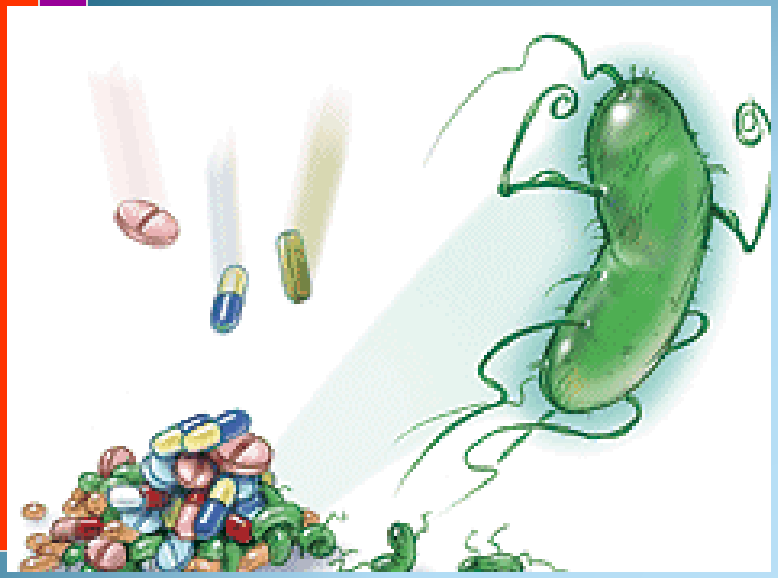
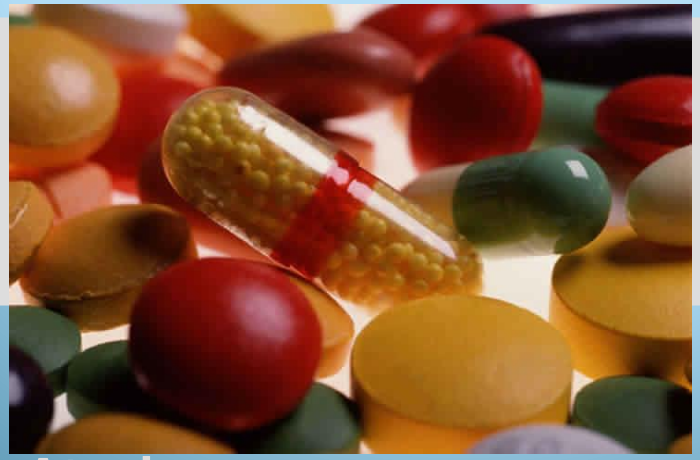
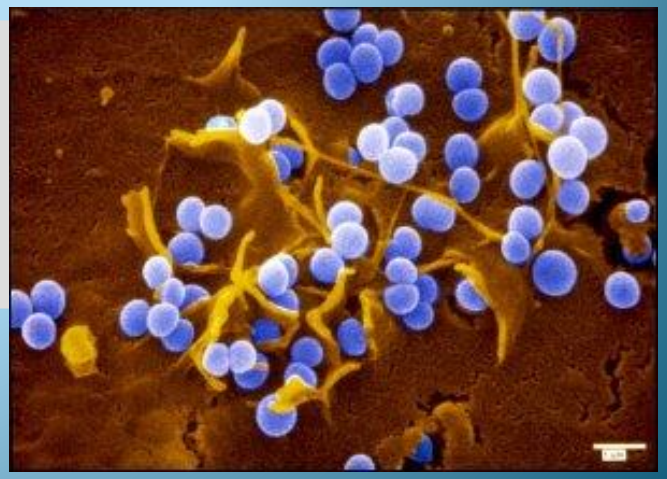
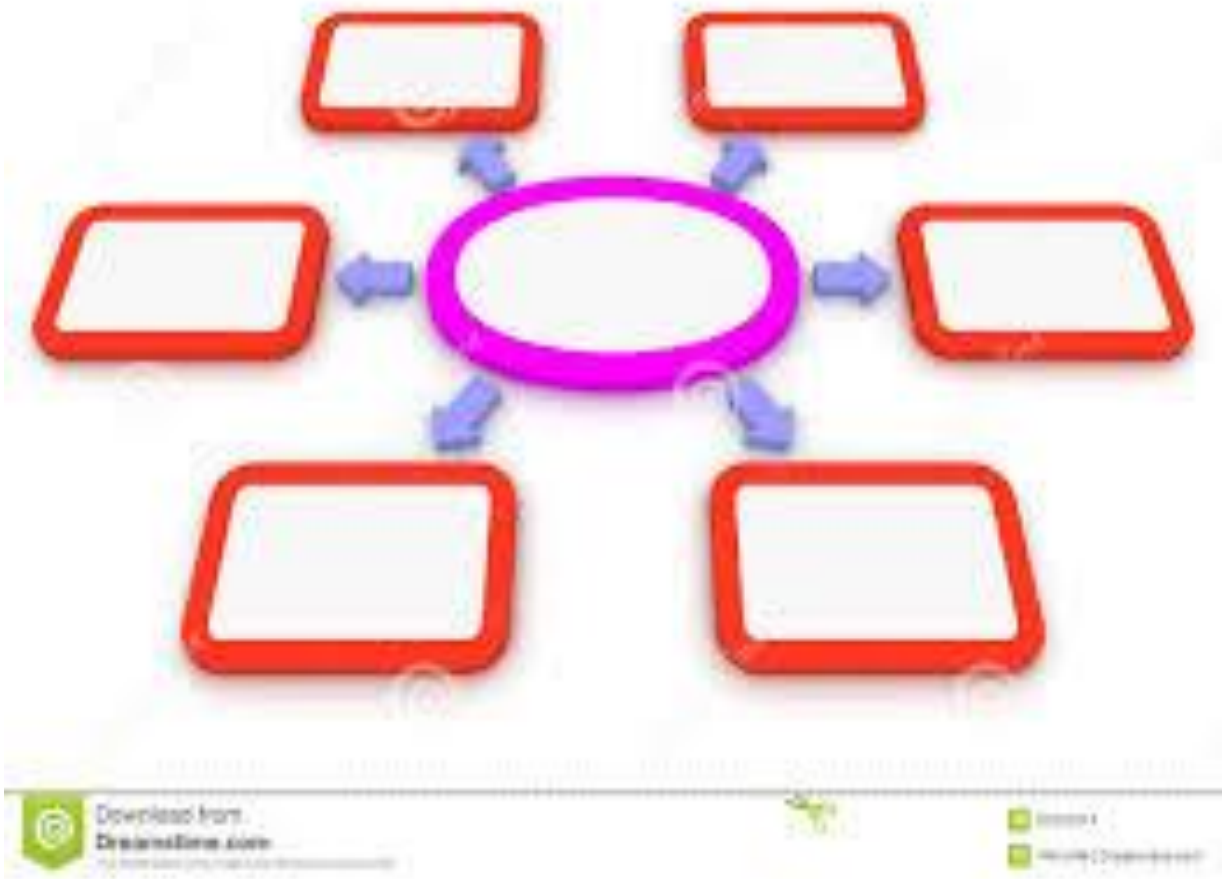


ANTIBIOTICS



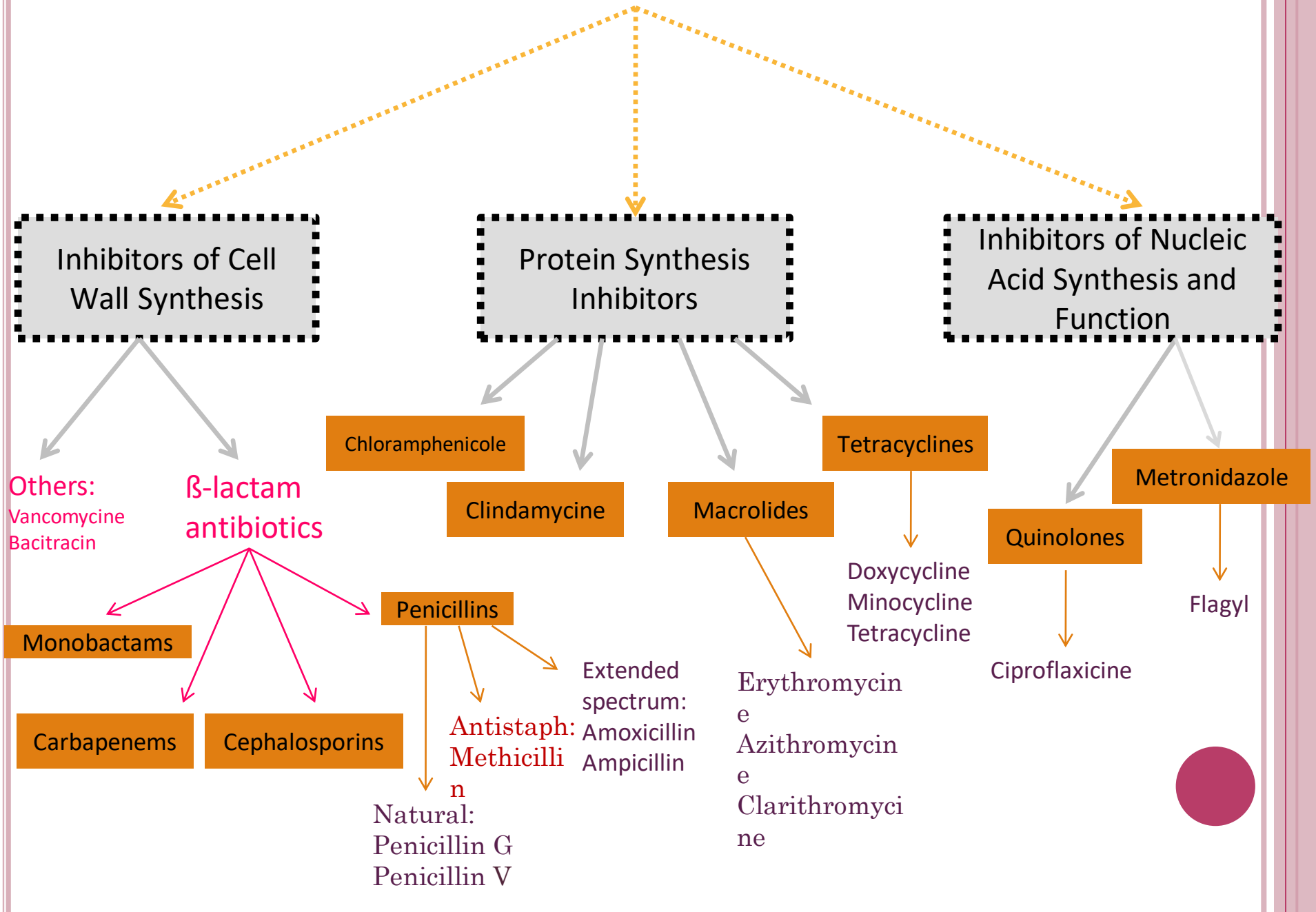


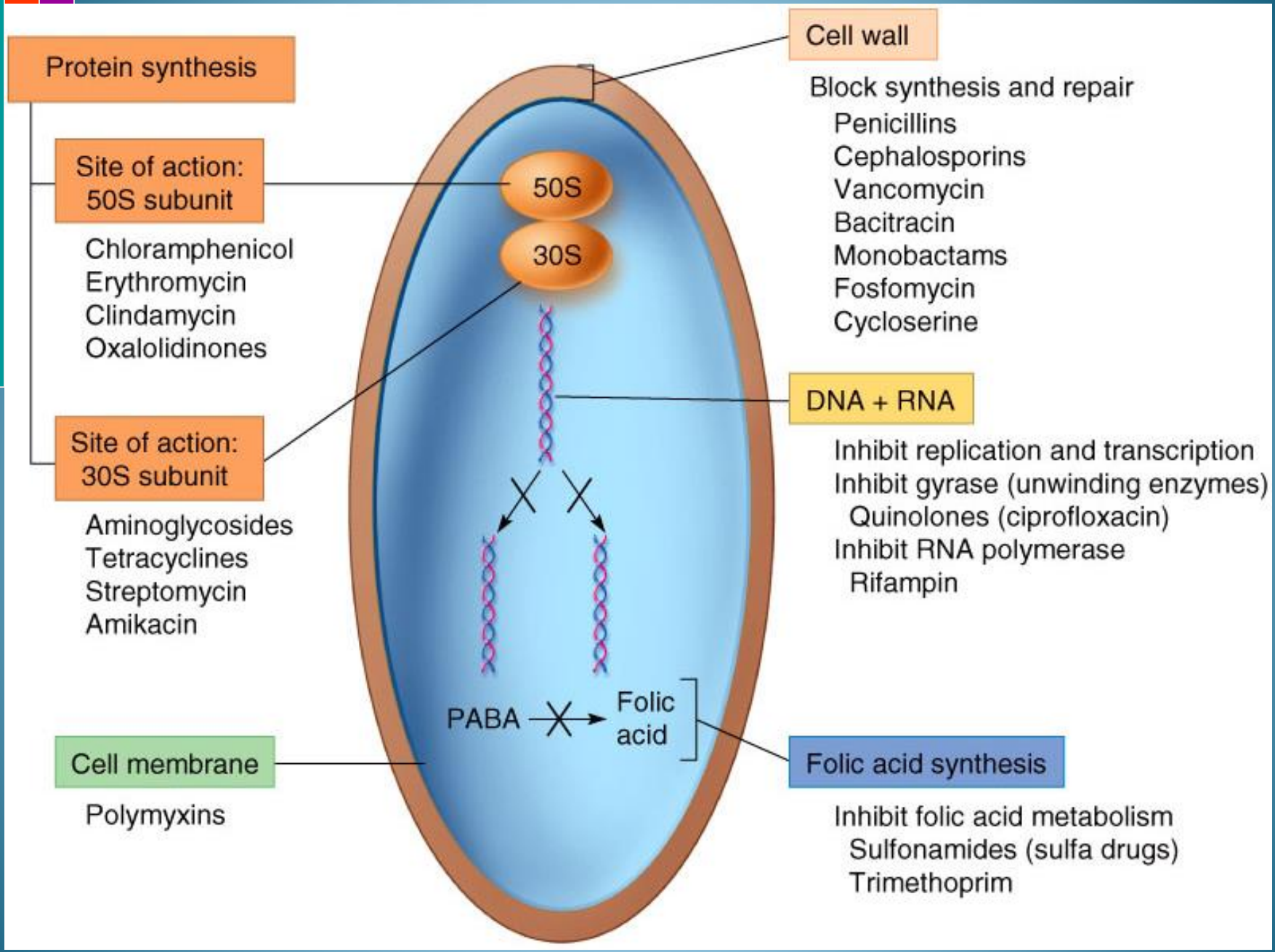
BY: Dr. Shekoufeh Atashpour



CLASSIFICATION

Classification of Antibiotics




Protein synthesis
Site of action: 50S subunit
Chloramphenicol
Erythromycin
Clindamycin
Oxalolidinones
Site of action: 30S subunit
Aminoglycosides
Tetracyclines
Streptomycin
Amikacin
Cell membrane
Polymyxins
50S
30S
PABA
Folic acid
Cell wall
Block synthesis and repair
Penicillins
Cephalosporins
Vancomycin
Bacitracin
Monobactams
Fosfomycin
Cycloserine
DNA + RNA
Inhibit replication and transcription
Inhibit gyrase (unwinding enzymes)
Quinolones (ciprofloxacin)
Inhibit RNA polymerase
Rifampin
Folic acid synthesis
Inhibit folic acid metabolism
Sulfonamides (sulfa drugs)
Trimethoprim

β-Lactam Antibiotics

Cephalosporins
- *First-generation*
  - Cefadroxil (Duricef)
  - Cefazolin (Ancef)
  - Cephalexin (Keflex)
- *Second-generation*
  - Cefaclor (Ceclor)
  - Cefamandole (Mandol)
  - Cefonicid (Monocid)
  - Ceforanide (Precef)
  - Cefotetan (Cefotan)
  - Cefoxitin (Mefoxin)
  - Cefprozil (Cefzil)
  - Cefuroxime (Zinacef)
  - Cefuroxime axetil (Ceftin)
- *Third-generation*
  - Cefdinir (Omnicef)
  - Cefditoren (Spectracef)
  - Cefixime (Suprax)
  - Cefotaxime (Claforan)
  - Cefpodoxime proxetil (Vantin)
  - Ceftazidime (Fortaz)
  - Ceftibuten (Cedax)
  - Ceftizoxime (Cefizox)
  - Ceftriaxone (Rocephin)
- *Fourth-generation*
  - Cefepime (Maxipime)
- *Fifth-generation*
  - Ceftaroline (Teflaro)

Carbacephems
- Loracarbef (Lorabid)

Monobactams
- Aztreonam (Azactam)

Penems
- Doripenem (Doribax)
- Ertapenem (Invanz)
- Imipenem (Primaxin)
- Meropenem (Merem)

Penicillins
- *Natural penicillins*
  - Penicillin G
  - Penicillin V
- *Aminopenicillins*
  - Ampicillin (Omnipen)
  - Amoxicillin (Amoxil)
  - Bacampicillin (Spectrobid)

β-Lactam Antibiotics

- *Penicillinase-resistant penicillins*
  - Isoxazolyl penicillins (dicloxacillin, oxacillin, cloxacillin)
  - Nafcillin (Unipen)
- *Combination with β-lactamase inhibitors*
  - Augmentin (amoxicillin plus clavulanic acid)
  - Timentin (ticarcillin plus clavulanic acid)
  - Unasyn (ampicillin plus sulbactam)
  - Zosyn (piperacillin plus tazobactam)

Aminoglycosides
- Amikacin (Amikin)
- Gentamicin (Garamycin)
- Neomycin (Mycifradin)
- Netilmicin (Netromycin)
- Streptomycin
- Tobramycin (Nebcin)

Protein synthesis inhibitors
- Azithromycin (Zithromax)
- Clarithromycin (Biaxin)
- Clindamycin (Cleocin)
- Chloramphenicol (Chloromycetin)
- Dalfopristin/Quinupristin (Synercid)
- Dirithromycin (Dynabac)
- Erythromycin (Erythrocin)
- Linezolid (Zyvox)
- Telithromycin (Ketek)
- Tetracyclines (doxycycline, minocycline, tetracycline, tigecycline)

Folate inhibitors
- Sulfadiazine
- Sulfadoxine (Fansidar)
- Trimethoprim (Trimpex)
- Trimethoprim-sulfamethoxazole (Bactrim, Septra)

Quinolones
- Ciprofloxacin (Cipro)
- Gemifloxacin (Factive)
- Levofloxacin (Levoquin)
- Moxifloxacin (Avelox)
- Norfloxacin (Noroxin)
- Ofloxacin (Floxin)

Daptomycin (Cubicin)

Televancin (Vibativ)

Vancomycin (Vancocin)

Metronidazole (Flagyl)

D. SPECTRUM OF ACTIVITY

NARROW SPECTRUM

Penicillin –G

Streptomycin

Erythromycin

BROAD SPECTRUM

- Tetracyclines

-Chloramphenicol

E. TYPE OF ACTION

PRIMARILY BACTERIOSTATIC

Sulphonamides

Tetracyclines

Chloramphenicol

Erythromycin

PRIMARILY BACTERIOCIDAL

Penicillin

Cephalosporins

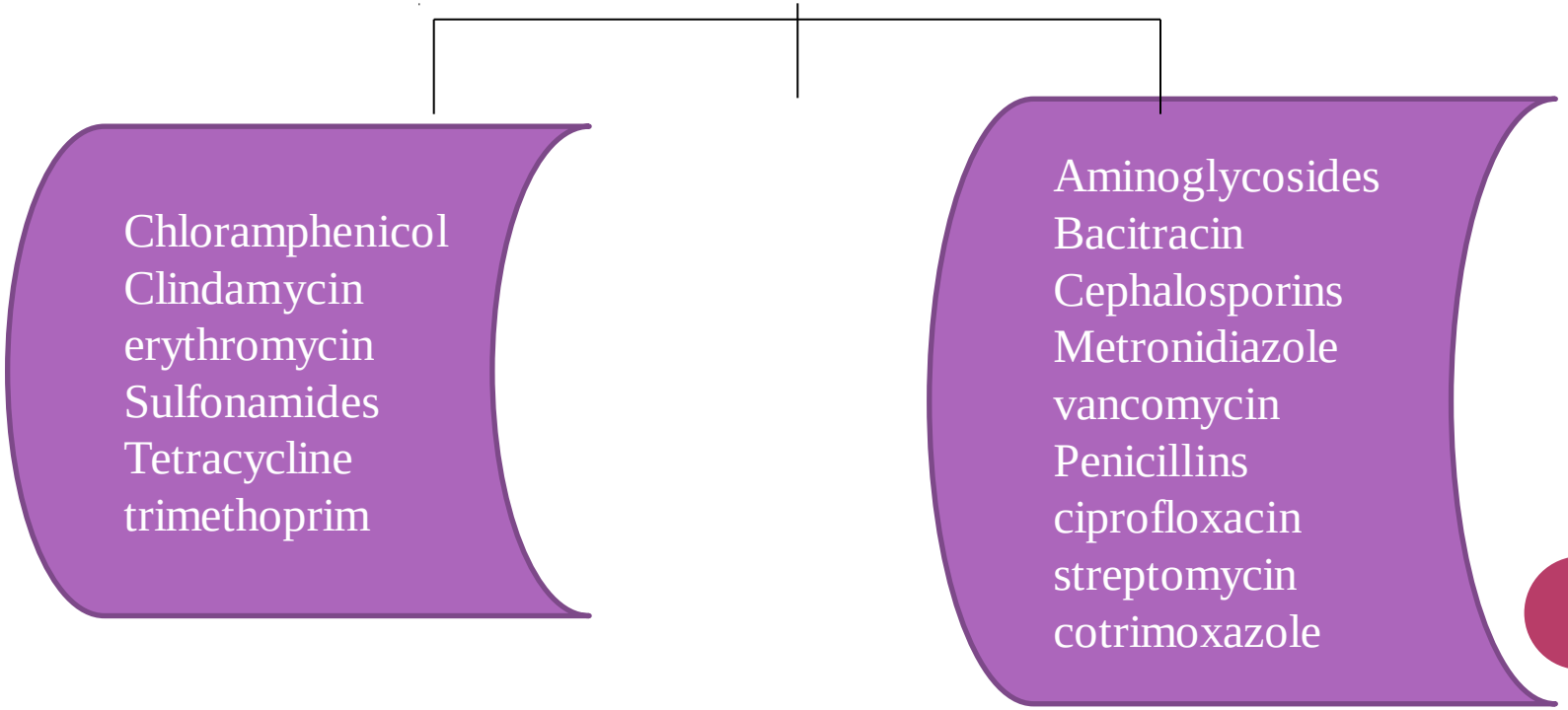
Aminoglycosides

Polypeptides

Ciprofloxacin

Bactericidal- the ability to kill the bacteria
Bacteriostatic- the ability to inhibit or retard the growth of bacteria

BACTERIOSTATIC V/S BACTERICIDAL



BETA-LACTAMS

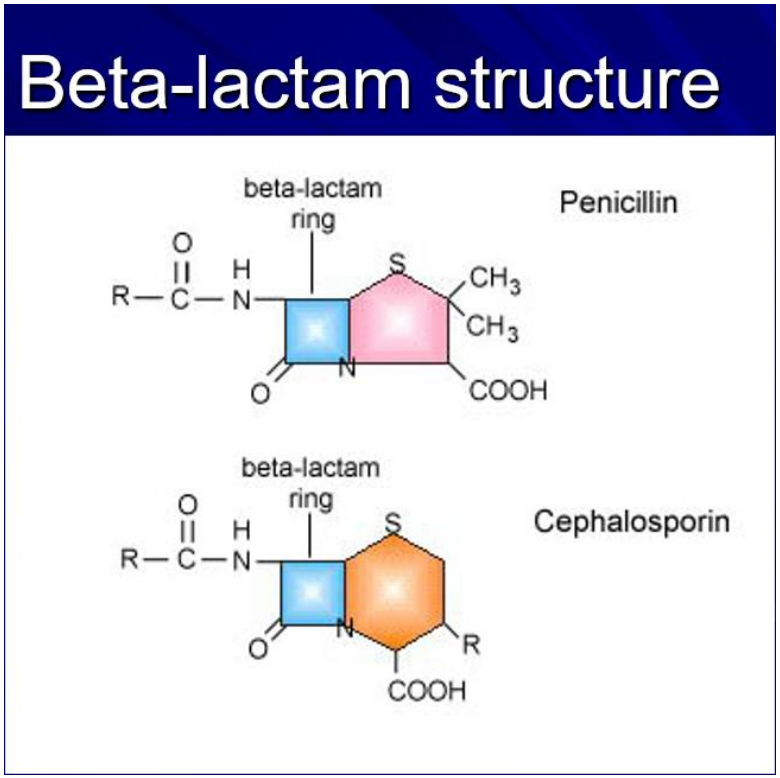
1. Penicillins (e. g. Penicillin G)

2. Cephalosporines (e. g. Cephalexin, Ceftriaxone)

3. Carbapenems (e. g. Imipenem)

4. Monobactams (e.g. Aztreonam)

Why are they called beta-lactam?



