closely related compounds characterized by a macrocyclic lactone ring (usually containing 14 or 16 atoms) to which deoxy sugars are attached. The prototype drug, erythromycin, which consists of two sugar moieties attached to a 14-atom lactone ring, was obtained in 1952 from *Streptomyces erythreus*.

Clarithromycin and azithromycin are semisynthetic derivatives of erythromycin.

Antimicrobial Activity

Erythromycin is effective against gram-positive organisms, especially pneumococci, streptococci, staphylococci, and corynebacteria, in plasma concentrations of 0.02-2 mcg/mL. Mycoplasma, legionella, *Chlamydia trachomatis, C psittaci, C pneumoniae*, helicobacter, listeria, and certain mycobacteria *(Mycobacterium kansasii, M scrofulaceum)* are also susceptible. Gram-negative organisms such as *Neisseria* sp, *Bordetella pertussis, Bartonella henselae*, and *B quintana* (etiologic agents of cat-scratch disease and bacillary angiomatosis), some rickettsia sp, *Treponema pallidum*, and campylobacter sp are susceptible. *Haemophilus influenzae* is somewhat less susceptible.

Mechanism of action

The antibacterial action of erythromycin may be inhibitory or bactericidal, particularly at higher concentrations, for susceptible organisms. Activity is enhanced at alkaline pH. Inhibition of protein synthesis occurs via binding to the 50S ribosomal RNA,

Pharmacokinetics:-

Absorption by the oral (entric coated)prepration protect from gastric acid destruction, widely distribution all tissue except CNS,

Azithromycin **has similar spectrum of activity but is more active against H infuenzae ,because of its long half –life a single dose ,Azithromycin dose not inhibit hepatic cytochrome P450**

Erythromycin inhibit several form of hepatic cytochrome p450 and can increase the plasma level of anticoagulants,,,,,several drugs

Averse effect :-

-GIT upset

-skin rash,hypersensitivity . may occur hepatitis with erythromycin

-pain,irritation at IM

-sever diarrhea.

AMINOGLYCOSIDES:-

Consist of two or three amino sugars joined to amino cyclitol

the aminoglycosides are destroy bacteria rather inhibit growth therefore bactericidal antibiotic. These agent can be given by several different routs but they are not given orally because of their poor oral absorption an **except neomycine.**

The aminoglycosides include **streptomycin, neomycin, kanamycin, amikacin, gentamicin, tobramycin, sisomicin, netilmicin**, and others. They are used most widely against gram-negative enteric bacteria, especially in bacteremia and sepsis, in combination with vancomycin or a penicillin for endocarditis, and for treatment of tuberculosis.

MECHANISM OF ACTION

The mode of action of streptomycin has been studied far more closely than that of other aminoglycosides, but probably all act similarly. Aminoglycosides are irreversible inhibitors of protein synthesis, but the precise mechanism for bactericidal**.**

MECHANISMS OF RESISTANCE

Three principal mechanisms have been established: (1) production of a transferase enzyme or enzymes inactivates the aminoglycoside by adenylylation, acetylation, or phosphorylation.

(2) There is impaired entry of aminoglycoside into the cell.

(3) The receptor protein on the 30S ribosomal subunit may be deleted or altered as a result of a mutation.

ADVERSE EFFECTS

All aminoglycosides **are ototoxic and nephrotoxic.**

Streptomycin:- old class broad spectrum Clinical Uses

A. MYCOBACTERIAL INFECTIONS

Streptomycin is mainly used as a second-line agent for treatment of tuberculosis.

B. NONTUBERCULOUS INFECTIONS

given intramuscularly in combination with an oral tetracycline. Penicillin plus streptomycin is effective for enterococcal endocarditis and 2-week therapy of viridans streptococcal endocarditis.

Gentamicin has largely replaced streptomycin for these indications.

Streptomycin remains a useful agent for treating enterococcal infections, however, because approximately 15% of enterococcal isolates that are resistant to gentamicin

Neomycin-is administration oraly and topical

Gentamicin-amikacin are effective against psudomounas ,protus,staphylococcus,and Gram-negative aerobs

Kanamycin smilar gentamicin except not effective against psudomounas