PENICILLINS

- Penicillin was first antibiotic to be used clinically in 1941.
- It was originally obtained from the fungus *Penicillium notatum*, but the present source is a high yeilding mutant of *P.chrysogenum.*

- Penicillinase is a beta lactamase developed by most staphylococci and many gram negative organisms, that is responsible for the breakdown of beta lactam ring

Classification of penicillins

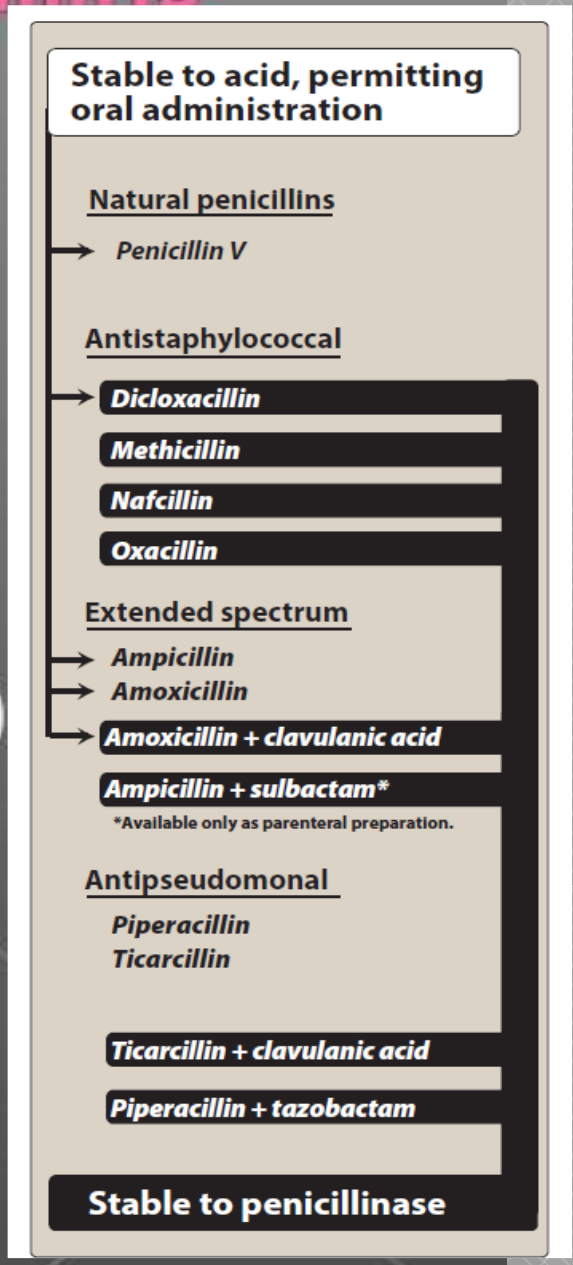
- Natural Penicillins
  - Penicillin G
  - Penicillin VK
- Semisynthetic penicillins:
  - Acid-stable penicillins

    (Penicillin V);
  - Penicillinase-Resistant Penicillins

    (Nafcillin, Oxacillin, Methicillin)
  - Extended-spectrum penicillins

    (Ampicillin and Amoxycillin);
  - Antipseudomonal

    (Carbenicillin, Ticarcillin)



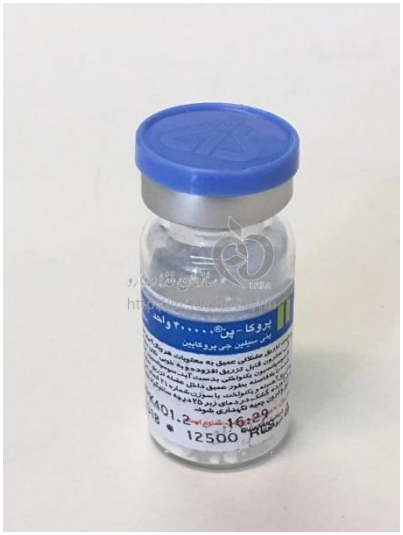
Penicillin V

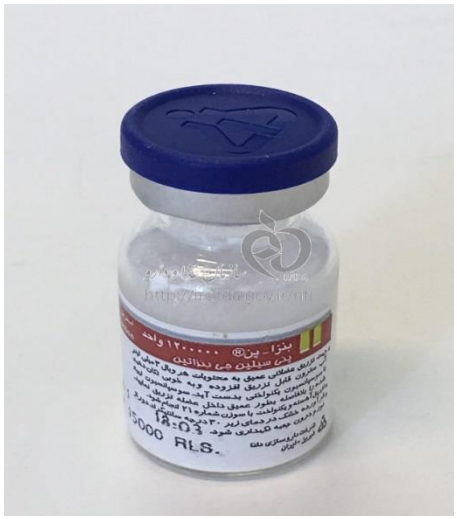
- *Tablet 500 mg*
- *Powder for oral suspension 125 & 250 mg/5 ml*

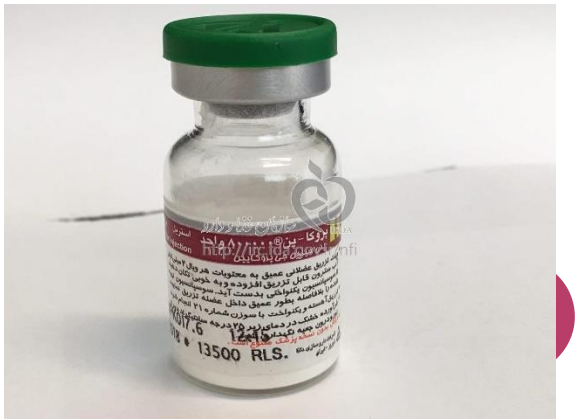
Oral loading dose of 1000 mg followed by 500 mg eve
six hours for 6 – 10 days.
For severe infections antibiotics is taken every 4 hours
maintain more constant serum level

Penicillin G

- Penicillin G sodium or potassium (1,000,000 & 5,000,000 U)
- Penicillin G procaine (400,000 & 800,000U) 24 hours
- Penicillin G benzathin (pen.LA, Pen 1,200,000 U, Penadur®) 21-28 days







Penicillin 6-3-3	**INJECTION, POWDER,**	**Benzathine penicillin G 600,000U+Potassium Penicillin G 300,000U+Procaine Penicillin G 300,000U**
Penicillin G Benzathin 1,200,000 U	**INJECTION,POWDER,EXTENDED RELEASE**	**-**
Penicillin G Benzathine 600,000 U	**INJECTION,POWDER,EXTENDED RELEASE**	**-**
Penicillin G Potassium 1,000,000 U	**INJECTION, POWDER,**	**-**
Penicillin G Potassium 5000000 U	**INJECTION, POWDER**	**-**
Penicillin G Procaine 400,000 U	**INJECTION, POWDER,**	**Potassium Penicillin G 100,000U+Procaine Penicillin G 300,000U**
Penicillin G procaine 800,000 U	**INJECTION, POWDER,**	**Potassium Penicillin G 200,000U+ Procaine Penicillin G 600,000U**
Penicillin G Sodium 5,000,000 U	**INJECTION, POWDER,**	**-**
Penicillin V 125 mg/5ml	**POWDER, FOR SOLUTION**	****(As Potassium) 200,000 U****
Penicillin V 250 mg/5ml	**POWDER, FOR SUSPENSION**	****(As Potassium)****
Penicillin V 500 mg	**TABLET**	****(As Potassium) 800.000 U****
Penicillin V Benzathine 200,000 IU/5ml	**POWDER, FOR SUSPENSION**	**-**
Penicillin V Benzathine 400,000 IU/5ml	**POWDER, FOR SUSPENSION**	**-**

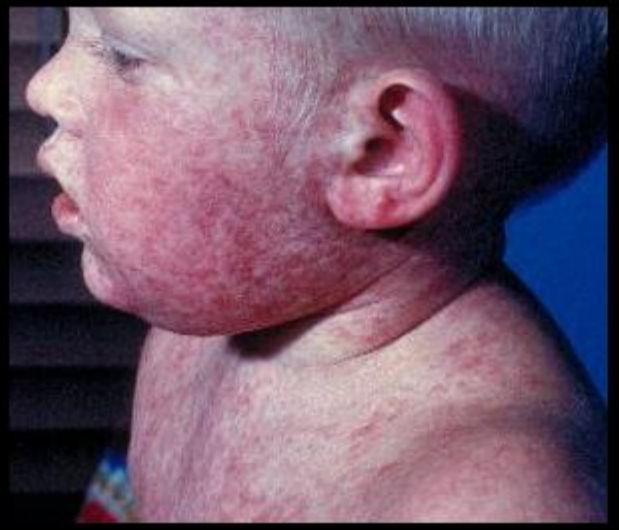
Uses :

PnG and PnV is the drug of choice for infections

1. Streptococcal infections
2. Pneumococcal infections
3. Meningococcal infections
4. Gonorrhoea
5. Syphilis
6. Diphtheria
7. Endocarditis
8. Oral and dental infection
9. Prophylactic uses (streptococcal infection, rheumatic fever, syphilis)

Greatest activity against gram-positive organisms, gram-negative cocci, and non-ß-lactamase producing anaerobes.
They have little activity against gram-negative rods

After 3 days of treatment beginning, J. K. complains of annoying pruritic rash on his trunk and limbs. What's happened?

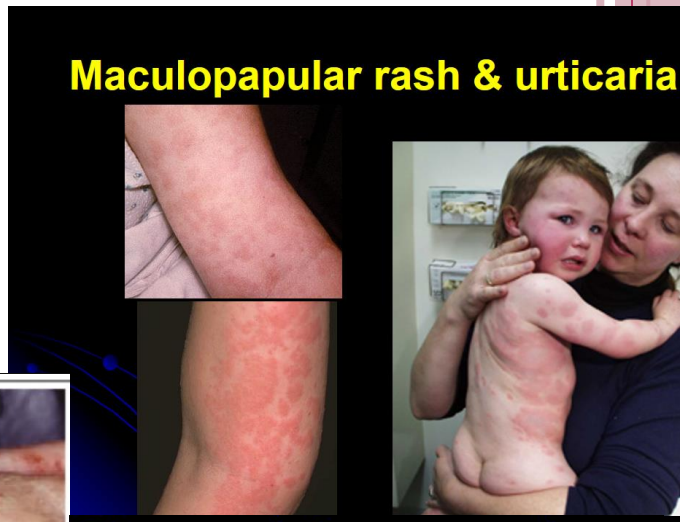


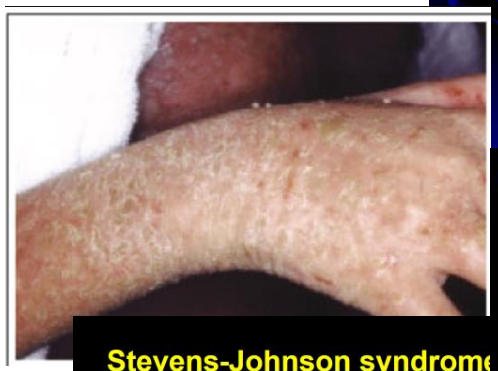
What are adverse effects of penicillin?

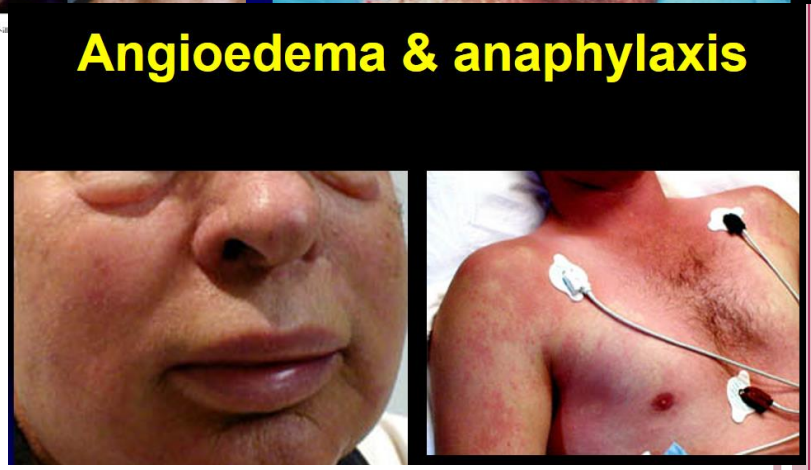
Adverse reactions of penicillins

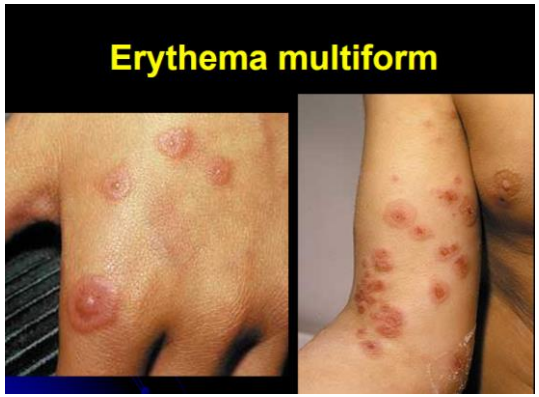
- **Hypersensitivity reaction:**
  - Maculopapular rash
  - Urticaria
  - Fever
  - Exfoliative dermatitis
  - Erythema multiform
  - Steven-Johnson syndrome
  - Immediate allergic reaction

  (early urticarial, angioedema, anaphylaxis)





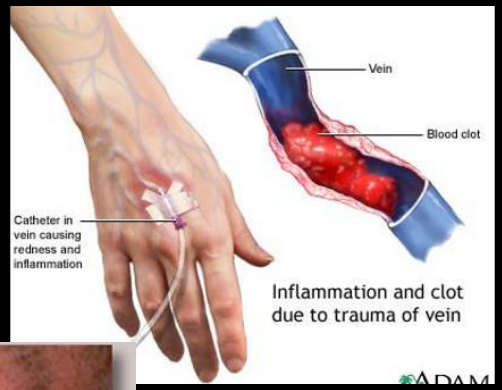


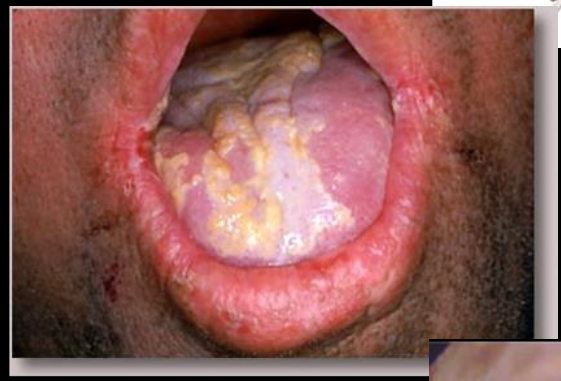


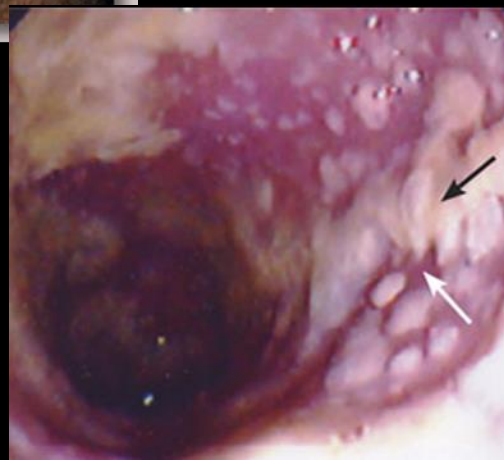
Adverse Reactions of Penicillins

Other Reactions:

- Nausea with or without vomiting
- Mild to moderate diarrhea
- Pain at the im injection site, Thrombophlebitis in iv injection site
- Electrolyte disturbances (high doses)
- Superinfections
  - Candidiasis
  - Pseudomembranous colitis







SEMI SYNTHETIC PENICILLINS

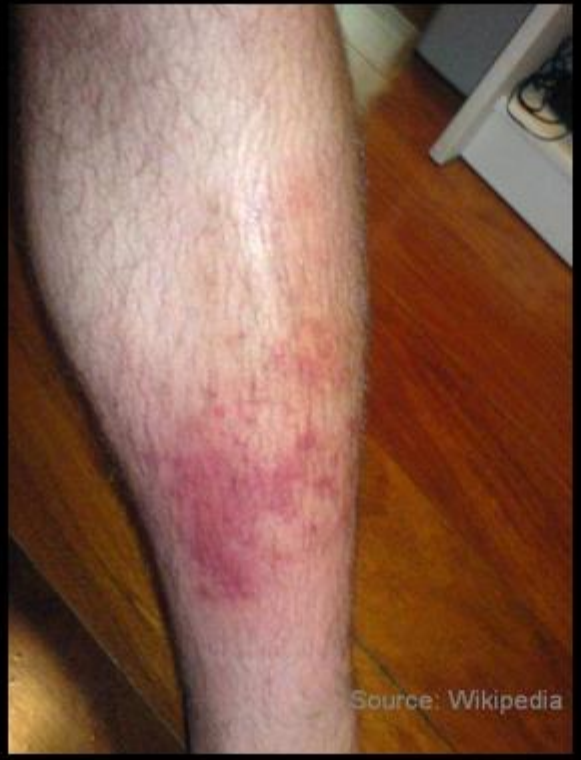
The major drawbacks of benzyl penicillin are :

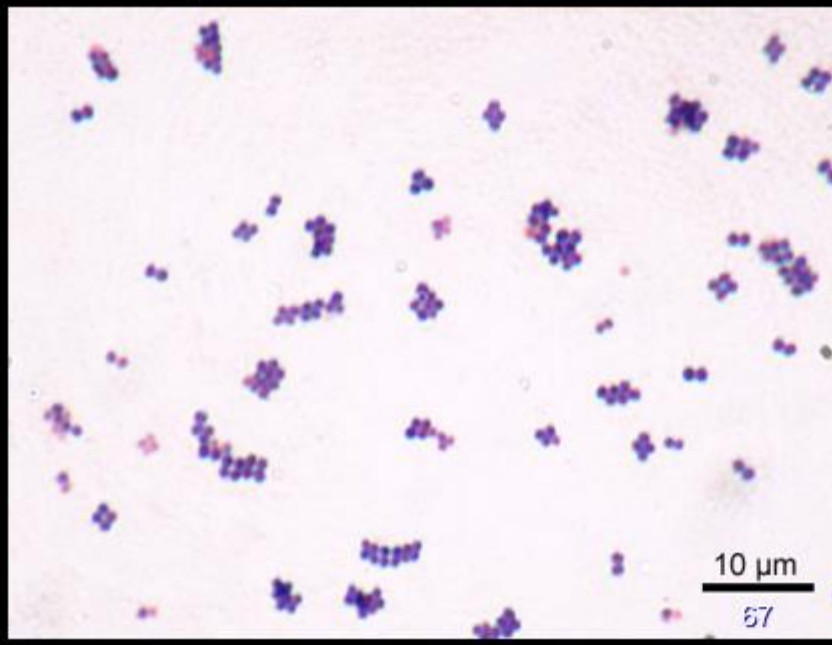
1. Inactivation by the gastric hydrochloric acid
2. Short duration of action
3. Activity mainly against gram +ve organism
4. Possibility of anaphylaxis

Attempts therefore have been made to synthesize pencillin free from such drawbacks.

Case 2: cellulitis

- Which microrganisms cause cellulitis?
- Do penicillin G & V work in this case? Why?
- What kind of penicillins, do you suggest?





Pencillinase resistant pencillins (antistaphylococcal Pen):

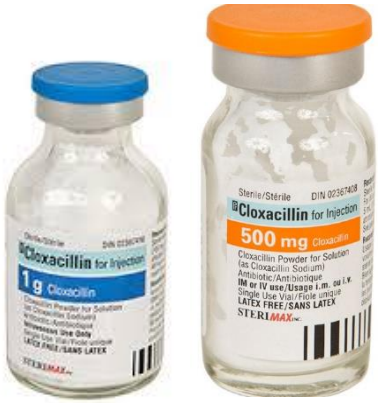
- Activity Against Staph and Strep producing beta-lactamase
- Lower activity against other G+-organism compared to natural Pen
- No activity against G- oraganism

Methicillin

1. Effective in staphylococci
2. It is given IM or IV (slow) in the dose of 1 gm every 4-6 hours.
3. Haematuria, albuminuria and reversible interstitial nephritis are the special adverse effect of methicillin.

- Cloxacillin

1. Weaker antibacterial activity.
2. Distributed throghtout the body, but highest concentration in kidney and liver. 30% excreted in urine.
3. Oral dose for adults 2-4 gm divided into 4 portions children 50-100mg/kg/day.
4. IM adults 2-12 gm/day, children 100-300 mg/kg/day every 4-6 hours.



Cloxacillin	**1g**	**INJECTION, POWDER,**
Cloxacillin	**250 mg**	**CAPSULE**
Cloxacillin	**250 mg**	**INJECTION, POWDER,**
Cloxacillin	**250 mg**	**TABLET**
Cloxacillin	**500 mg**	**CAPSULE**
Cloxacillin	**500 mg**	**INJECTION, POWDER,**
Cloxacillin	**500 mg**	**TABLET**

❑ Nafcillin :

More active than methicillin and cloxacillin but less active than PnG

80% of drug bonds with plasma proteins excreted by liver

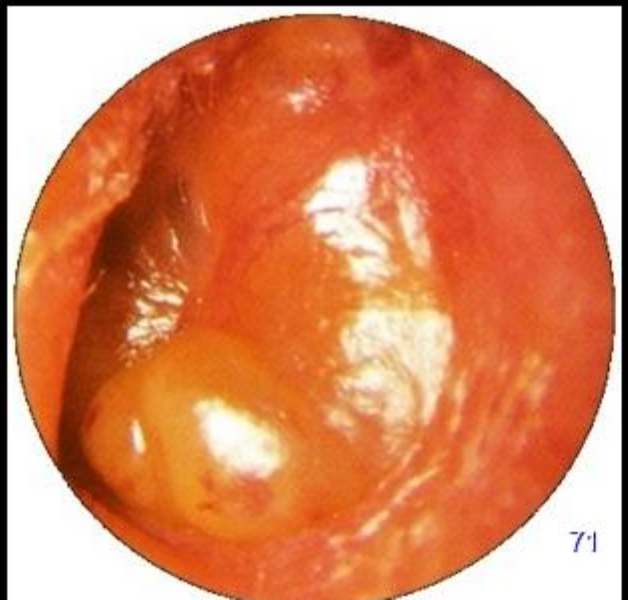
500mg- 2 g IV/IM q 4-6 hr/ 50-200mg/kg/day IV/IM q6hr

Nafcillin Sodium 1 g	INJECTION, POWDER,
Nafcillin Sodium 500 mg	INJECTION, POWDER,

Case 3

- V. O., a 10 month old, 9 Kg boy is brought to ED with a history of increased irritability and fever over last 2 days. He has been observed pulling his left ear and is refusing to take his bottle feedings.

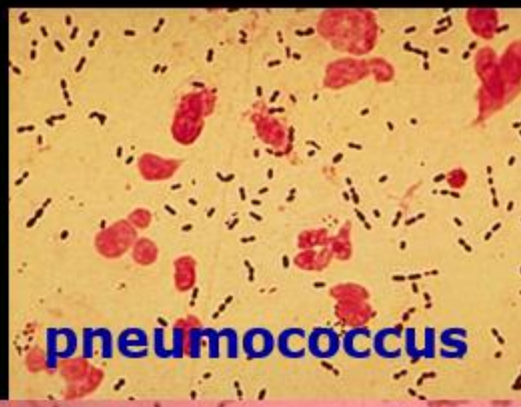
- PE: left tympanic membrane is red, inflamed, opaque, bulging and immobile.

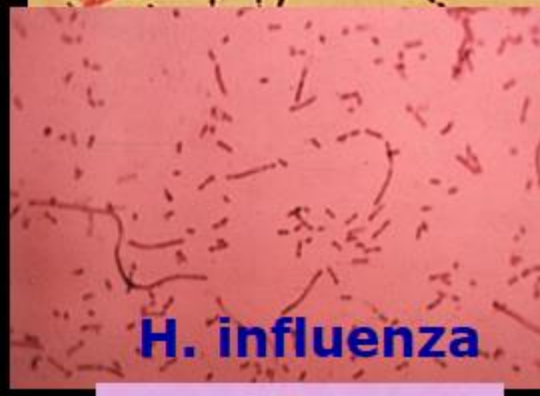


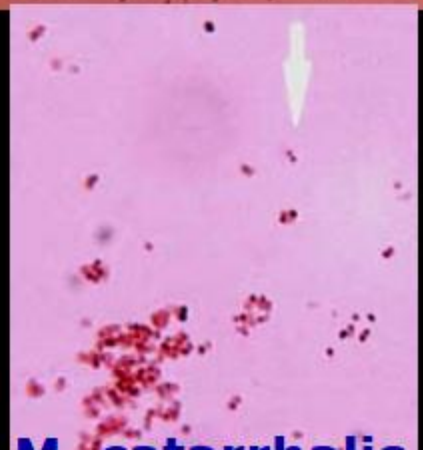
- He is diagnosed to suffer from acute otitis media.

Case 3: Acute otitis media

- Which microrganisms are the most common causes of otitis media?
- Do previously mentioned penicillins work?
- Why?
- What kind of penicillins, do you suggest?







(AMPICILLIN) آمپی سیلین

III) Extended spectrum pencillins :

1. Amino pencillins

    1. Ampicillin –

    - Antibacterial activity is similar to that of PnG that is more effective than PnG against a variety of gram-ve bacteria
    - Drug is effective against H.influenzae strep.viridans, N.gonorrhea, Salmonella, shigellae, Klebsilla and enterococci.

    Absorption, fate and excretion :

    - Oral absorption is incomplete but adequate
    - Food interferes with absorption

Dose : 0.5-2 gm oral/IM or IV depending on severity of infection every 6 hours

Children : 25-50 mg/kg/day

USES :

- Urinary tract infections
- Respiratory tract infections
- Meningitis
- Gonorrhoea
- Typhoid fever
- Septicaemias

Ampicillin 1 g	INJECTION, POWDER,
Ampicillin 250 mg	INJECTION, POWDER,
Ampicillin 500 mg	INJECTION, POWDER,
Ampicillin 125 mg/5ml	POWDER, FOR SUSPENSION
Ampicillin 250 mg	CAPSULE
Ampicillin 250 mg/5ml	POWDER, FOR SUSPENSION
Ampicillin 500 mg	CAPSULE
Ampicillin/Sulbactam 2 g /1 g (3g)	INJECTION, POWDER
Ampicillin/Sulbactam 1 g /0.5 g (1.5 g)	INJECTION, POWDER+C19

Adverse effects :

- Diarrhea is frequent
- Skin rashes is more common
- Unabsorbed drug irritates lower intestines
- Patient with history of hypersensitivity to PnG should not be given ampicillin.

AMOXYCILLIN :

- Antibacterial spectrum is similar to ampicillin but less effective than ampicillin for shigellosis.
- Oral absorption is better; food does not interfere; higher and more sustained blood levels are produced.
- It is less protein bond and urinary excretion is higher than that of ampicillin.
- Incidence of diarrhea is less

Dose : 0.25-1 g TDS oral;

- Typhoid
- Bronchitis
- Urinary infection
- Gonorrhoea
- H. pylori peptic ulcer

Amoxicillin 250 mg	POWDER, FOR SUSPENSION
Amoxicillin 125 mg	TABLET, DISPERSIBLE
Amoxicillin 250 mg	TABLET, CHEWABLE
Amoxicillin 250 mg	TABLET, DISPERSIBLE
Amoxicillin 500 mg	TABLET
Amoxicillin 125 mg/5ml	POWDER, FOR SUSPENSION
Amoxicillin 250 mg	CAPSULE
Amoxicillin 250 mg/5ml	POWDER, FOR SUSPENSION
Amoxicillin 400 mg/5ml	POWDER, FOR SUSPENSION
Amoxicillin 500 mg	CAPSULE
Amoxicillin 200 mg/5ml	POWDER, FOR SUSPENSION

Case 3: Acute otitis media

- After 2 days of treatment, V. O.'s mother calls you and says there is no improvement in her son's condition.

What is the possible causes?
What would you do?

Co-Amoxiclav

- *Co-amoxiclav= amoxicillin + calvulanic acid*
- *Clavulanic acid is a β-lactamase inhibitor.*
- *Sulbactam & tazobactam are congeners of calvulanic acid*
- *Co-amoxiclav is effective against **some** β-lactamase producing bacteria including: H. influenza, M. catarralis, E.coli, Staphylococci, Gonococci, B. fragilis.*
- *The main indications are: otitis media, sinusitis, animal and human bite*

Co-amoxiclav 125/31.25 mg	POWDER, FOR SUSPENSIO
Co-amoxiclav 125/31.25 mg/5ml	POWDER, FOR SUSPENSIO
Co-amoxiclav 200/28.5 mg/5ml	POWDER, FOR SUSPENSIO
Co-amoxiclav 250/125 mg	TABLET
Co-amoxiclav 250/62.5 mg	POWDER, FOR SUSPENSIO
Co-amoxiclav 250/62.5 mg/5ml	POWDER, FOR SUSPENSIO
Co-amoxiclav 400/57 mg/5ml	POWDER, FOR SUSPENSION
Co-amoxiclav 500/125 mg	TABLET
Co-amoxiclav 500/125 mg	TABLET
Co-amoxiclav 500/125 mg	TABLET, DISPERSIBLE
Co-amoxiclav 600/42.9 mg /5ml	POWDER, FOR SUSPENSION
Co-amoxiclav 250/125 mg	TABLET
Co-amoxiclav 500/100 mg	INJECTION, POWDER, FOR SOLUTION
Co-amoxiclav 1000/200 mg	INJECTION, POWDER, FOR SOLUTION

Antipseudomonal penicillins: piperacillin

Antimicrobial Activity:

- *Greatest activity against G^- bacteria (eg. Pseudomonas, Enterobacter, Klebsiella, E. coli, Proteus)*

- *Weaker than penicillin G against G^+ bacteria.*

Note: They are sensitive to many beta-lactamases

- *Piperacillin + tazobactam is now available*

Antipseudomonal penicillins: piperacillin

Clinical Uses:

- Treatment of serious infections (usually, nosocomial) caused by G^- bacteria (generally with an aminoglycoside)

Piperacillin Sodium/Tazobactam Sodium 2g/250mg	INJECTION, POWDER
Piperacillin Sodium/Tazobactam Sodium 3g/375mg	INJECTION, POWDER,
Piperacillin Sodium/Tazobactam Sodium 4g/500mg	INJECTION, POWDER
Piperacillin 1 g	INJECTION, POWDER,
Piperacillin 2 g	INJECTION, POWDER,

Usual dosage range:

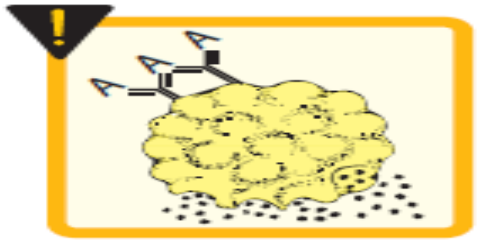
IV: 3-4g/dose q4-6 hr, not exceed 24g/24hr

IM: 2-3g/dose **q6-12hr,** not exceed 24g/24hr

Antibiotic (Route of Administration)	Adult Dose	Pediatric Dose[1]	Neonatal Dose[2]	Adjusted Dose as a Percentage of Normal Dose for Renal Failure Based on Creatinine Clearance (Cl_{cr})	
				Cl_{cr} Approx 50 mL/min	*Cl_{cr} Approx 10 mL/min*
Penicillins					
Penicillin G (IV)	1–4 × 10^6 units q4–6h	25,000–400,000 units/kg/d in 4–6 doses	75,000–150,000 units/kg/d in 2 or 3 doses	50–75%	25%
Penicillin V (PO)	0.25–0.5 g qid	25–50 mg/kg/d in 4 doses		None	None
Antistaphylococcal penicillins					
Cloxacillin, dicloxacillin (PO)	0.25–0.5 g qid	25–50 mg/kg/d in 4 doses		100%	100%
Nafcillin (IV)	1–2 g q4–6h	50–100 mg/kg/d in 4–6 doses	50–75 mg/kg/d in 2 or 3 doses	100%	100%
Oxacillin (IV)	1–2 g q4–6h	50–100 mg/kg/d in 4–6 doses	50–75 mg/kg/d in 2 or 3 doses	100%	100%
Extended-spectrum penicillins					
Amoxicillin (PO)	0.25–0.5 g tid	20–40 mg/kg/d in 3 doses		66%	33%
Amoxicillin/potassium clavulanate (PO)	500/125 tid–875/125 mg bid	20–40 mg/kg/d in 3 doses		66%	33%
Piperacillin (IV)	3–4 g q4–6h	300 mg/kg/d in 4–6 doses	150 mg/kg/d in 2 doses	50–75%	25–33%
Ticarcillin (IV)	3 g q4–6h	200–300 mg/kg/d in 4–6 doses	150–200 mg/kg/d in 2 or 3 doses	50–75%	25–33%

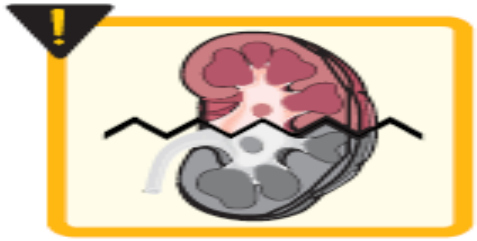
[1]The total dose should not exceed the adult dose.

[2]The dose shown is during the first week of life. The daily dose should be increased by approximately 33–50% after the first week of life. The lower dosage range should be used for neonates weighing less than 2 kg. After the first month of life, pediatric doses may be used.

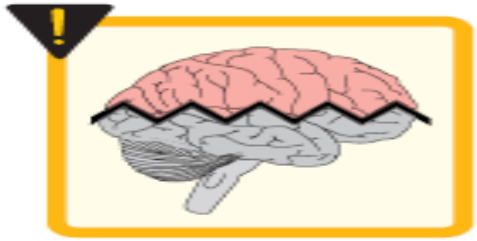


Hypersensitivity

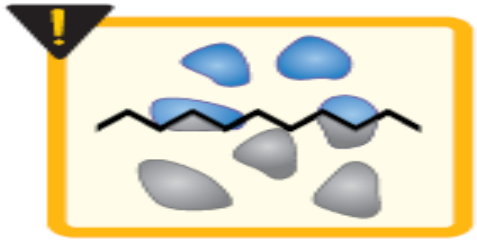
Diarrhea



Nephritis



Neurotoxicity



Hematologic toxicities

CEPHALOSPORINS

- Group of semi-synthetic antibiotics derived from cephalosporin, “C” obtained from fungus *Cephalosporium.*
- Chemically related to penicillins (contain β-lactum ring), Like penicillin acts similar
- Have been classified as first, second, third and fourth generation.

Based on:

- ❖When the were introduced
- ❖spectrum of activity
- ❖Resistance to β-lactamase
- ❖Pharmacokinetics

CEPHALOSPORINES: classification

First Generation:
cephalexin, cefazolin

Second Generation:
cefuroxime

CEPHALOSPORINS

- **Third Generation:** cefixime, cefotaxime, ceftriaxone, ceftazidime, ceftizoxime

CEPHALOSPORINS

- **Fourth Generation:** cefepime

- **Fifth Generation:** ceftobiprole

Cephalosporins

Gram + activity — 1st Generation — β-lactamase sensitive

2nd Generation

Gram — activity — 3rd Generation — β-lactamase resistant

4th Generation: good Gram + and Gram - activity;
more resistant to β-lactamase

FIRST GENERATION

These are active against gram-positive bacteria but weaker against gram-negative bacteria. *e.g.Cephalothin, cephalexin.*

SECOND GENERATION

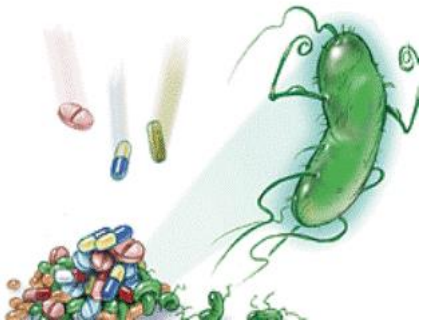
More active against gram-negative organisms with some members active against anaerobes. *e.gCefuroxime, Cefaclor*

THIRD GENERATION

Very active against gram–negative and gram-positive, but not effective against anaerobes. *e.gCefotaxime, Cefixime*

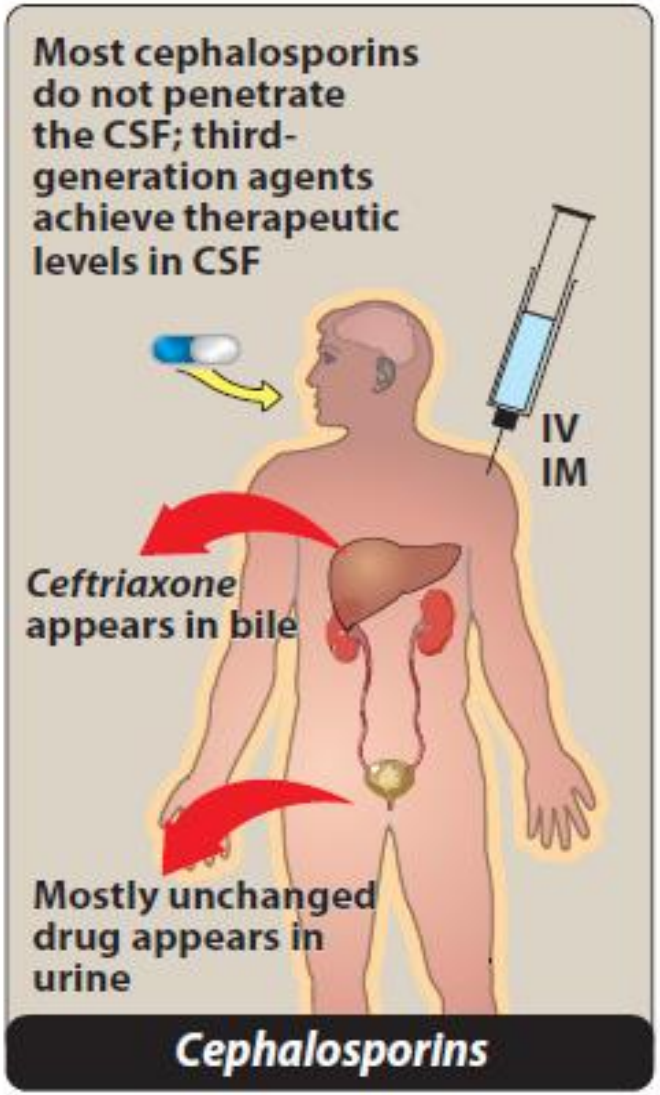
FOURTH GENERATION

Very effective against anaerobes and resistant to beta lactamase *.e.g.Cefipime*



Advantages with Newer generations

- Each newer generation of cephalosporins has significantly greater gram-negative antimicrobial properties than the preceding generation, in most cases with decreased activity against gram-positive organisms. Fourth generation cephalosporins, however, have true broad spectrum activity



Generations	First	second	Third
Drugs	Cephalexin (O) Cefadroxil (O) Cefazolin (im, iv) Cephalothin (o,im)	Cefaclor (o) Cefuroxime (o) Cefoxatin (im, iv) Cefotetan (im)	Cefixime (o) Ceftriaxone (o) Cefotaxime (im, iv) Cefoperazone
Antibacterial spectrum			
G+Ve	+++	++	+
G -ve	+	++	+++
Anaerobes	Efective against B.Fragalis	Very effective (cefotetan & cefoxitin)	Effective (Cefoperazone)
Pseudomonas	- -	--	effective
Salmonella	--	-	effective
Betalactamase	Resistant to staphylococcal	H, resistant to G-ve	Highly resistant
BBB	---	Only cefuroxime	Most drugs

Cephalosporins Indications

- ***1st Generation (cefazolin, cephalexin):***
  - **Surgical site *infections*,**
  - ***Substitution for penicillins in some G^+ (streptococcal and staphylococcal) and G^- (eg. UTI) infections***

- ***2nd Generation (cefuroxime):***
  - ***Sinusitis & Otitis media,***
  - ***G^--induced pneumonia***
  - ***Gonorrhoea***

Cephalosporins Indications

3rd Generation:

Serious infections caused by G⁻ bacteria like Klebsiella, E. coli, Enterobacter, Proteus, Haemophilus and P.aeroginosa. Microorganisms which become resistant to the older agents (e.g. Pneumococcus, Gonococcus, Salmonella, H. influenzae & ...)

4th Generation:

Infections caused by agents resistant to the 3rd generation (G- bacilli nosocomial infections)

Cephalosporins Indications

Note: ***All the cephalosporins are ineffective against Enterococci & Listeria***

Cephalosporins Adverse Reactions

Hypersensitivity reactions (maculopapular rash, urticaria bronchospasm, anaphylaxis)

GI upset, diarrhea

Pain at the injection site, thrombophlebitis

Biliary sludge with ceftriaxone (especially in children)

Cefalexin	125 mg		POWDER, FOR SUSPENSION
Cefalexin	125 mg/5ml		POWDER, FOR SUSPENSION
Cefalexin	250 mg	25-50mg/kg/day, Q6h	CAPSULE
Cefalexin	250 mg		POWDER, FOR SUSPENSION
Cefalexin	250 mg		TABLET
Cefalexin	250 mg/5ml		POWDER, FOR SUSPENSION
Cefalexin	500 mg		CAPSULE
Cefalexin	500 mg		TABLET

1-4g/day, Q6h

Cefazolin	**1 g**	25-100 mg/kg/day IV, IM Q6-8h	**INJECTION, POWDER**	0.5-2gIV, Q8h
Cefazolin	**250 mg**		**INJECTION, POWDER**	
Cefazolin	**500 mg**		**INJECTION, POWDER**	

Cephalothin 1 g

INJECTION, POWDER

50-150mg/kg/day
IV, IM , Q6h

1-2g IV, IM
Q6h

Cefuroxime	1.5 g	30mg/kg/day PO divided Q12h 75-150mg/kg/day IV/IM Divided Q8h	INJECTION, POWDER
Cefuroxime	125 mg		TABLET
Cefuroxime	125 mg/5ml		POWDER, FOR SUSPENSION
Cefuroxime	250 mg		INJECTION, POWDER
Cefuroxime	250 mg		TABLET
Cefuroxime	250 mg/5ml		POWDER, FOR SUSPENSION
Cefuroxime	750 mg		INJECTION, POWDER
Cefuroxime	500 mg		TABLET

250-500mg PO Q12h
500-750mg IV/IM q12h

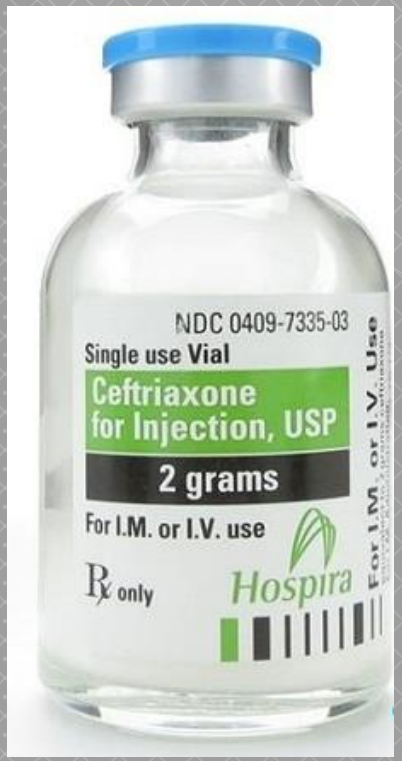
Cefixime	100 mg		POWDER, FOR SUSPENSION
Cefixime	100 mg/5ml		POWDER, FOR SUSPENSION
Cefixime	200 mg	8mg/kg/day QD or divided Q12h	CAPSULE
Cefixime	200 mg		TABLET
Cefixime	400 mg		CAPSULE
Cefixime	400 mg		TABLET
Cefixime	50 mg		POWDER, FOR SUSPENSION

400mg/day QD or divided Q12h

Cefotaxime	**1 g**	50/200mg/kg/day IV,IM Divided Q6-8hr	**INJECTION, POWDER**	0.5-2 g Iv, IM Q6-12h Max: 12g/day
Cefotaxime	**500 mg**		**INJECTION, POWDER**	

Ceftazidime (As Pentahydrate)	1 g	30-50mg/kg, IV, Q8-12h	INJECTION, POWDER	1-2 g, IV/IM, Q8-12h
Ceftazidime (As Pentahydrate)	2 g		INJECTION, POWDER	
Ceftazidime (As Pentahydrate)	500 mg		INJECTION, POWDER	

Ceftriaxone	250 mg	50-100 mg/kg/day IV, IM Q12-24h	INJECTION, POWDER	1-2g, IV, IM, Q12-24h
Ceftriaxone	500 g		INJECTION, POWDER	
Ceftriaxone	1 g		INJECTION, POWDER	
Ceftriaxone	2 g		INJECTION, POWDER	



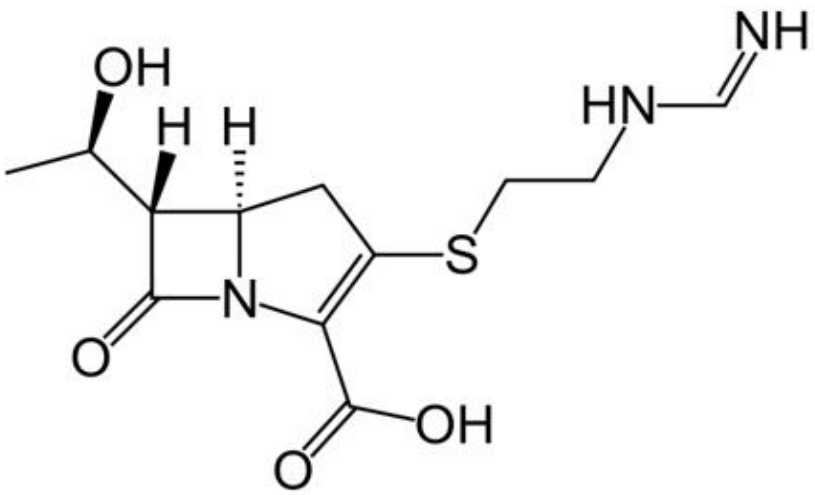
Ceftizoxime	**1 g**	100-200mg/kg IV Q8-12h	**INJECTION, POWDER**	0.5-2g IV, IM Q8-12h
Ceftizoxime	**500 mg**		**INJECTION, POWDER**	

Cefepime 500mg	50mg/kg IV Q8-12h	**INJECTION, POWDER**	0.5-2g IV Q8-12h
Cefepime 1 g		**INJECTION, POWDER**	
Cefepime 2 g		**INJECTION, POWDER**	

Carbapenems: imipenem & meropenem

Antimicrobial activity:

- wide spectrum (G^+ & G^- bacteria), anaerobes
- MRS & Cl. Difficile are resistant



Imipenem /Cilastatin	250/250 mg
Imipenem /Cilastatin	500/500 mg
Imipenem /Cilastatin	750/750 mg

500mg, 1 g

Carbapenems: imipenem & meropenem

Clinical uses:

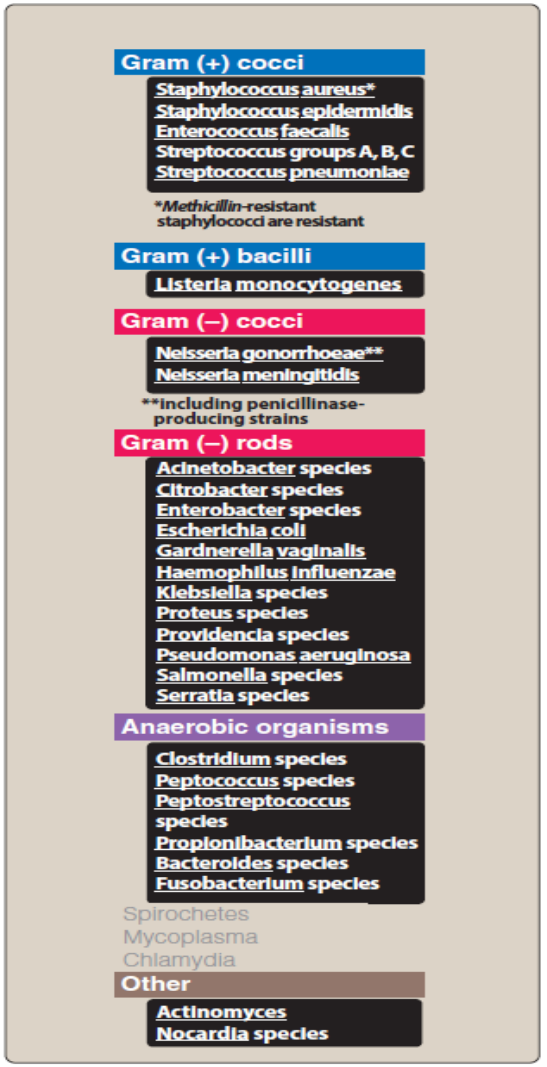
Nosocomial infections

ADRs:

Nausea & vomiting (1-20%)

Other reactions same as penicillins

Convulsion with imipenem (1.5 %; meropenem is safer)



Vancomycin

Antimicrobial activity:

G+ microorganisms including: methicillin-resistant staphylococci, penicillin resistant enterococci and pneumococci

Some anaerobics including: Cl. Difficile

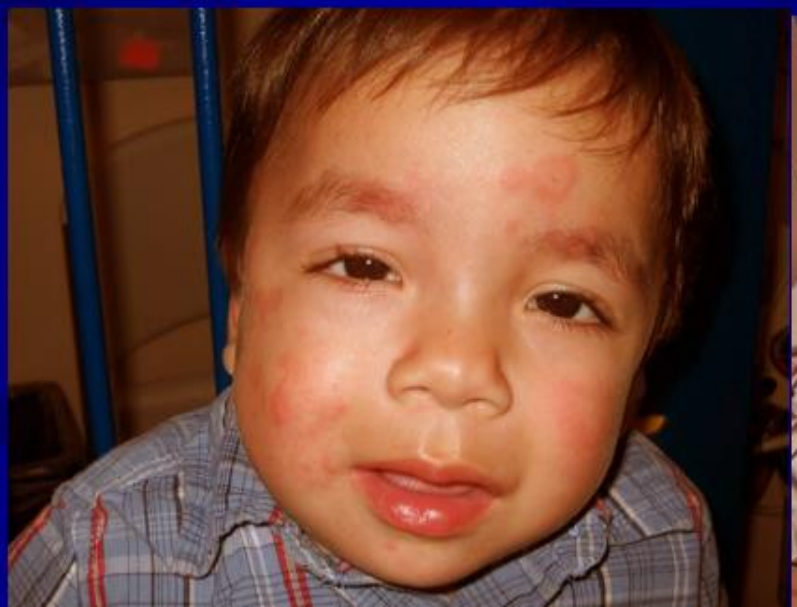
No GI absorption
Renal excretion

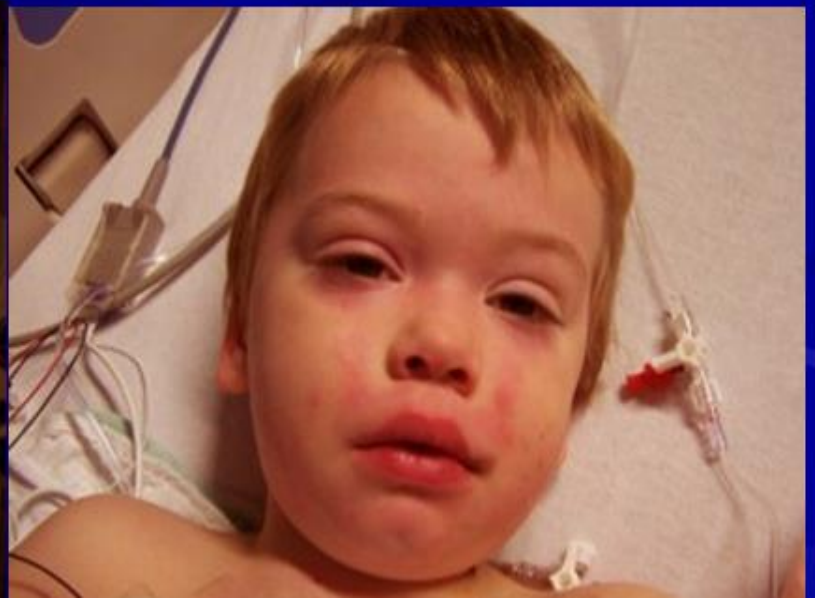
Vancomycin

- ***Clinical Uses:***
  - MRS infections
  - Penicillin resistant enterococci endocarditis and bacteremia
  - Highly penicillin-resistant pneumococci meningitis
  - Pseudomemberanous colitis (oral form of vancomycin)

Vancomycin: adverse effects

- Red man syndrome
  - Eerythema of the neck and back, chill & fever, hypotension, paresthesia





Vancomycin: adverse effects

اطلاعیه شماره ۸۶

تاریخ: ۱۳۸۷/۱۰/۳۰

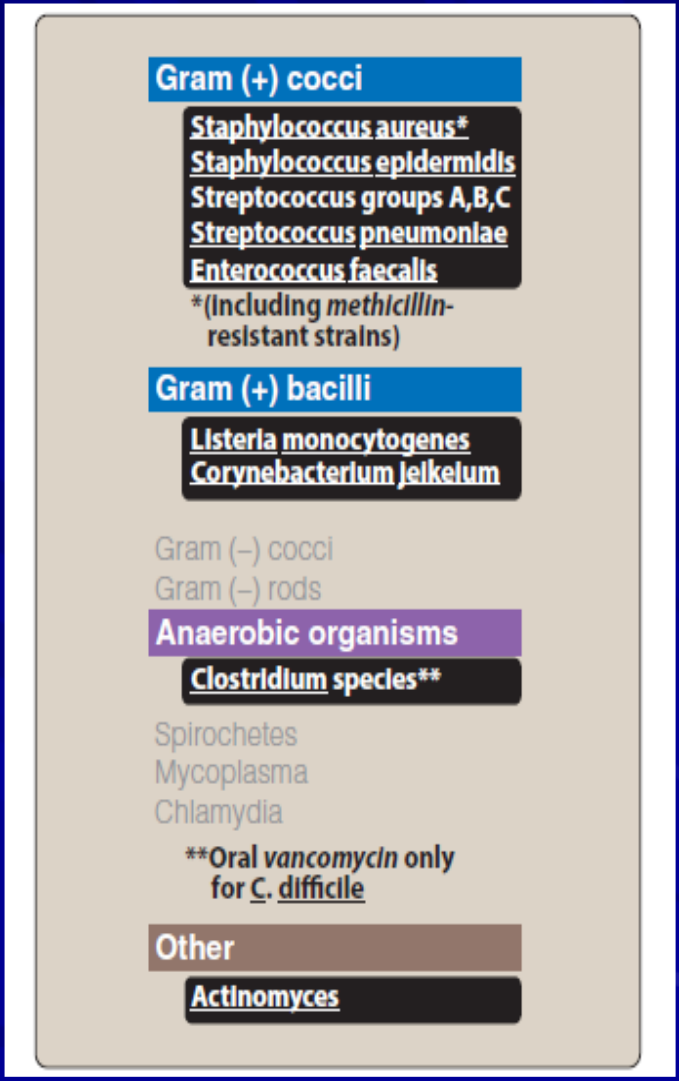
هشدار مجدد در خصوص عوارض ناشی از انفوزیون سریع وانکومایسین

واکنشهای حساسیتی از جمله سندرم گردن قرمز یا Red-neck Syndrome از دسته عوارض ناشی از تزریق وانکومایسین می باشند که تاکنون طی ۳۸۱ مورد گزارش ارسالی در مرکز ADR به ثبت رسیده ا ند. رعایت مدت زمان انفوزیون حداقل به مدت یک ساعت می تواند منجر به کاهش فراوانی وقوع و یا شدت بروز این قبیل عوارض شود.

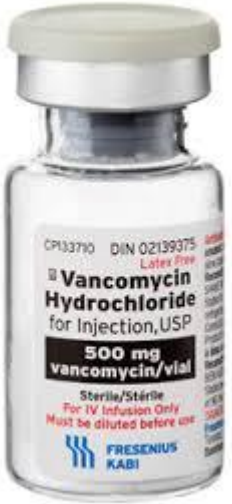
پیرو اطلاعیه شماره ۶۶ مرکز ثبت و بررسی عوارض ناخواسته داروها (ADR) در خصوص انفوزیون وریدی وانکومایسین، به اطلاع همکاران محترم می رساند که این مرکز تا پایان دی ماه ۱۳۸۷، ۳۸۱ مورد گزارش عارضه متعاقب

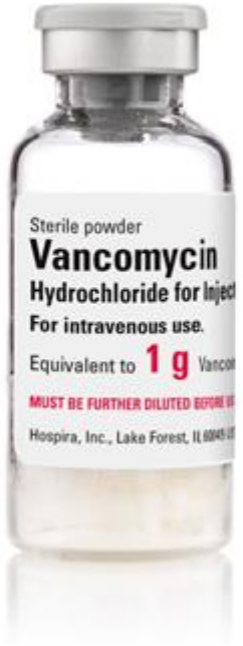
Vancomycin: adverse effects

- Red man syndrome
  - Eerythema of the neck and back, chill & fever, hypotension, paresthesia
- Macular rashes
- Phlebitis
- Ototoxicity & nephrotoxicity (in combination with other ototoxic/nephrotoxic drugs)



Vancomycin 250 mg	CAPSULE LIQUID FILLED
Vancomycin 500 mg/6ml	POWDER, FOR SUSPENSION
Vancomycin (As Hydrochloride) 1 g	INJECTION, POWDER,
Vancomycin (As Hydrochloride) 500 mg	INJECTION, POWDER,





Is it possible for bacteria to become resistant to Vancomycin?

Unforatunately, Yes

What is the solution?

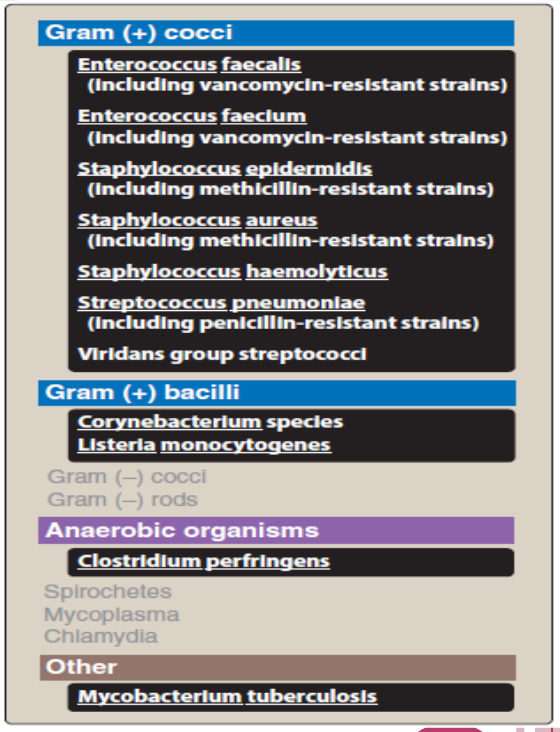
LINEZOLIDE

Antibacterial properties:

G+ bacteria including staphylococci, enterococci and other streptococci

Usually bacteriostatic

No activity against gram negative bacteria



Clinical Uses:

- Very expensive
- MRS & VRS osteomyelitis and soft tissue infections

Adverse Effects

- gastrointestinal upset, nausea, diarrhea, headache, and rash.
- The principal toxicity of linezolid is hematologic:
  - Thrombocytopenia is the most common manifestation particularly when the drug is administered for longer than 2 weeks.
  - Anemia and neutropenia most commonly in patients with a predisposition to or underlying bone marrow suppression.
- There are case reports of serotonin syndrome occurring when linezolid is coadministered with serotonergic drugs, most frequently SSRI.

TETRACYCLINES

- Obtained from soil actinomycetes.
- Resistance - Common
- These bind to 30S ribosomal subunit and inhibit the binding of *aminoacyl-tRNA* to the A site.
- On the basis of chronology of development they may be divided in to 3 groups

Group – I	**Group – II**	**Group – III**
Chlortetracycline	Domeclocycline	Doxycycline
Oxytetracycline	Methacycline	Minocycline
Tetracycline		

- Commonly used to treat sexually transmitted disease
- Tetracycline: oint 1 & 3%, cap 250mg
- Doxycycline: cap 50 & 100mg, inj 100mg/vial

Tetracyclines

Antimicrobial Activity:

Brucella

V. cholera

mycoplasma, chlamydia, legionella

H. pylori

ureaplasma

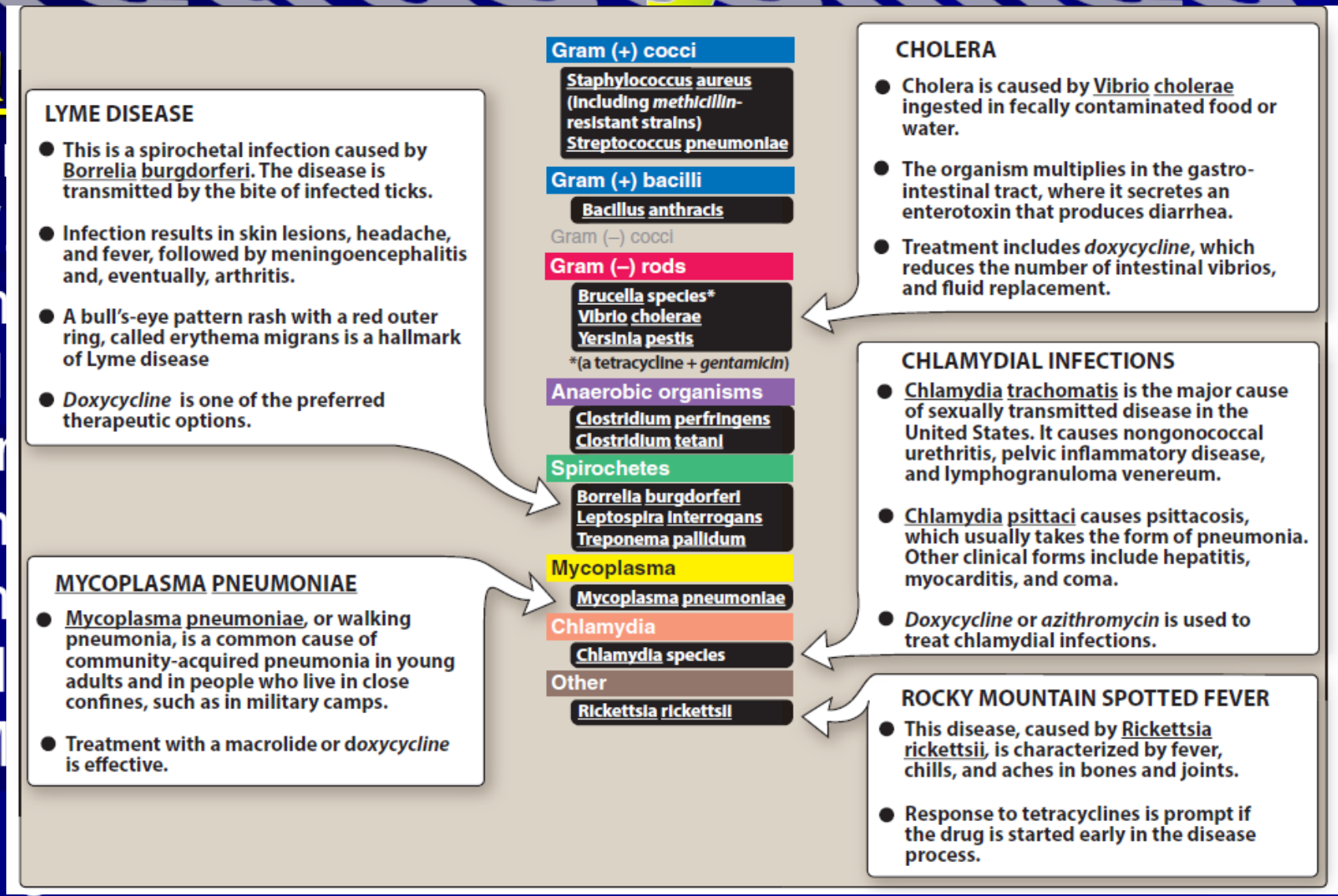
many spirochetes

many anaerobes

plasmodium

Many of previously sensitive microorganisms are now resistant: pneumococci, staphylococci, gonococcus

Tetracyclines



Tetracyclines

Clinical uses:

Brucellosis

Cholera

STDs (chlamydia, ureaplasma and treponema but not gonococcus)

Atypical pneumonia

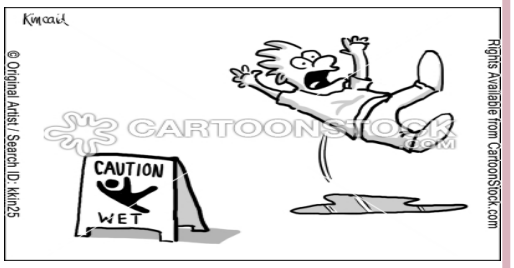
Trachoma

H. Pylori eradiaction regimen

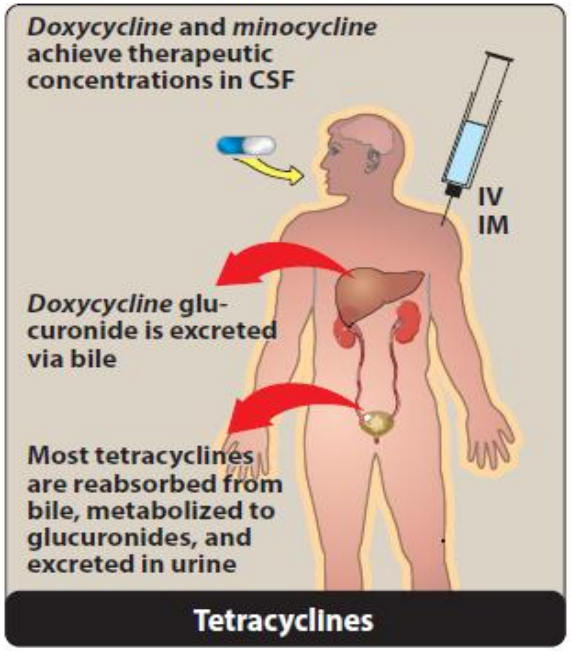
Prophylaxis and treatment of chloroquine-resistant falciparum malaria

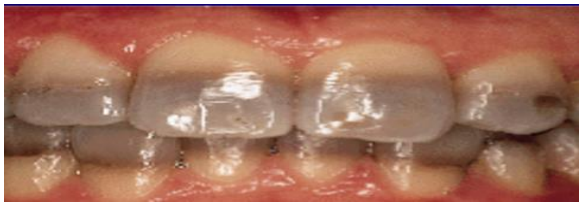
Acne

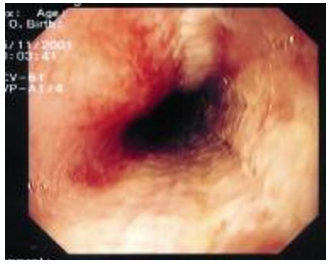
PRECAUTIONS

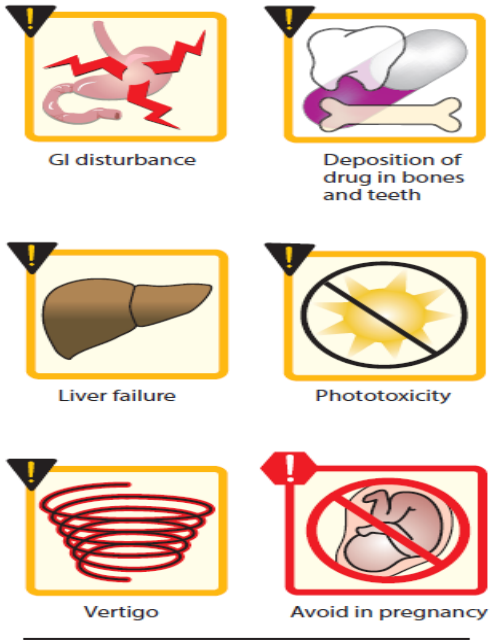


- Not used during pregnancy, lactation ,childhood.
- Used cautiously in renal and hepatic patients.
- Adverse effects – esophagitis, nausea, vomiting, diarrhea, Destruction of normal intestinal flora resulting in increased secondary infections; staining and impairment of the structure of bone and teeth. Not used in children



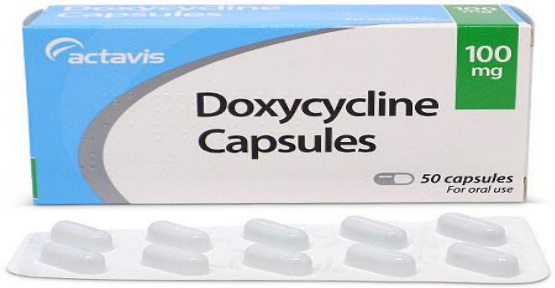






Tetracycline Hydrochloride 1%	OINTMENT
Tetracycline Hydrochloride 250 mg	CAPSULE
Tetracycline Hydrochloride 3%	OINTMENT

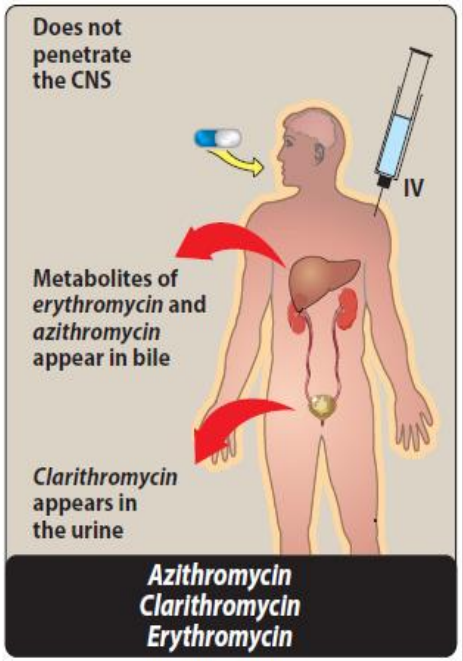
Doxycycline 100 mg	CAPSULE
Doxycycline 100 mg	TABLET
Doxycycline 50 mg	CAPSULE
Doxycycline 100 mg/ Vial	INJECTION



Macrolides

Erythromycin, Clarithromycin Azithromycin

Macrolides: kinetics



- *Better absorption on an empty stomach for azithromycin.*
- *Clarithromycin and azithromycin have longer duration of action compared to erythromycin.*
  - ***Erythromycin: QID***
  - ***Calrithromycin: BID***
  - **Azithromycin: QD**
- Azithromycin remains in tissue for a long time

  → Shorter duration of treatment

ERYTHROMYCIN

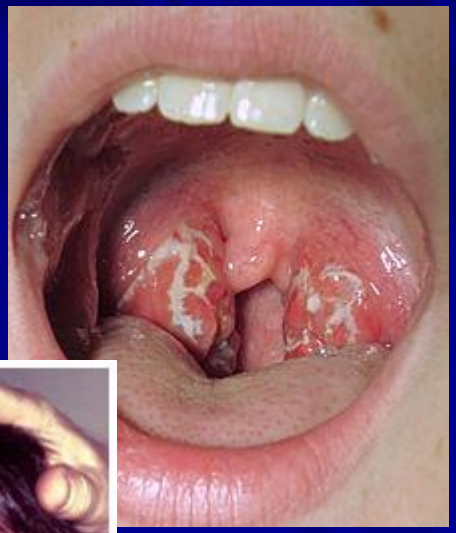
- ✓ It was Isolated from ***Streptomyces erythreus*** in 1952.
- ✓ Water solubility of erythromycin is limited and the solution remains stable only when kept in cold.
- ✓ It acts by inhibiting bacterial protein synthesis. It combines with 50S ribosomes subunits and interferes with *translocation*.

ANTIMICROBIAL SPECTRUM

It is narrow, includes mostly gram positive organisms and few gram negative bacteria and overlaps considerably with that of Penicillin G.

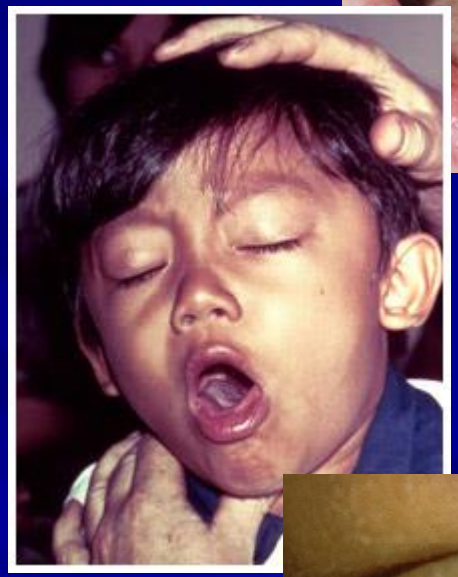
	Erythro-mycin	*Clarithro-mycin*	*Azithro-mycin*
Oral absorption	Yes	Yes	Yes
Half-life (hours)	2	3.5	>40
Conversion to an active metabolite	No	Yes	Yes
Percent excretion in urine	15	50	12

Erythromycin



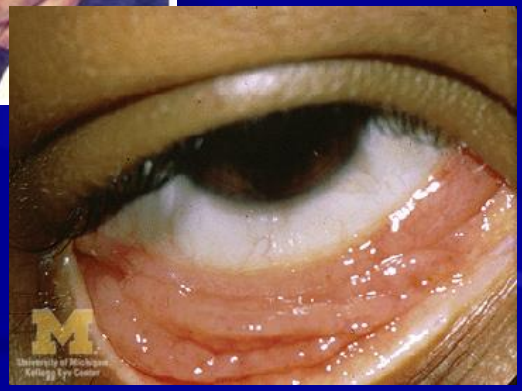
Clinical Uses:

Pharyngitis



Oral & dental infections

Pneumonia



Pertussis

Chlamydia urethritis & conjuctivitis

Azithromycin & Clarithromycin

Clinical uses:

Pharyngitis

Otitis media, Sinusitis

CAP

Chlamydia urethritis & conjuctivitis

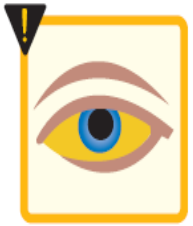
H. pylori eradication regimen (clarithromycin)

Shigellosis, gonorrhea, acne (azithromycin)

Company
LOG

Macrolides: adverse reactions


GI disturbance


Jaundice


Ototoxicity

1. GI disturbances
   Erythromycin>clarithromycin> azithromycin

2. Drug interactions due to inhibition of metabolism of other drugs:
   phenytoin, carbamazepine, valproate theophylline warfarin, terfenadine, cyclosporine, statins (e.g. lovastatin)

erythromycin≥clarithromycin>>azithromycin

1. Hepatitis
2. QT prolongation and polymorphic VT
3. Skin rash and fever

DRUG INTERACTIONS

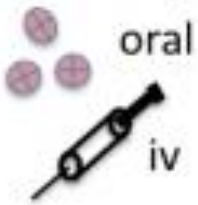
1) Interaction with warfarin leads to serious bleeding in patients undergoing anticoagulation therapy.

2) Interaction with lovastatin, drug given for cholesterol reduction leads to severe muscle weakness.

3) Interaction with Theophylline, a bronchodilator used for asthmatic patients leads to toxic concentrations of the same resulting in cardiac arrhythmias

Macrolide Uses

Routes:



Pharmacokinetics:

- Azithromycin $t_{1/2}$ =3 days
- a 1 g dose provides 7 day coverage
- common therapy consists of 500 mg loading dose & 250 mg/day for 4 more days.

Upper Respiratory Tract:
- *Pharyngitis*
- *Tonsillitis*
- *Sore throat*

Otitis Media

Lower respiratory tract infections:
Pneumonia
MAC (Mycobacterium avis complex)
Legionnaire's
Anthrax

Ulcers (H. pylori)
drug combo including Clarithromycin

Uncompliated skin infections (staph)

STDs
Chancroid disease in men
Chlamydia
Gonorrhea

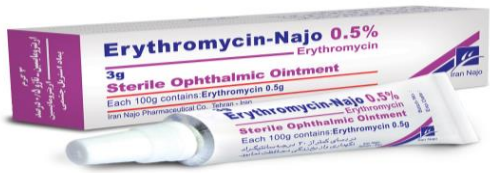
Mechanism:

Bind to 50S & block translocation step in protein synthesis

bacteriostatic

Adverse Effects:

- nausea, vomiting, diarrhea
- abdominal pain
- liver toxicity (estolate related)
- erythromycin inhibits P-450 (drug interactions) & ↑ QTc



Erythromycin

Erythromycin	1 g	INJECTION, POWDER,
Erythromycin	200 mg	TABLET
Erythromycin	200 mg/5ml	POWDER, FOR SUSPENSION
Erythromycin	400 mg	TABLET
Erythromycin	0.5%	OINTMENT
Erythromycin	2%	GEL
Erythromycin	2%	SOLUTION
Erythromycin	4%	GEL
Erythromycin	4%	SOLUTION

Azithromycin –loading dose;500mg 1st day Followed by 250mg daily.

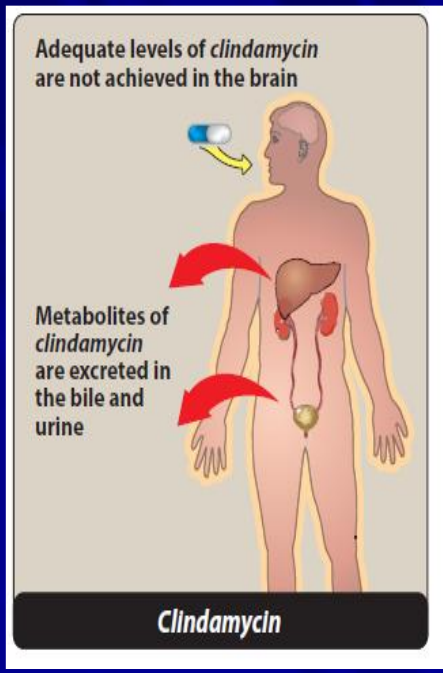
Azithromycin	1g/sachet	POWDER, FOR SUSPENSION
Azithromycin	1%	DROPS, SOLUTION
Azithromycin	100 mg/5ml	POWDER, FOR SUSPENSION
Azithromycin	2 g	POWDER, FOR SOLUTION
Azithromycin	200 mg/5ml	POWDER, FOR SUSPENSION
Azithromycin	250 mg	CAPSULE
Azithromycin	250 mg	TABLET
Azithromycin	500 mg	CAPSULE
Azithromycin	500 mg	INJECTION, POWDER
Azithromycin	500 mg	TABLET

Clarithromycin – 250-500mg every 12 hrs for 6-10 days.

Clarithromycin	125 mg/5ml	POWDER, FOR SUSPENSION
Clarithromycin	250 mg	TABLET
Clarithromycin	250 mg/5ml	POWDER, FOR SUSPENSION
Clarithromycin	250 mg/sachet	GRANULE, FOR SUSPENSION
Clarithromycin	500 mg	TABLET


RANBAXY
CLINDAMYCIN
HYDROCHLORIDE
Capsules, USP
150 mg
Rx only
100 Capsules


CLINDAMYCIN
INJECTION USP
150 mg/mL
Rx ONLY


Adequate levels of clindamycin are not achieved in the brain
Metabolites of clindamycin are excreted in the bile and urine
Clindamycin


(۶۰ میلی‌لیتر)
کلیندامایسین
فسفات ۱٪
محلول موضعی
دسته دارویی: ضد آکنه
دستور پزشک:


داروسازی بهـــــوزان
کلیندامایسین فسفات
کرم واژینال ۲٪
Clindamycin 2%
40g

CLINDAMYCIN

MOA: Same as erythromycin (but fewer chance of resistance)

Antibacterial activity:

- Streptococci (not enterococci), pneumococci, staphylococci
- Very good effects against anaerobic bacteria (but not Cl. difficile)
- Plasmodia, toxoplasma
- No effect against G^- bacilli

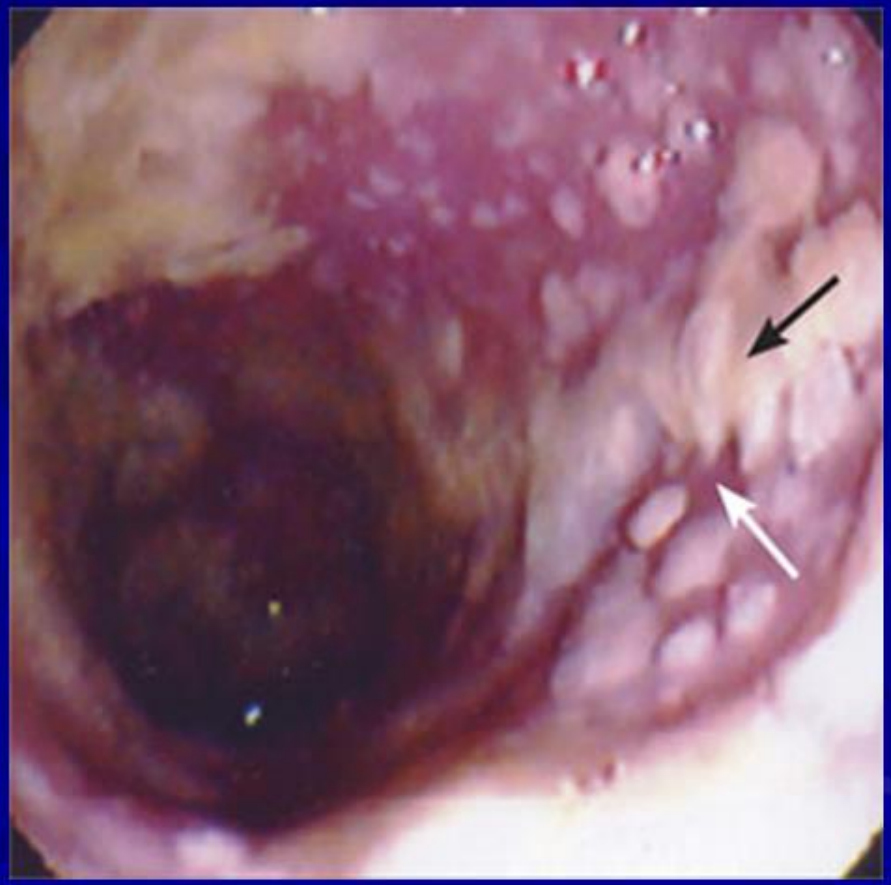
CLINDAMYCIN

Clinical uses

- Mixed aerobic-anaerobic infections (usually with an anti-aerobic drug in PID, intraabdominal/pelvic and lung abcess, diabetic foot)
- Sometimes in staphylococcal infections (especially, osteomyelitis)
- Acne
- Bacterial vaginosis
- Falciparum malaria, toxoplasmosis

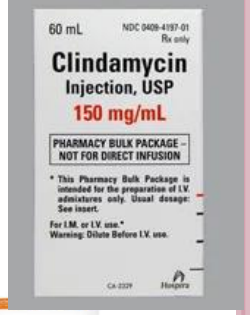
Clindamycin: adverse effects

- Diarrhea
- Pseudomemberanous colitis (abdominal pain & tenderness, fever, severe diarrhea, mucus and blood in stool)



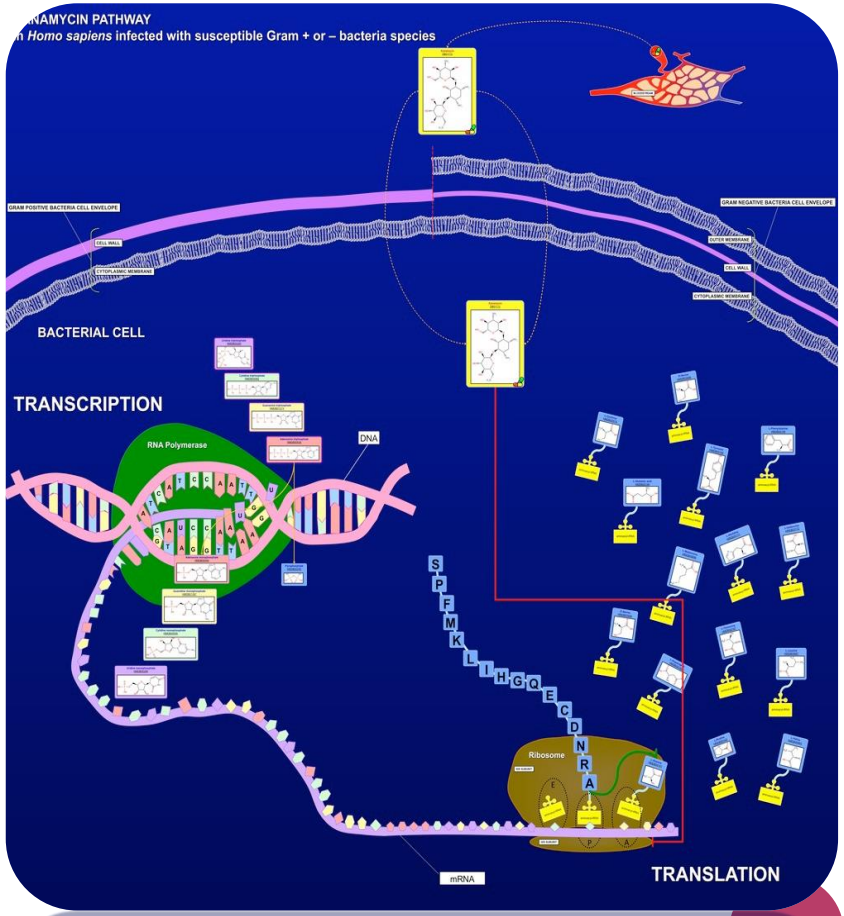
150-450mg PO q6-8hr
1.2-2.7g/day IV/IM divided q6-12hr

indamycin	CREAM	2%	VAGINAL
indamycin	CAPSULE	150 mg	ORAL
indamycin	INJECTION	150 mg/ml	PARENTERA
mycin	CAPSULE	300 mg	ORAL
mycin	SUSPENSION	75 mg/5ml	ORAL
mycin	POWDER, FOR SOLUTION	75 mg/5ml	ORAL
mycin	GEL	1%	TOPICAL
mycin	SOLUTION	1%	TOPICAL
mycin	SUPPOSITORY	100 mg	VAGINAL
indamycin+Clotrimazole	CREAM		VAGINAL
indamycin+Tretinoin	GEL		TOPICAL



AMINOGLYCOSIDES

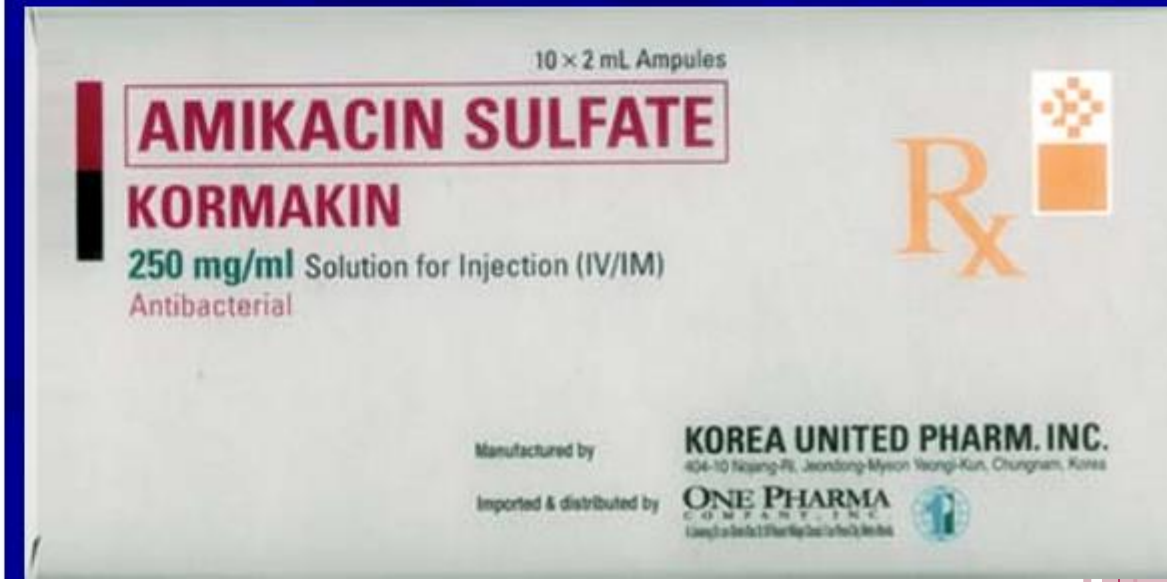
- **Aminoglycosides** are group of antibiotics in which amino sugars liked by glycoside bonds
- Eg Streptomycin,
- Act at the level of Ribosome's and inhibits protein synthesis
- Other Aminoglycosides – **Gentamycin,** neomycins,paromomycins,tobramycins Kanamycins



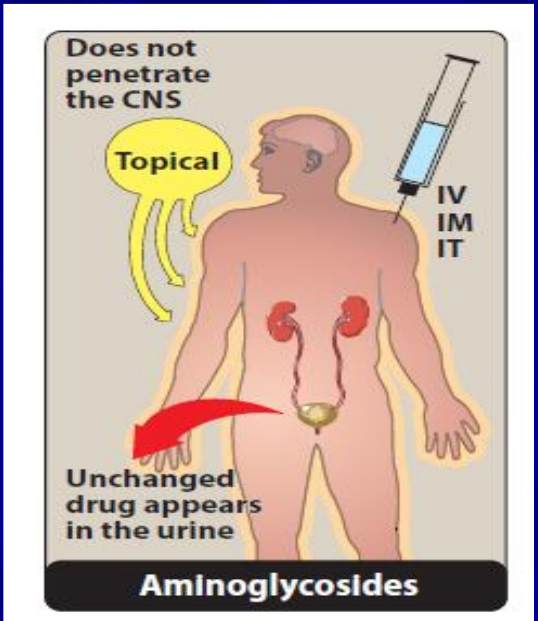
AMINOGLYCOSIDES

- **Available agents:**

Gentamicin, Tobramycin, Amikacin, Streptomycin, Kanamycin, Neomycin, Netilmicin



AMINOGLYCOSIDES



Kinetics:

- No oral absorption
- No penetration to CNS
- Poor tissue penetration
- Concentrated in inner ear and renal cortex
- Excretion as intact form via glumerolar filtration
- Narrow therapeutic window

AMINOGLYCOSIDES

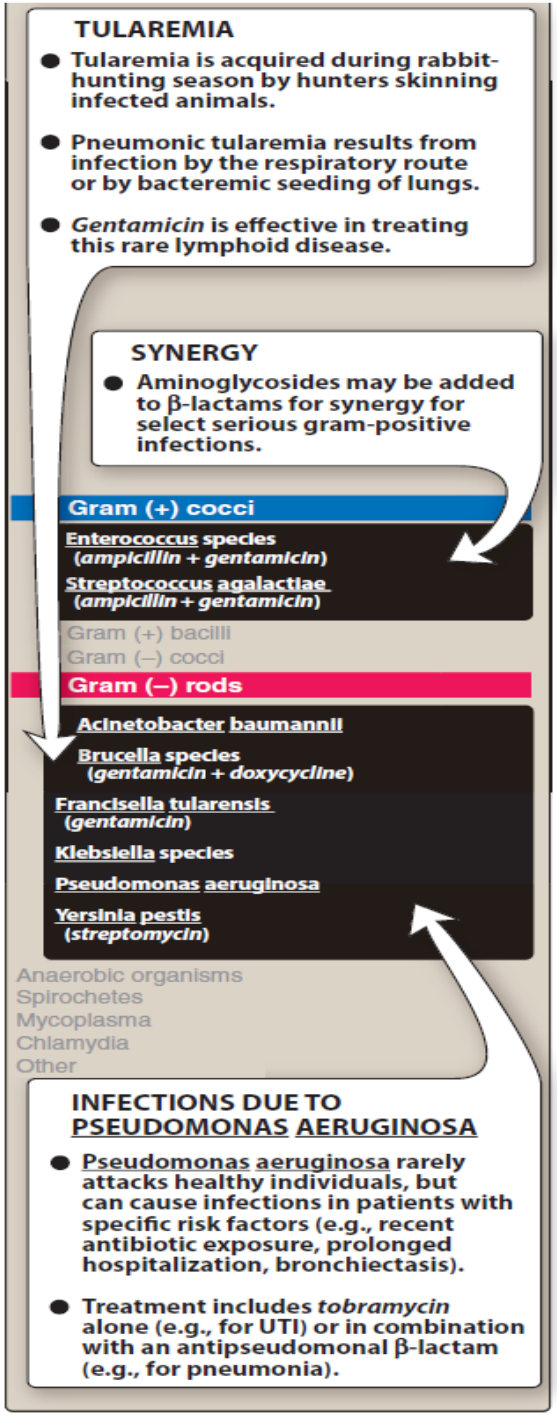
Antibacterial Activity:

- Aerobic G^- bacilli (E. coli, K. pneumoniae, P. mirabilis, P. aeroginosa, Serratia, Enterobacter)

- Streptococci (only viridans group), staphylococci & enterococci (in combination with a cell wall-active agent)

⇒ Gentamicin has much greater activity against G+ bacteria, compared to amikacin

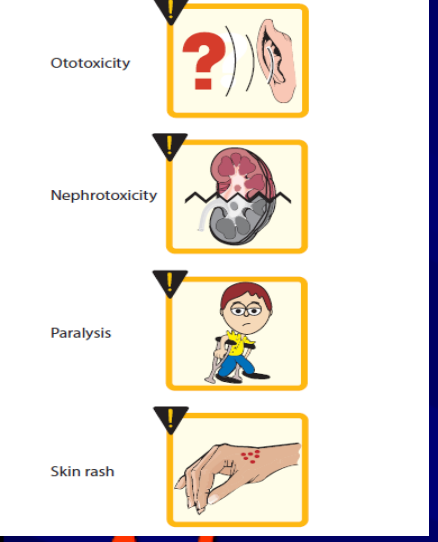
- ⇔little activity against anaerobic microorganisms


TULAREMIA
Tularemia is acquired during rabbit-hunting season by hunters skinning infected animals.
Pneumonic tularemia results from infection by the respiratory route or by bacteremic seeding of lungs.
Gentamicin is effective in treating this rare lymphoid disease.
SYNERGY
Aminoglycosides may be added to β-lactams for synergy for select serious gram-positive infections.
Gram (+) cocci
Enterococcus species (ampicillin + gentamicin)
Streptococcus agalactiae (ampicillin + gentamicin)
Gram (+) bacilli
Gram (–) cocci
Gram (–) rods
Acinetobacter baumannii
Brucella species (gentamicin + doxycycline)
Francisella tularensis (gentamicin)
Klebsiella species
Pseudomonas aeruginosa
Yersinia pestis (streptomycin)
Anaerobic organisms
Spirochetes
Mycoplasma
Chlamydia
Other
INFECTIONS DUE TO PSEUDOMONAS AERUGINOSA
Pseudomonas aeruginosa rarely attacks healthy individuals, but can cause infections in patients with specific risk factors (e.g., recent antibiotic exposure, prolonged hospitalization, bronchiectasis).
Treatment includes tobramycin alone (e.g., for UTI) or in combination with an antipseudomonal β-lactam (e.g., for pneumonia).

AMINOGLYCOSIDES

Clinical Uses:

- Bacterial Endocarditis
- G^- Bacillary UTI, Pneumonia and Sepsis
- Brucellosis (gentamicin & streptomycin)
- Tuberculosis (streptomycin)
- Atypical mycobacterial infections (amikacin)
- Plague (streptomycin)
- With the exception of UTI, they are usually administered with other antibiotics



AMINOGLYCOSIDES

Adverse Drug Reactions:

1. Ototoxicity (auditory & vestibular)
2. Nephrotoxicity

Ototoxicity ▶ **Neo > Strep > Amik=Genta=Tobra** ◀ **Nephrotoxicity**

3. Neuromuscular Blockade

Aminoglycoside Uses

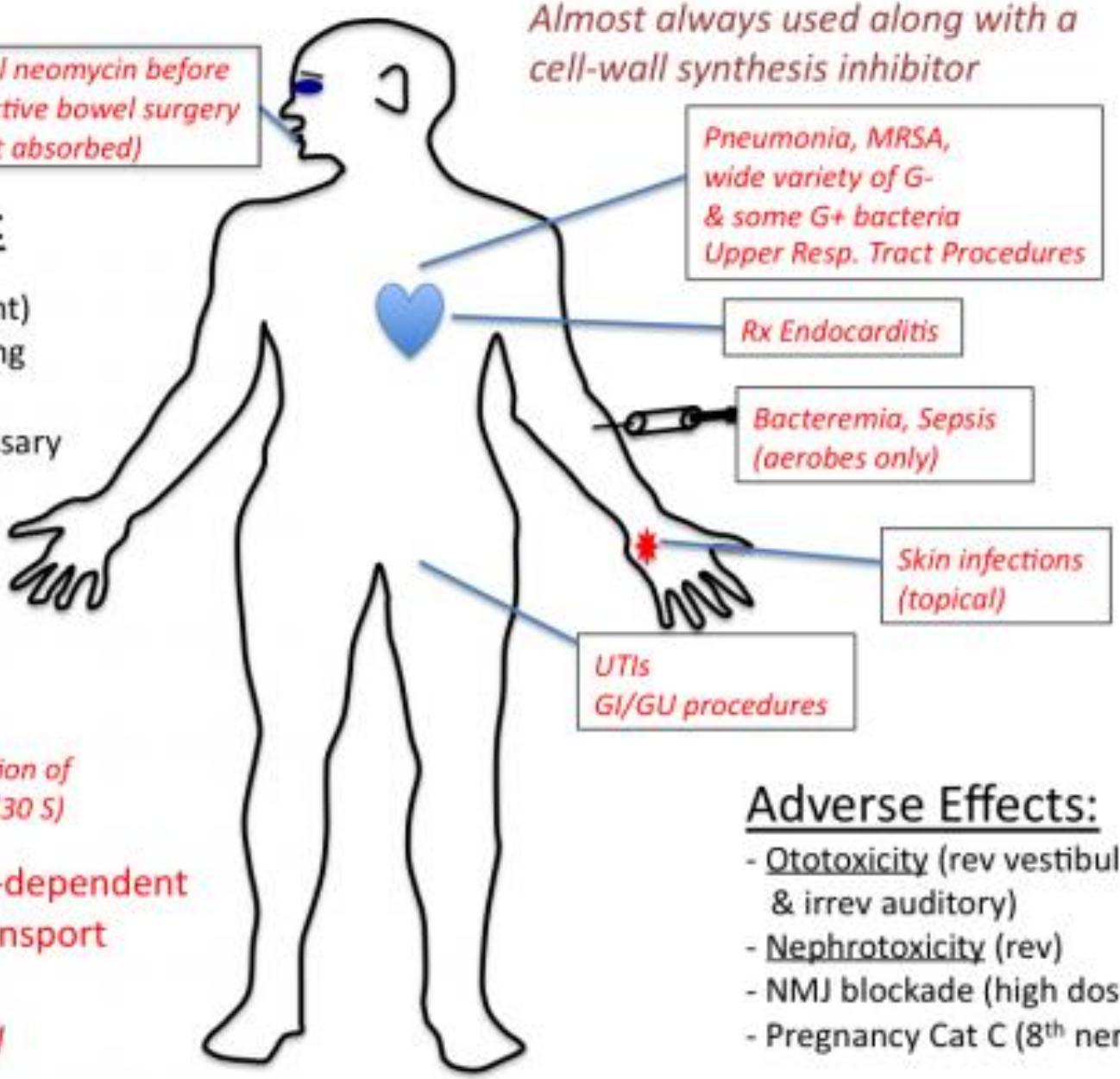
Routes:

im *or* iv,
topical

Pharmacokinetics:

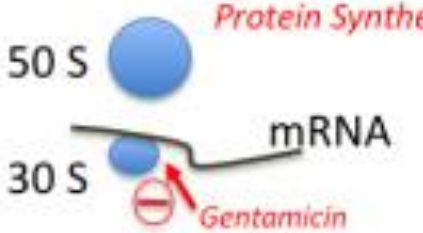
-Vd = ECS (25% body weight)
- adjust maintenance dosing based upon [creatinine]
- plasma monitoring necessary

Almost always used along with a cell-wall synthesis inhibitor



Mechanism:

Irreversible inhibition of Protein Synthesis (30 S)



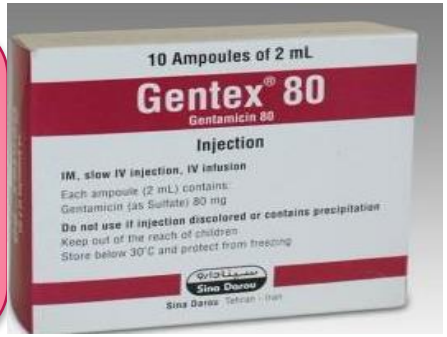
O_2-dependent transport

bactericidal

Adverse Effects:

- Ototoxicity (rev vestibular & irrev auditory)
- Nephrotoxicity (rev)
- NMJ blockade (high dose)
- Pregnancy Cat C (8th nerve)

pediatric: 2-2.5mg/kg/day
IV/IM divided q8h



Gentamicin	3 mg/g	OINTMENT
Gentamicin	3 mg/ml	DROPS, SOLUTION
Gentamicin	40 mg/ml, 1ml	INJECTION
Gentamicin	40 mg/ml, 2ml	INJECTION
Gentamicin	0.8 mg/ml , 100 ml	INJECTION
Gentamicin	10 mg/ml, 2ml	INJECTION

ADULTS: 3-5mg/kg/day
IV/IM divided q8h
Or
4-7 mg/kg/dose IV QD

Neomycin Sulfate 125 mg/5ml	SOLUTION
Neomycin Sulfate 500 mg	TABLET

Pre-op intestinal antiseptic: 1g PO at 19, 18, 9 hours pre-op * children:90mg/kg/day PO divided q4hr for 2-3 days

Hepatic encephalopathy: 4-12g/day PO divided q6hr for 5-6 days or 3-6g/day for 1-2 weeks * children: 50-100mg/kg/day PO divided q8hr for 5-6 days

Spectinomycin	**2 g**	**INJECTION, POWDER,**

Tobramycin	**OINTMENT**	**0.30%**	**OPHTHALMIC**
Tobramycin	**INJECTION**	**10 mg/ml**	**PARENTERAL**
Tobramycin	**POWDER**	**28 mg**	**RESPIRATORY**
Tobramycin	**NEBULISATION**	**300mg/4 ml**	**INHALATION**
Tobramycin	**NEBULISATION**	**300mg/5 ml**	**INHALATION**
Tobramycin	**INJECTION**	**40 mg/ml**	**PARENTERAL**
Tobramycin	**INJECTION**	**50 mg / ml**	**PARENTERAL**
Tobramycin	**NEBULISATION**	**60 mg/ml**	**RESPIRATORY**
Tobramycin	**NEBULISATION**	**75mg/ml**	**RESPIRATORY**

3-6mg/kg/day IM, IV divided q8hr or 4-7mg/kg/dose IV,IM QD

Pediatric: 2-2.5 mg/kg/dose IV,IM Q8hr

300mg inhaled QD-BID

Amikacin	**INJECTION**	**250 mg/ml**	**PARENTERAL**
Amikacin	**INJECTION**	**50 mg/ml**	**PARENTERAL**

15mg/kg/day divided q8-12hr, IV,IM

15-22.5 mg/kg/day IV,IM q8h

STREPTOMYCIN

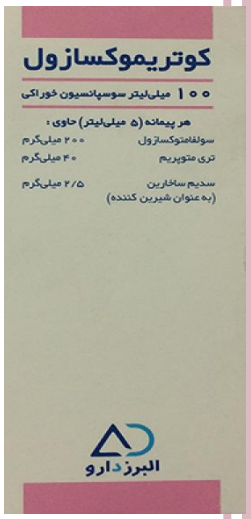
1-2g/day IM divided Q6-12hr

20-40mg/kg/day IM q6-12hr

Trimethoprim-Sulfamethoxazole (co-Trimoxazole)

1-2 tab Po q12-24hr
8-20mgTMP/kg/day IV q6-12hr

Co-trimoxazole		INJECTION, SOLUTION	(Sulfamethoxazole 400mg+Trimethoprim 80mg)/5ml
Co-trimoxazole		SUSPENSION	(Sulfamethoxazole 200mg+Trimethoprim 40mg)/5ml
Co-trimoxazole		TABLET	Sulfamethoxazole 100mg+Trimethoprim 20mg
Co-trimoxazole		TABLET	Sulfamethoxazole 400mg+Trimethoprim 80mg
Co-trimoxazole		TABLET	Sulfamethoxazole 800mg+Trimethoprim 160mg



Trimethoprime-Sulfamethoxazole

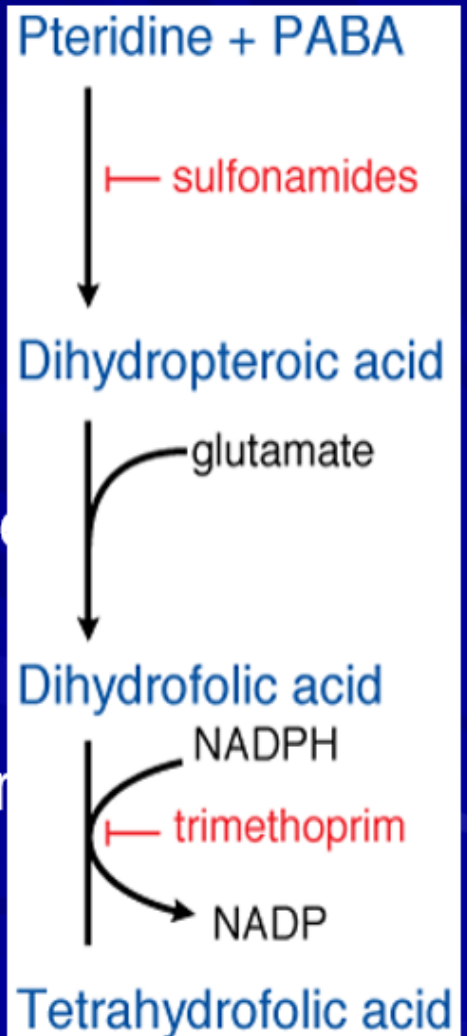
Trimethoprime-Sulfamethoxazole

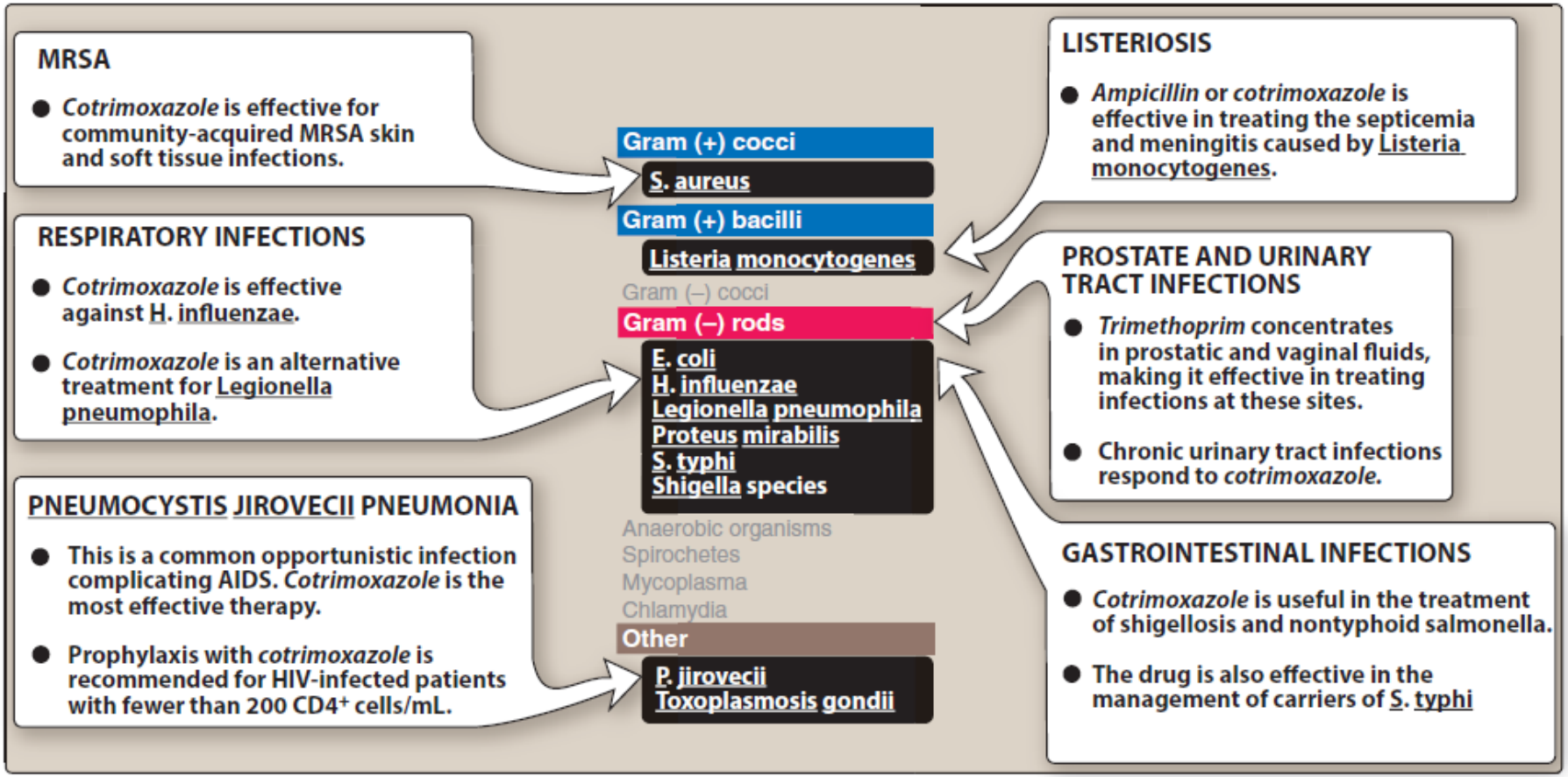
Co-Trimoxazole

- **MOA:**
  Sulfamethoxazole (and all of the sulfonamides):
  - Inhibition of dihydropteroate synthetase

- ***Trimethoprime:***
  - Inhibition of dihydrofolate (DHF)-reductas

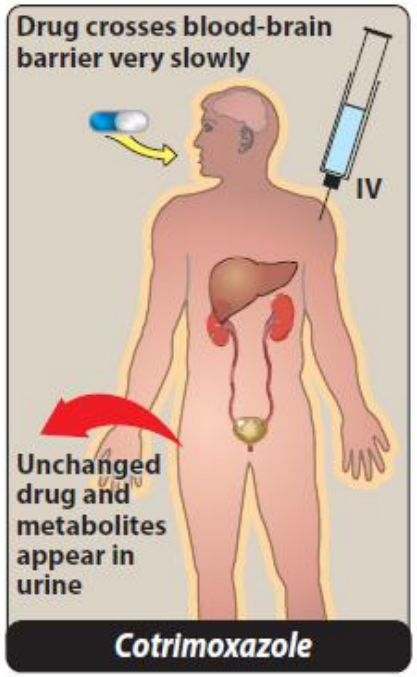
- Inhibition of folic acid synthesis and turn over and eventually inhibition of growth or cell death



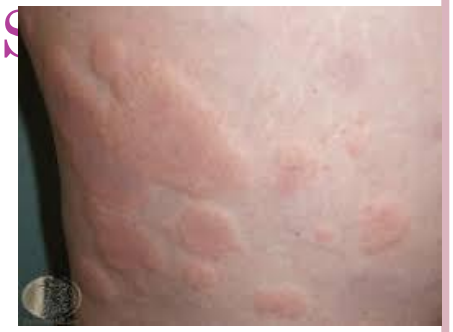

MRSA
Cotrimoxazole is effective for community-acquired MRSA skin and soft tissue infections.
RESPIRATORY INFECTIONS
Cotrimoxazole is effective against H. influenzae.
Cotrimoxazole is an alternative treatment for Legionella pneumophila.
PNEUMOCYSTIS JIROVECII PNEUMONIA
This is a common opportunistic infection complicating AIDS. Cotrimoxazole is the most effective therapy.
Prophylaxis with cotrimoxazole is recommended for HIV-infected patients with fewer than 200 CD4+ cells/mL.
Gram (+) cocci
S. aureus
Gram (+) bacilli
Listeria monocytogenes
Gram (–) cocci
Gram (–) rods
E. coli
H. influenzae
Legionella pneumophila
Proteus mirabilis
S. typhi
Shigella species
Anaerobic organisms
Spirochetes
Mycoplasma
Chlamydia
Other
P. jirovecii
Toxoplasmosis gondii
LISTERIOSIS
Ampicillin or cotrimoxazole is effective in treating the septicemia and meningitis caused by Listeria monocytogenes.
PROSTATE AND URINARY TRACT INFECTIONS
Trimethoprim concentrates in prostatic and vaginal fluids, making it effective in treating infections at these sites.
Chronic urinary tract infections respond to cotrimoxazole.
GASTROINTESTINAL INFECTIONS
Cotrimoxazole is useful in the treatment of shigellosis and nontyphoid salmonella.
The drug is also effective in the management of carriers of S. typhi

Trimethoprim-Sulfamethoxazole (co-Trimoxazole)

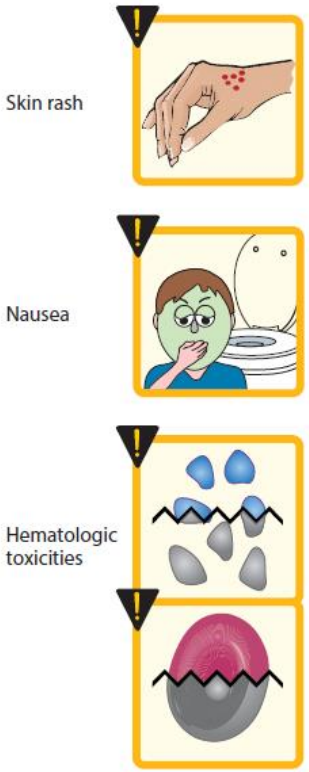
- Pneumocystis pneumonia (**PCP**)
- Listeria meningitis(in the case of penicillin sensitivity)
- Brucellosis(not as a first choice)
- UTI
- Prostatitis
- Otitis media
- sinusitis



CO-TRIMOXAZOLE: ADVERSE EFFECTS



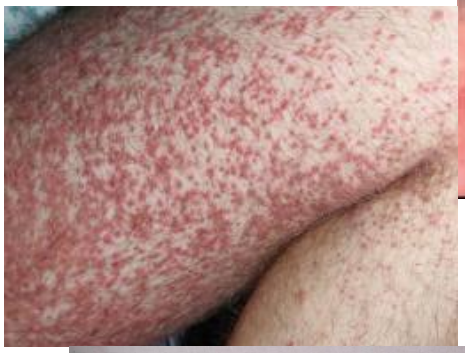
- Dermal reaction:
  - Sulfonamides are the most involved antibiotics in producing adverse dermal reactions
  - Dermal reactions constitute 75% of reported adverse reactions of sulfonamides
- Other adverse effects:
  - Anorexia, nausea, vomiting
  - Crystalluria
  - Hemolytic anemia(in G6PD deficiency)
  - Not suitable for infants< 2months(also for lactating mother)

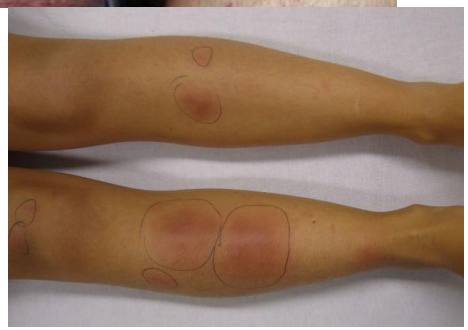


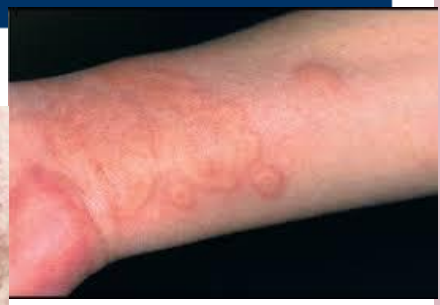
Compa
LOGO

Co-trimoxazole: adverse effects

- **Dermal reactions**
  - Urticaria
  - Purpura
  - Exfoliative dermatitis
  - Erythema nodosum
  - Erythema multiform
  - Stevens-Johnson syndrome
  - Toxic epidermal necrosis (Lyell's syndrome)

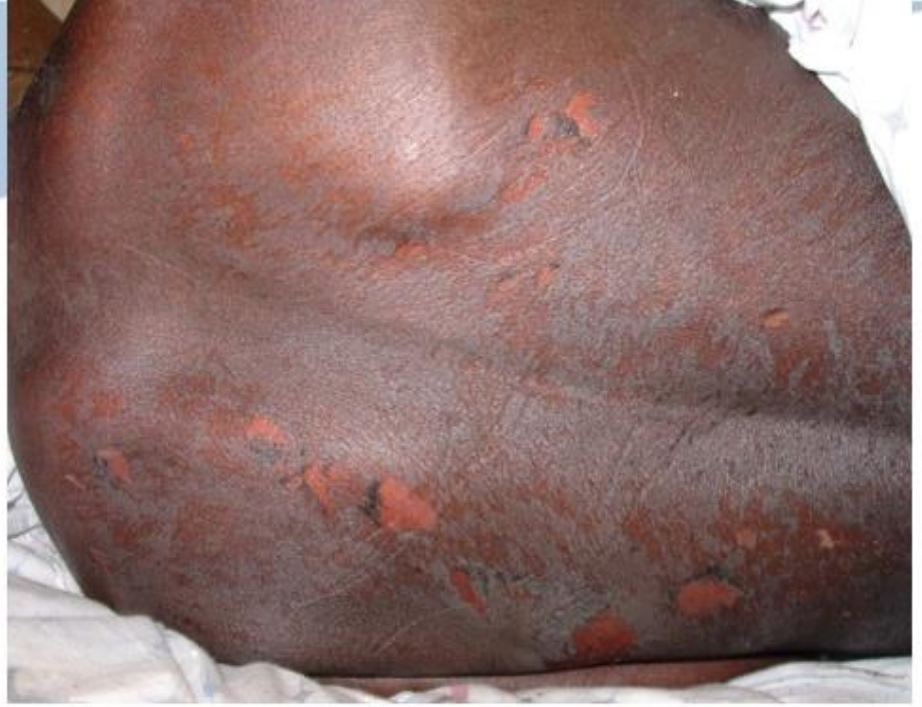


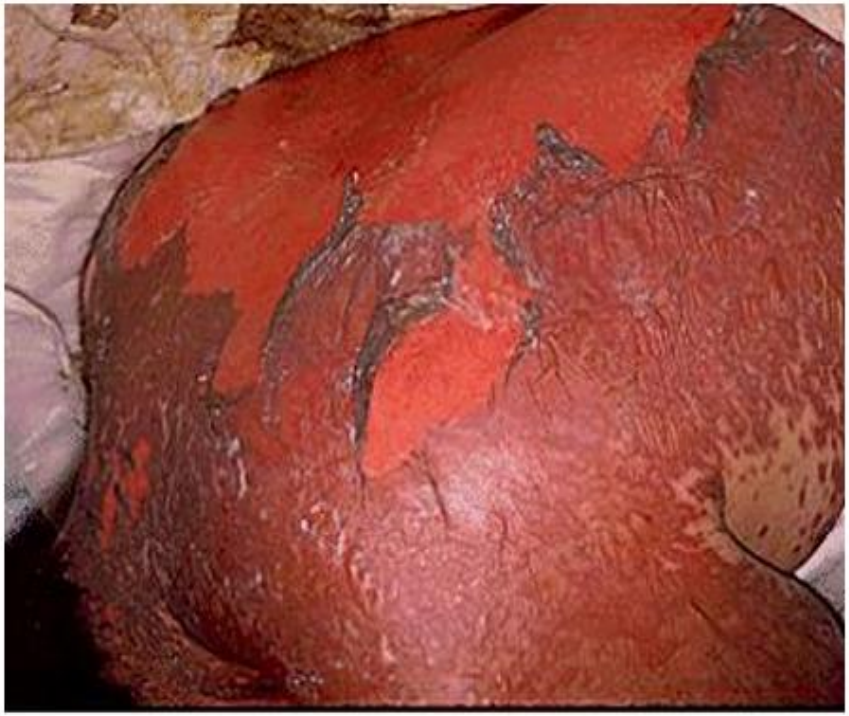




Company
LOGO

Toxic Epidermal Necrosis





Co-trimoxazole: adverse effects

- Drug interactions:
  - Increase plasma levels of:
    - Warfarin
    - sulfonylurea agents
    - phenytoin

Case : UTI

- I. B., a 32 year old female presents with a community acquired UTI. Results of culture and sensitivity are pending.
- What are the potentially effective agents?
- I. B. has experienced a rash with co-trimoxazole and type I hypersensitivity reaction to penicillin. How does the story change?

Case : UTI

- Based on lab results, the microorganism is E. coli and it is sensitive to nalidixic acid and ciprofloxacin.

- To what class of antibiotcs, do these drugs belong?

fluoroquinolones

- **First Generation**

  Gram-negative
  treatment of lower urinary tract infections.

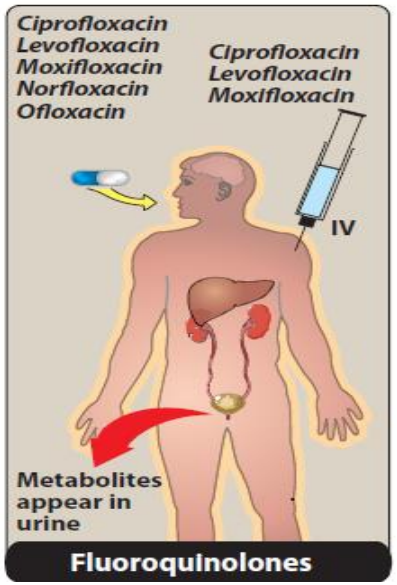
- **Second Generation**

  excellent gram-negative activity and moderate to good activity against gram-positive bacteria

  Ciprofloxacin is the most active agent of this group against gram-negative organisms, P aeruginosa in particular. Levofloxacin has superior activity against gram-positive organisms, including Streptococcus pneumoniae.

- **Third and Fourth Generation**

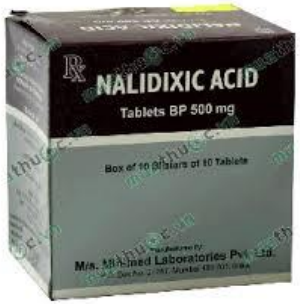
  Have increased activity against gram-positive pathogens including *S. pneumoniae.* They are also active against mycobacteria.



Moxifloxacin is excreted primarily by the liver

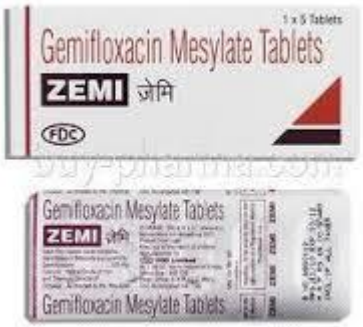
fluoroquinolones

- **First Generation**
  - Nalidixic Acid



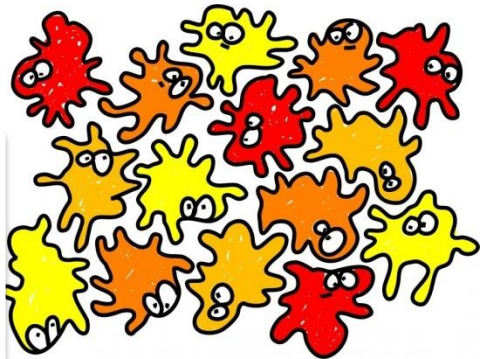
- **Second Generation**
  - Ciprofloxacin
  - Levofloxacin
  - Ofloxacin

- **Third Generation**
  - Gatifloxacin



- **Fourth Generation**
  - Gemifloxacin
  - Moxifloxacin

Fluoroquinolones also are active against agents of atypical pneumonia (eg, mycoplasmas and chlamydiae) and against intracellular pathogens such as *Legionella pneumophila* and some mycobacteria ,including *Mycobacterium*

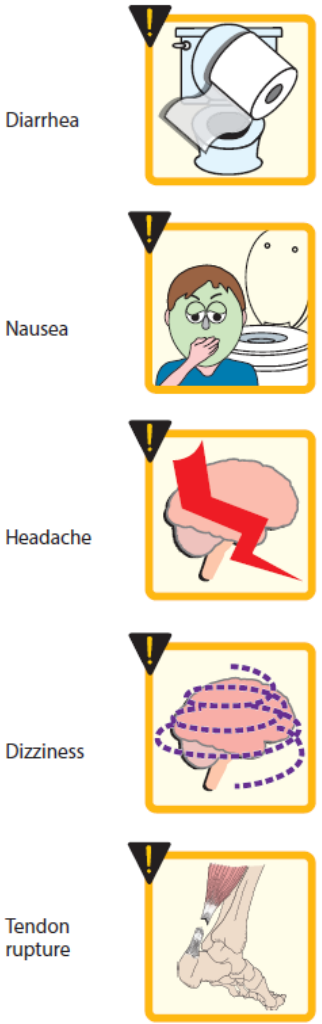


Quinolones: indications

- UTI
- prostatitis, gonorrhea, chlamydial urethritis/cervicitis, pelvic infections
- Traveler's diarrhea, shigellosis, cholera, typhoid fever
- Meningococcal carrier state
- Sinusitis, otitis media
- Pneumonia, acute exacerbation of chronic bronchitis
- Bone, joint & soft tissue infections
- Diabetic foot infection
- Multidrug-resistant tubercolosis and atypical mycobacterial infections

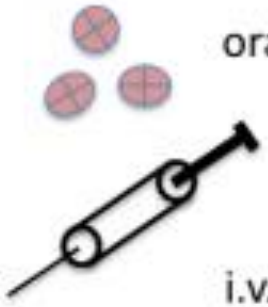
Adverse effects

- Gastrointestinal effects: nausea, vomiting, and diarrhea
- Hemolytic anemia (nalidixic acid)
- phototoxicity
- Headache, dizziness, insomnia, rarely hallucination, delirium and seizure
- Damage to growing cartilage (not recommended for use in children).
- Tendonitis, a rare complication, reported in adults, is potentially more serious because of the risk of tendon rupture. Risk factors for tendonitis include advanced age, renal insufficiency, and concurrent steroid use.
- Theophylline interaction (with ciprofloxacin)
- Multivalent catión



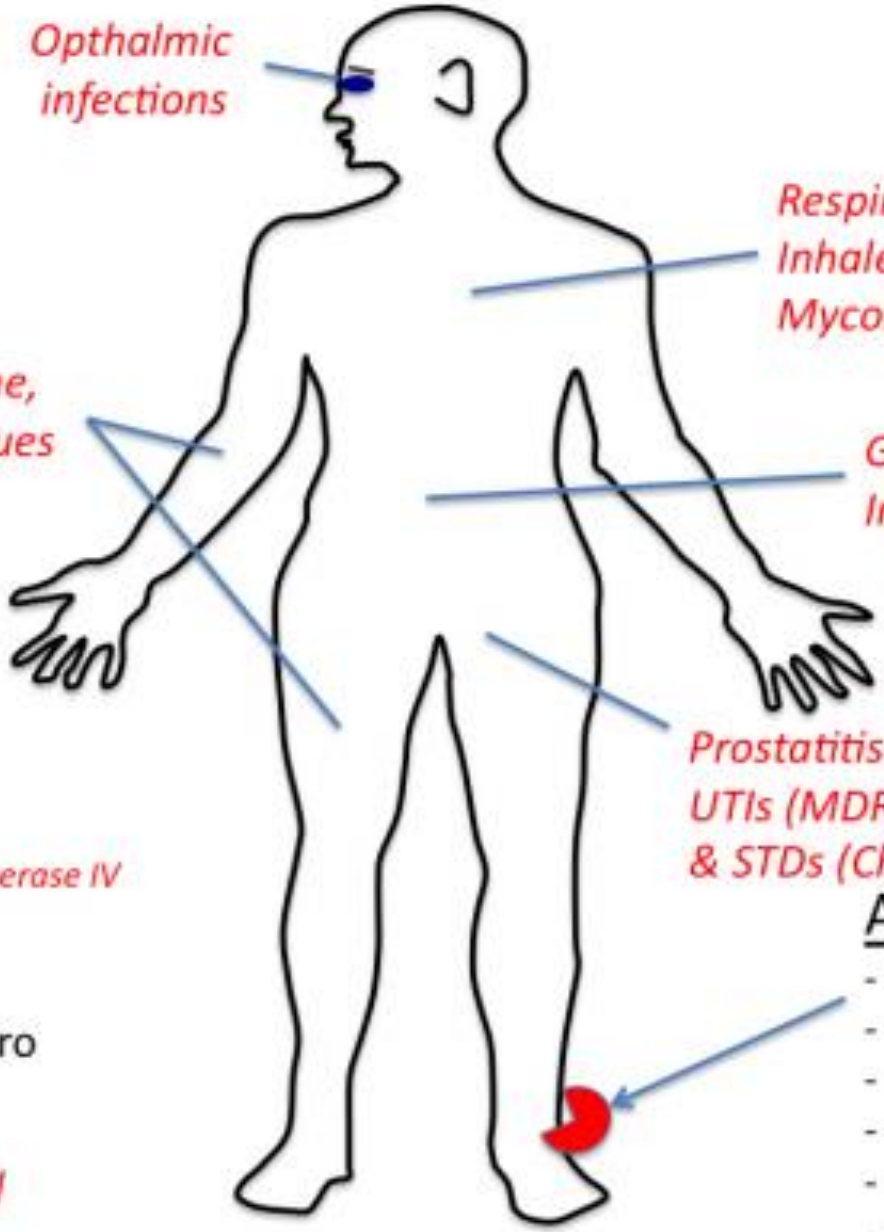
Fluoroquinolone Uses

Routes:



oral

i.v.



Opthalmic infections

Respiratory Infections, Inhaled Anthrax, Mycobacteria (TB)

Infections of bone, joints & soft tissues

GI & Abdominal Infections

Prostatitis
UTIs (MDR strains)
& STDs (Chlamydia)

Mechanism:

Inhibits DNA Gyrase & Topoisomerase IV

Cipro

bactericidal

Adverse Effects:

- Tendon rupture
- Children <18 yo (cartilage)
- Pregnancy Category C
- Seizures, prolong QT
- Dizziness, Confusion
- Photosensitivity

Ciprofloxacin 0.3%	DROPS, SOLUTION
Ciprofloxacin 0.3%	OINTMENT
Ciprofloxacin 10 mg/ml, 20ml	INJECTION, SOLUTION
Ciprofloxacin 2 mg/ml, 100ml	INJECTION, SOLUTION
Ciprofloxacin 250 mg	TABLET
Ciprofloxacin 500 mg	TABLET
Ciprofloxacin 250 mg/5ml	SUSPENSION
Ciprofloxacin/Dexamethasone 0.3/0.1%	DROPS, SUSPENSION
Ciprofloxacin 400 mg/200ml	INJECTION

200- 400 mg q12 h

Gemifloxacin 320 mg	TABLET

320 mg QD

Ofloxacin 0.3%	DROPS, SOLUTION
Ofloxacin 200 mg	TABLET
Ofloxacin 300 mg	TABLET
Ofloxacin 400 mg	TABLET

Moxifloxacin 400 mg	TABLET
Moxifloxacin 0.5%	Opht SOLUTION

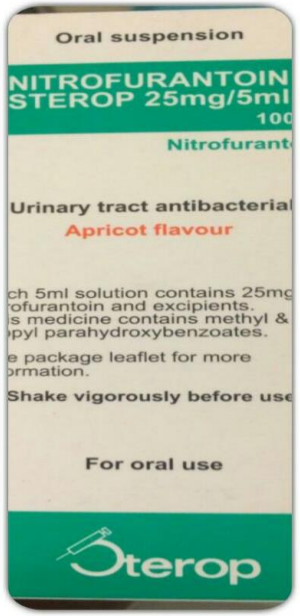
400mg QD

250-750 mg QD

Levofloxacin 250 mg	TABLET
Levofloxacin 500 mg	TABLET
Levofloxacin 500 mg/100ml	INJECTION , SOLUTION
Levofloxacin 750 mg	TABLET
Levofloxacin Hemihydrate 0.5%	DROPS, SOLUTION
Levofloxacin 25mg/ml	INJECTION, SOLUTION CONCENTRATE

Nitrofurantoin

- MOA: Drug reduction in bacteria and invasion to DNA
- Effective against: E.coli, Staphylococci, enterococci
- Urinary antiseptic



Nitrofurantoin

- ***Uses:***

  Cystitis (treatment & prophylaxis)

- ***Adverse effects:***

  - Anorexia, nausea & vomiting (most common reactions)
  - Allergic reactions
  - Hemolytic anemia (in G6PD deficient patients)
  - Discoloration of urine
  - Hepatitis
  - Neuropathies
  - Pulmonary toxicity (pneumonitis, fibrosis)

Metronidazole

- Introduced in 1959 for the treatment of "Trichomonas Vulgaris".
- Used especially for serous anaerobic infections, including those of the orofacial region.
- Bactericidal
  - DNA synthesis inhibition (reduction by enzymatic system of anaerobic microorganism)

Metronidazole

- DNA synthesis inhibition (reduction by enzymatic system of anaerobic microorganism)

METRONIDAZOLE

- **METRONIDAZOLE-250mg every 8 hrs**

Metronidazole	125 mg/5ml	SUSPENSION
Metronidazole	0.75%	GEL
Metronidazole	250 mg	TABLET
Metronidazole	5 mg/ml, 100ml	INJECTION, SOLUTION
Metronidazole	500 mg	SUPPOSITORY
Metronidazole	500 mg	TABLET

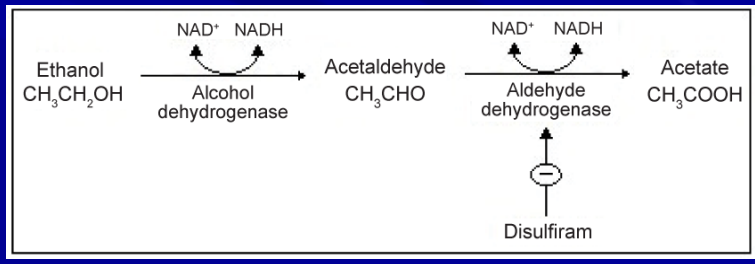
Metronidazol: clinical uses

- Amoebic dysentery
- Giardiasis
- Trichomonas vaginitis, bacterial vaginosis
- Obligatory anaerobic bacterial infections
- Mixed aerobic-anaerobic infections (with an anti-aerobic drug in PID, pelvic, lung & brain abcess)
- Peptic ulcer

Metronidazole

ADRs:

- Common: nausea, headache, dry mouth, metallic taste
- Uncommon: vomiting, diarrhea, insomnia, weakness, oral thrush, paresthesia and other neurotoxicities
- Others: disulfiram-like syndrome



PRINCIPLES OF ANTIBIOTIC ADMINISTRATION

APPROACHING THE PROBLEM

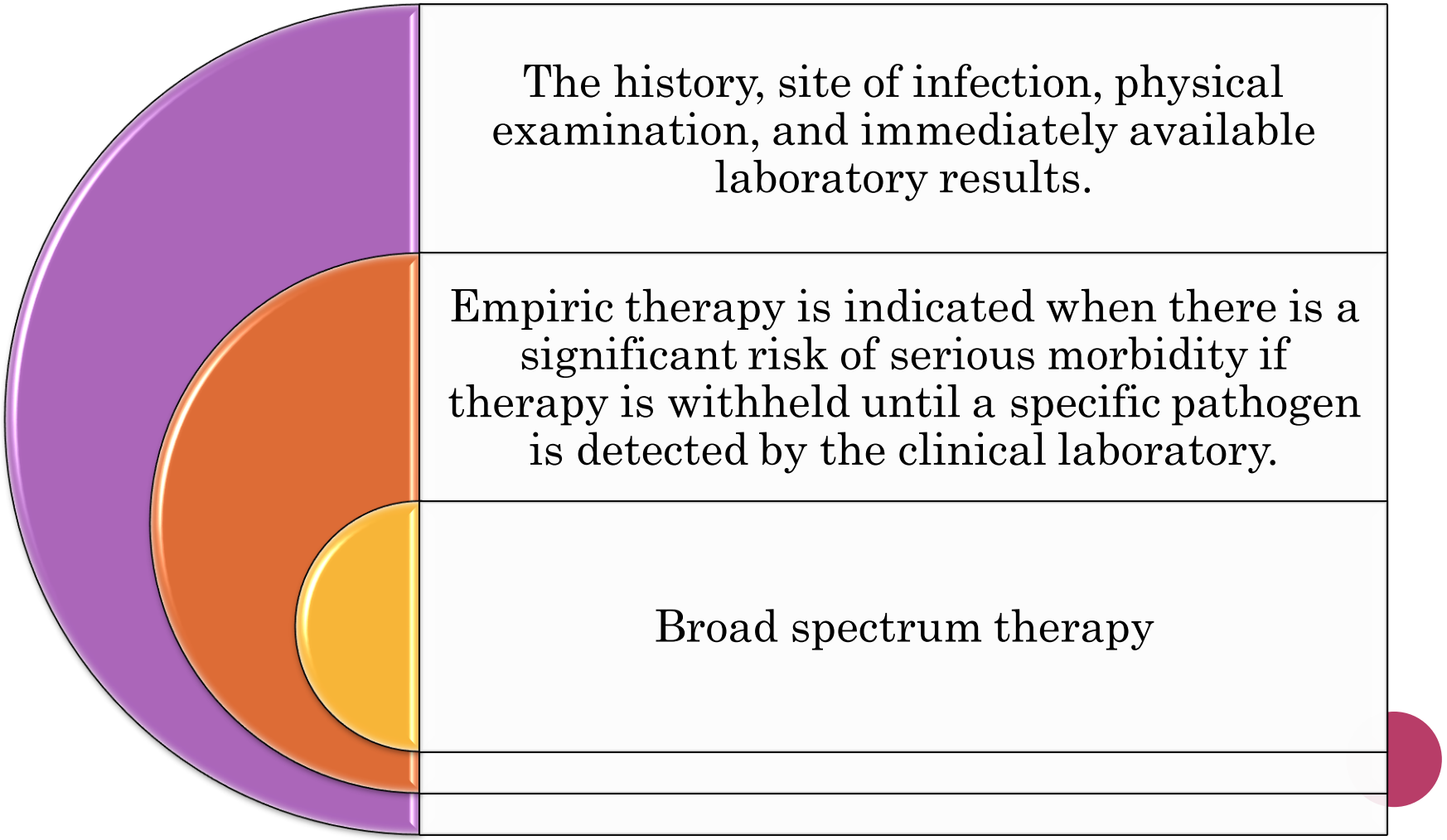
- Confirm an infectious versus noninfectious process.
- Most likely site must be identified according to signs and symptoms.
- Laboratory tests, including the Gram stain, serologic analysis, and antimicrobial susceptibility testing.
- Spectrum of activity, established clinical efficacy, adverse effect profile, pharmacokinetic disposition, and cost considerations
- Once an agent has been selected, the dosage and duration should be based on the size of the patient, site of infection, route of elimination, and other factors.

EMPIRIC ANTIMICROBIAL THERAPY

empiric (or presumptive) therapy

definitive therapy.

EMPIRIC ANTIMICROBIAL THERAPY



Choice of antimicrobial agent depends upon

Host factors:

History of allergy

Immune system

renal and hepatic function.

ability to tolerate drugs by mouth

severity of illness

Age (meningitis: H.influenza, S. pneumoniae and Neisseria meningitides).

if female whether pregnant, breast-feeding or taking oral contraceptive.

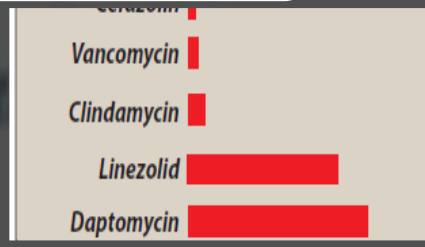
The duration of therapy, dosage and route of administration depend on site, type and severity of infection and response.

The dose varies according to a number of factors including age, weight, renal function and severity of infection.

II. Pharmacologic factors:

- The kinetics of absorption, distribution and elimination.
- The ability of the drug to be delivered to the site of infection.
- The potential toxicity of an agent.
- The pharmacokinetic or pharmcodynamic interaction with other drug.

III cost of antimicrobial therapy



Site/Type of Infection	Suspected Organisms
1. Respiratory	
Pharyngitis	Viral, group A streptococci
Bronchitis, otitis	Viral, *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis*
Acute sinusitis	Viral, *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*
Chronic sinusitis	Anaerobes, *Staphylococcus aureus* (as well as suspected organisms associated with acute sinusitis)
Epiglottitis	Viral, *Haemophilus influenzae*
Pneumonia	
Community -acquired	
Normal host	*Streptococcus pneumoniae*, viral, mycoplasma
Aspiration	Normal aerobic and anaerobic mouth flora
Pediatrics	*Streptococcus pneumoniae, Haemophilus influenzae*
COPD	*Streptococcus pneumoniae, Haemophilus influenzae, Legionella, Chlamydia, Mycoplasma*
Alcoholic	*Streptococcus pneumoniae, Klebsiella*
Hospital-acquired	
Aspiration	Mouth anaerobes, aerobic gram-negative rods, *Staphylococcus aureus*
Neutropenic	Fungi, aerobic gram-negative rods, *Staphylococcus aureus*
HIV	Fungi, *Pneumocystis, Legionella, Nocardia, Streptococcus pneumoniae, Pseudomonas*
2. Urinary Tract	
Community-acquired	*Escherichia coli*, other gram-negative rods, *Staphylococcus aureus, Staphylococcus epidermidis*, enterococci
Hospital-acquired	Resistant aerobic gram-negative rods, enterococci
3. Skin and Soft Tissue	
Cellulitis	Group A streptococci, *Staphylococcus aureus*
IV catheter infection	*Staphylococcus aureus, Staphylococcus epidermidis*
Surgical wound	*Staphylococcus aureus*, gram-negative rods
Diabetic ulcer	*Staphylococcus aureus*, gram-negative aerobic rods, anaerobes
Furuncle	*Staphylococcus aureus*
4. Intra-Abdominal	*Bacteroides fragilis, Escherichia coli*, other aerobic gram-negative rods, enterococci
5. Gastroenteritis	*Salmonella, Shigella, Helicobacter, Campylobacter, Clostridium difficile*, amoeba, *Giardia*, viral, enterotoxigenic-hemorrhagic *Escherichia coli*
6. Endocarditis	
Pre-existing valvular disease	*Viridans streptococci*
IV drug user	*Staphylococcus aureus*, aerobic gram-negative rods, enterococci, fungi
Prosthetic valve	*Staphylococcus epidermidis, Staphylocccus aureus*
7. Osteomyelitis and Septic Arthritis	*Staphylococcus aureus*, aerobic gram-negative rods
8. Meningitis	
<2 months	*Escherichia coli*, group B streptococci, *Listeria*
2 months–12 years	*Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae*
Adults	*Streptococcus pneumoniae, Neisseria meningitidis*
Hospital-acquired	*Streptococcus pneumoniae, Neisseria meningitidis*, aerobic gram-negative rods
Postneurosurgery	*Staphylococcus aureus*, aerobic gram-negative rods

COPD, chronic obstructive pulmonary disease; IV, intravenous.

TABLE 51–1 Empiric antimicrobial therapy based on microbiologic etiology.

Suspected or Proven Disease or Pathogen	Drugs of First Choice	Alternative Drugs
Gram-negative cocci (aerobic)		
Moraxella (Branhamella) catarrhalis	TMP-SMZ,[1] cephalosporin (second- or third-generation)[2]	Quinolone,[3] macrolide[4]
Neisseria gonorrhoeae	Ceftriaxone, cefixime	Spectinomycin, azithromycin
Neisseria meningitides	Penicillin G	Chloramphenicol, ceftriaxone, cefotaxime
Gram-negative rods (aerobic)		
E coli, Klebsiella, Proteus	Cephalosporin (first- or second-generation),[2] TMP-SMZ[1]	Quinolone,[3] aminoglycoside[5]
Enterobacter, Citrobacter, Serratia	TMP-SMZ,[1] quinolone,[3] carbapenem[6]	Antipseudomonal penicillin,[7] aminoglycoside,[5] cefepime
Shigella	Quinolone[3]	TMP-SMZ,[1] ampicillin, azithromycin, ceftriaxone
Salmonella	Quinolone,[3] ceftriaxone	Chloramphenicol, ampicillin, TMP-SMZ[1]
Campylobacter jejuni	Erythromycin or azithromycin	Tetracycline, quinolone[3]
Brucella species	Doxycycline + rifampin or aminoglycoside[5]	Chloramphenicol + aminoglycoside[5] or TMP-SMZ[1]
Helicobacter pylori	Proton pump inhibitor + amoxicillin + clarithromycin	Bismuth + metronidazole + tetracycline + proton pump inhibitor
Vibrio species	Tetracycline	Quinolone,[3] TMP-SMZ[1]
Pseudomonas aeruginosa	Antipseudomonal penicillin ± aminoglycoside[5]	Antipseudomonal penicillin ± quinolone,[3] cefepime, ceftazidime, antipseudomonal carbapenem,[6] or aztreonam ± aminoglycoside[5]
Burkholderia cepacia (formerly *Pseudomonas cepacia*)	TMP-SMZ[1]	Ceftazidime, chloramphenicol
Stenotrophomonas maltophilia (formerly *Xanthomonas maltophilia*)	TMP-SMZ[1]	Minocycline, ticarcillin-clavulanate, tigecycline, ceftazidime, quinolone[3]
Legionella species	Azithromycin or quinolone[3]	Clarithromycin, erythromycin
Gram-positive cocci (aerobic)		
Streptococcus pneumoniae	Penicillin[8]	Doxycycline, ceftriaxone, antipneumococcal quinolone,[3] macrolide,[4] linezolid
Streptococcus pyogenes (group A)	Penicillin, clindamycin	Erythromycin, cephalosporin (first-generation)[2]
Streptococcus agalactiae (group B)	Penicillin (± aminoglycoside[5])	Vancomycin
Viridans streptococci	Penicillin	Cephalosporin (first- or third-generation),[2] vancomycin
Staphylococcus aureus		
β-Lactamase negative	Penicillin	Cephalosporin (first-generation),[2] vancomycin
β-Lactamase positive	Penicillinase-resistant penicillin[9]	As above
Methicillin-resistant	Vancomycin	TMP-SMZ,[1] minocycline, linezolid, daptomycin, tigecycline
Enterococcus species[10]	Penicillin ± aminoglycoside[5]	Vancomycin ± aminoglycoside[5]
Gram-positive rods (aerobic)		
Bacillus species (non-*anthracis*)	Vancomycin	Imipenem, quinolone,[3] clindamycin
Listeria species	Ampicillin (± aminoglycoside[5])	TMP-SMZ[1]
Nocardia species	Sulfadiazine, TMP-SMZ[1]	Minocycline, imipenem, amikacin, linezolid
Anaerobic bacteria		
Gram-positive (clostridia, *Peptococcus, Actinomyces, Peptostreptococcus*)	Penicillin, clindamycin	Vancomycin, carbapenem,[6] chloramphenicol
Clostridium difficile	Metronidazole	Vancomycin, bacitracin
Bacteroides fragilis	Metronidazole	Chloramphenicol, carbapenem,[6] β-lactam–β-lactamase-inhibitor combinations, clindamycin

Suspected or Proven Disease or Pathogen	Drugs of First Choice	Alternative Drugs
Fusobacterium, Prevotella, Porphyromonas	Metronidazole, clindamycin, penicillin	As for *B fragilis*
Mycobacteria		
Mycobacterium tuberculosis	Isoniazid + rifampin + ethambutol + pyrazinamide	Streptomycin, moxifloxacin, amikacin, ethionamide, cycloserine, PAS, linezolid
Mycobacterium leprae		
Multibacillary	Dapsone + rifampin + clofazimine	
Paucibacillary	Dapsone + rifampin	
Mycoplasma pneumoniae	Tetracycline, erythromycin	Azithromycin, clarithromycin, quinolone[3]
Chlamydia		
C trachomatis	Tetracycline, azithromycin	Clindamycin, ofloxacin
C pneumoniae	Tetracycline, erythromycin	Clarithromycin, azithromycin
C psittaci	Tetracycline	Chloramphenicol
Spirochetes		
Borrelia recurrentis	Doxycycline	Erythromycin, chloramphenicol, penicillin
Borrelia burgdorferi		
Early	Doxycycline, amoxicillin	Cefuroxime axetil, penicillin
Late	Ceftriaxone	
Leptospira species	Penicillin	Tetracycline
Treponema species	Penicillin	Tetracycline, azithromycin, ceftriaxone
Fungi		
Aspergillus species	Voriconazole	Amphotericin B, itraconazole, caspofungin
Blastomyces species	Amphotericin B	Itraconazole, fluconazole
Candida species	Amphotericin B, echinocandin[11]	Fluconazole, itraconazole, voriconazole
Cryptococcus	Amphotericin B ± flucytosine (5-FC)	Fluconazole, voriconazole
Coccidioides immitis	Amphotericin B	Fluconazole, itraconazole, voriconazole, posaconazole
Histoplasma capsulatum	Amphotericin B	Itraconazole
Mucoraceae (*Rhizopus, Absidia*)	Amphotericin B	Posaconazole
Sporothrix schenckii	Amphotericin B	Itraconazole

TABLE 51–2 Empiric antimicrobial therapy based on site of infection.

Presumed Site of Infection	Common Pathogens	Drugs of First Choice	Alternative Drugs
Bacterial endocarditis			
Acute	*Staphylococcus aureus*	Vancomycin + gentamicin	Penicillinase-resistant penicillin[1] + gentamicin
Subacute	*Viridans* streptococci, enterococci	Penicillin + gentamicin	Vancomycin + gentamicin
Septic arthritis			
Child	*H influenzae, S aureus,* β-hemolytic streptococci	Ceftriaxone	Ampicillin-sulbactam
Adult	*S aureus,* Enterobacteriaceae	Cefazolin	Vancomycin, quinolone
Acute otitis media, sinusitis	*H influenzae, S pneumoniae, M catarrhalis*	Amoxicillin	Amoxicillin-clavulanate, cefuroxime axetil, TMP-SMZ
Cellulitis	*S aureus,* group A streptococcus	Penicillinase-resistant penicillin, cephalosporin (first-generation)[2]	Vancomycin, clindamycin, linezolid, daptomycin
Meningitis			
Neonate	Group B streptococcus, *E coli, Listeria*	Ampicillin + cephalosporin (third-generation)	Ampicillin + aminoglycoside, chloramphenicol, meropenem
Child	*H influenzae,* pneumococcus, meningococcus	Ceftriaxone or cefotaxime ± vancomycin[3]	Chloramphenicol, meropenem
Adult	Pneumococcus, meningococcus	Ceftriaxone, cefotaxime	Vancomycin + ceftriaxone or cefotaxime[3]
Peritonitis due to ruptured viscus	Coliforms, *B fragilis*	Metronidazole + cephalosporin (third-generation), piperacillin/tazobactam	Carbapenem, tigecycline
Pneumonia			
Neonate	As in neonatal meningitis		
Child	Pneumococcus, *S aureus, H influenzae*	Ceftriaxone, cefuroxime, cefotaxime	Ampicillin-sulbactam
Adult (community-acquired)	Pneumococcus, *Mycoplasma, Legionella, H influenzae, S aureus, C pneumonia,* coliforms	**Outpatient:** Macrolide,[4] amoxicillin, tetracycline	**Outpatient:** Quinolone
		Inpatient: Macrolide[4] + cefotaxime, ceftriaxone, ertapenem, or ampicillin	**Inpatient:** Doxycycline + cefotaxime, ceftriaxone, ertapenem, or ampicillin; respiratory quinolone[5]
Septicemia[6]	Any	Vancomycin + cephalosporin (third-generation) or piperacillin/tazobactam or imipenem or meropenem	
Septicemia with granulocytopenia	Any	Antipseudomonal penicillin + aminoglycoside; ceftazidime; cefepime; imipenem or meropenem; consider addition of systemic antifungal therapy if fever persists beyond 5 days of empiric therapy	

In Vitro Antimicrobial Susceptibility: Gram-Negative Aerobes

Drugs	Escherichia Coli	Klebsiella Pneumoniae	Enterobacter Cloacae	Proteus Mirabilis	Serratia Marcescens	Pseudomonas Aeruginosa	Haemophilus Influenzae	Haemophilus Influenzae[a]
Ampicillin	++			+++			++++	
Augmentin	+++	++		++++			++++	++++
Aztreonam	++++	++++	+	++++	++++	++++	++++	++++
Cefazolin	+++	+++		++++			+	
Cefepime	++++	++++	+++	++++	++++	++++	++++	++++
Ceftazidime	++++	++++	+	++++	++++	++++	++++	++++
Cefuroxime	+++	+++		++++	+		++++	++++
Cotrimoxazole	++	+++	+++	++++	+++		++++	++++
Ertepenem	++++	++++	++++	++++	++++	+	++++	++++
Gentamicin	++++	++++	++++	++++	++++	+++	++	++
Imipenem/ meropenem/ doripenem	++++	++++	++++	+++	++++	++++	++++	++++
Quinolones	+++	++++	+++	++++	++++	++	++++	++++
TGC[b]	++++	++++	+	++++	++++	+	++++	++++
Tigecycline	++++	++++	++++	++	++++	–	++++	++++
Timentin	+++	++	+	++++	+++	+++	++++	++++
Tobramycin	++++	++++	++++	++++	+++	++++	++	++
Unasyn	+++	+++		++++	++		++++	++++
Zosyn	++++	++++	++	++++	++++	++++	++++	++++

[a] β-Lactamase-producing strains.
[b] Cefataxime, ceftizoxime, ceftriaxone.
TGC, third-generation cephalosporin.

In Vitro Antimicrobial Susceptibility: Aerobic Gram-Positive Cocci

Drugs	Staphylococcus Aureus	Staphylococcus Aureus (MR)	Staphylococcus Epidermidis	Staphylococcus Epidermidis (MR)	Streptococci[a]	Enterococci[b]	Pneumococci
Ampicillin	+		+		++++	++	+++
Augmentin	++++	+	++++		++++	++	++++
Aztreonam							
Cefazolin	++++		++++		++++		++
Cefepime	++++		++++		++++		+++
Cefoxitin/Cefotetan	++		++		++		+
Cefuroxime	++++		++++		++++		+++
Ciprofloxacin[c]	+++	++	+++	++	+	+	++
Clindamycin	++++	+	++++	+	+++		+++
Cotrimoxazole	++++	+++	++	+	++	+	+
Daptomycin[f]	++++	++++	++++	++++	++++	++++	++++
Erythromycin (azithromycin/ clarithromycin)	++		+		+++		++
Imipenem	++++		++++		++++	++	+++
Levofloxacin (gemifloxacin, moxifloxacin)	++++	++	+++	++	+++	++	++++
Linezolid[f]	++++	++++	++++	++++	++++	++++	++++
Nafcillin	++++		++++		++++		++
Penicillin	+		+		++++	++	+++
Quinupristin/ dalfopristin[d,f]	++++	++++	++++	++++	++++	++++	++++
TGC[e]	+++		++		++++		+++
Televancin	++++	++++	++++	++++	++++	++++	++++
Tigecycline[f]	++++	++++	++++	++++	++++	++++	++++
Timentin	++++		++++		++++	+	+
Unasyn	++++		++++		++++	++	+++
Vancomycin	++++	++++	++++	++++	++++	+++	++++
Zosyn	++++		++++		++++	++	+++

[a]Nonpneumococcal streptococci.
[b]Usually requires combination therapy (e.g., ampicillin and an aminoglycoside) for serious infection.
[c]Levofloxacin (gatifloxacin, gemifloxacin, moxifloxacin) is more active than ciprofloxacin against staphylococci and streptococci.
[d]Active against *E. faecium* but unpredictable against *E. faecalis*.
[e]Cefotaxime, ceftizoxime, ceftriaxone, cefoperazone. Ceftazidime has comparatively inferior antistaphylococcal and antipneumococcal activity. Cefotaxime and ceftriaxone are the most reliable cephalosporins versus *S. pneumoniae*.
[f]Active versus vancomycin-resistant *Enterococcus faecium*.
MR, methicillin resistant; TGC, third-generation cephalosporin.

Antimicrobials of Choice in the Treatment of Bacterial Infection

Organism	Drug of Choice	Alternatives	Comments
Aerobes			
Gram-positive cocci			
Streptococcus pyogenes (group A streptococci)	Penicillin	Clindamycin, macrolide, cephalosporin	Clindamycin is the most reliable alternative for penicillin-allergic patients.
Streptococcus pneumoniae	Ceftriaxone, ampicillin, oral amoxicillin	Macrolide, cephalosporin, doxycycline	Although the incidence of penicillin-nonsusceptible pneumococci is 20%–30%, high-dose penicillin or amoxicillin is active against most of these isolates. Penicillin-resistant pneumococci commonly demonstrate resistance to other agents, including erythromycin, tetracyclines, and cephalosporins. Antipneumococcal quinolones (gemifloxacin, levofloxacin, moxifloxacin), ceftriaxone, and cefotaxime are options for treatment of high-level penicillin-resistant isolates.
Enterococcus faecalis	Ampicillin ± gentamicin	Piperacillin-tazobactam; vancomycin ± gentamicin; daptomycin, linezolid, tigecycline	Most commonly isolated enterococcus (80%–85%). Most reliable antienterococcal agents are ampicillin (penicillin, piperacillin-tazobactam), vancomycin, and linezolid. Monotherapy generally inhibits but does not kill the enterococcus. Daptomycin is unique in its bactericidal activity against enterococci. Aminoglycosides must be added to ampicillin or vancomycin to provide bactericidal activity. High-level aminoglycoside resistance should be determined for endocarditis.
Enterococcus faecium	Vancomycin ± gentamicin	Linezolid, daptomycin, dalfopristin/quinupristin (D/Q), tigecycline	Second most common enterococcal organism (10%–20%) and is more likely than *E. faecalis* to be resistant to multiple antimicrobials. Most reliable agents are daptomycin, D/Q, and linezolid. Monotherapy generally inhibits but does not kill the enterococcus. Aminoglycosides must be added to cell wall–active agents to provide bactericidal activity. Ampicillin and vancomycin resistance is common. Daptomycin, D/Q, and linezolid are drugs of choice for vancomycin-resistant isolates.
Staphylococcus aureus (nafcillin-resistant)	Nafcillin	Cefazolin, vancomycin, clindamycin, trimethoprim-sulfamethoxazole linezolid,	10%–15% of isolates inhibited by penicillin. Most isolates susceptible to nafcillin, cephalosporins, trimethoprim-sulfamethoxazole, and clindamycin. First-generation cephalosporins are equal to nafcillin. Most second- and third-generation cephalosporins adequate in the treatment of infection (exceptions include ceftazidime and cefonicid). Methicillin-resistant *S. aureus* must be treated with vancomycin; however, trimethoprim-sulfamethoxazole, daptomycin, D/Q, linezolid, or minocycline can be used.
	Vancomycin	Trimethoprim-sulfamethoxazole, minocycline, daptomycin, tigecycline, televancin	
Staphylococcus epidermidis (nafcillin-resistant)	Nafcillin	Cefazolin, vancomycin, clindamycin	Most isolates are β-lactam-, clindamycin-, and trimethoprim-sulfamethoxazole–resistant. Most reliable agents are vancomycin, daptomycin, D/Q, and linezolid. Rifampin is active and can be used in conjunction with other agents; however, monotherapy with rifampin is associated with development of resistance.
	Vancomycin	Daptomycin, linezolid, D/Q	
Gram-positive Bacilli			
Diphtheroids	Penicillin	Cephalosporin	
Corynebacterium jeikeium	Vancomycin	Erythromycin, quinolone	
Listeria monocytogenes	Ampicillin (± gentamicin)	Trimethoprim-sulfamethoxazole	
Gram-negative Cocci			
Moraxella catarrhalis	Trimethoprim-sulfamethoxazole	Amoxicillin-clavulanic acid, erythromycin, doxycycline, second- or third-generation cephalosporin	
Neisseria gonorrhoeae	Cefixime	Ceftriaxone	
Neisseria meningitidis	Penicillin	Third-generation cephalosporin	

Gram-negative bacilli			
Campylobacter fetus	Imipenem	Gentamicin	
Campylobacter jejuni	Quinolone, erythromycin	A tetracycline, amoxicillin-clavulanic acid	
Enterobacter	Trimethoprim-sulfamethoxazole	Quinolone, carbapenem, aminoglycoside	Not predictably inhibited by third-generation cephalosporins. Carbapenems, quinolones, trimethoprim-sulfamethoxazole, cefepime, and aminoglycosides are most active agents.
Escherichia coli	Third-generation cephalosporin	First- or second-generation cephalosporin, gentamicin	Extended-spectrum β-lactamase (ESBL) –producers should be treated with a carbapenem.
Haemophilus influenzae	Third-generation cephalosporin	β-Lactamase inhibitor combinations, second-generation cephalosporin, trimethoprim-sulfamethoxazole	
Helicobacter pylori	Amoxicillin + clarithromycin + omeprazole	Tetracycline + metronidazole + bismuth subsalicylate	
Klebsiella pneumoniae	Third-generation cephalosporin	First- or second-generation cephalosporin, gentamicin, trimethoprim-sulfamethoxazole	Extended-spectrum β-lactamase (ESBL) –producers should be treated with a carbapenem.
Legionella	Fluoroquinolone	Erythromycin ± rifampin, doxycycline	
Proteus mirabilis	Ampicillin	First-generation cephalosporin, trimethoprim-sulfamethoxazole	
Other *Proteus*	Third-generation cephalosporin	β-Lactamase inhibitor combination, aminoglycoside, trimethoprim-sulfamethoxazole	
Pseudomonas aeruginosa	Antipseudomonal penicillin (or ceftazidime) ± aminoglycoside (or quinolone)	Quinolone or imipenem ± aminoglycoside	Most active agents include aminoglycosides, doripenem, imipenem, meropenem, ceftazidime, cefepime, aztreonam and the extended-spectrum penicillins. Monotherapy is adequate for most pseudomonal infections.
Salmonella typhi	Quinolone	Ceftriaxone	
Serratia marcescens	Third-generation cephalosporin	Trimethoprim-sulfamethoxazole, aminoglycoside	
Shigella	Quinolone	Trimethoprim-sulfamethoxazole, ampicillin	
Stenotrophomonas maltophilia	Trimethoprim-sulfamethoxazole	Ceftazidime, minocycline, β-lactamase inhibitor combination (Timentin)	
Anaerobes			
Bacteroides fragilis	Metronidazole	β-Lactamase inhibitor combinations, penems	Most active agents (95%–100%) include metronidazole, the β-lactamase inhibitor combinations (ampicillin-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanic acid), and penems. Clindamycin, cefoxitin, cefotetan, cefmetazole, ceftizoxime have good activity but not to the degree of metronidazole. Aminoglycosides and aztreonam are inactive.
Clostridia difficile	Metronidazole	Vancomycin	Oral vancomycin is the drug of choice for severe infection.
Fusobacterium	Penicillin	Metronidazole, clindamycin	
Other Oropharyngeal			
Prevotella	β-Lactamase inhibitor combination	Metronidazole, clindamycin	
Peptostreptococcus	Penicillin	Clindamycin, cephalosporin	Most β-lactams active (exceptions include aztreonam, nafcillin, ceftazidime).
Other			
Actinomyces israelii	Penicillin	Tetracyclines	
Nocardia	Trimethoprim-sulfamethoxazole	Amikacin, minocycline, imipenem	
Chlamydia trachomatis	Doxycycline	Azithromycin	
Chlamydia pneumoniae		Azithromycin, clarithromycin	
Mycoplasma pneumoniae	Doxycycline	Azithromycin, clarithromycin	
Borrelia burgdorferi	Doxycycline	Ampicillin, second- or third-generation cephalosporin	
Treponema pallidum	Penicillin	Doxycycline	

Antibiotic Adverse Effects and Toxicities

Antibiotic	Side Effects	Comments
β-Lactams, (penicillin, cephalosporins, monobactams, penems)	*Allergic:* anaphylaxis, urticaria, serum sickness, rash, fever	Many patients will have "ampicillin rash" or "β-lactam rash" with no cross-reactivity with any other penicillins/β-lactams. Most commonly observed in patients with concomitant EBV disease. Likelihood of IgE-mediated cross-reactivity between penicillins and cephalosporins approximately 5%–10%. Most recent data strongly suggest minimal IgE cross-reactivity between penicillins and imipenem/meropenem. No IgE cross-reactivity between aztreonam and penicillins.
	Diarrhea	Particularly common with ampicillin, augmentin, ceftriaxone, and cefoperazone. Antibiotic-associated colitis can occur with most antimicrobials.
	Hematologic: anemia, thrombocytopenia, antiplatelet activity, hypothrombinemia	Hemolytic anemia more common with higher doses. Antiplatelet activity (inhibition of platelet aggregation) most common with the antipseudomonal penicillins and high serum levels of other β-lactams. Hypothrombinemia more often associated with those cephalosporins with the methyltetrazolethiol side chain (cefamandole, cefotetan). Reaction preventable and reversible with vitamin K.
	Hepatitis or biliary sludging	Hepatitis most common with oxacillin. Biliary sludging and stones reported with ceftriaxone.
	Phlebitis	
	Seizure activity	Associated with high levels of β-lactams, particularly penicillins and imipenem.
	Potassium load	Penicillin G (K^+).
	Nephritis	Most common with methicillin; however, occasionally reported for most other β-lactams.
	Neutropenia	Nafcillin.
	Disulfiram reaction	Associated with cephalosporins with methyltetrazolethiol side chain (cefamandole, cefotetan).
	Hypotension, nausea	Associated with fast infusion of imipenem.
Aminoglycosides (gentamicin, tobramycin, amikacin, netilmicin)	Nephrotoxicity	Averages 10%–15% incidence. Generally reversible, usually occurs after 5–7 days of therapy. *Risk factors:* dehydration, age, dose, duration, concurrent nephrotoxins, liver disease.
	Ototoxicity	1%–5% incidence, often irreversible. Both cochlear and vestibular toxicity occur.
	Neuromuscular paralysis	Rare, most common with large doses administered via intraperitoneal instillation or in patients with myasthenia gravis.
Macrolides (erythromycin, azithromycin, clarithromycin)	Nausea, vomiting, "burning" stomach	Oral administration. Azithromycin and clarithromycin associated with less nausea than erythromycin.
	Cholestatic jaundice	Reported for all erythromycin salts, most common with estolate.
	Ototoxicity	Most common with high doses in patients with renal or hepatic failure.
Telithromycin	Hepatoxicity; upper GI	Severe, sometime fatal hepatoxicity associated with telithromycin.
Clindamycin	Diarrhea	Most common adverse effect. High association with antibiotic-associated colitis.
Tetracyclines (including tigecycline)	Allergic	
	Photosensitivity	
	Teeth and bone deposition and discoloration	Avoid in pediatrics (<8 years old), pregnancy, and breast-feeding.
	GI	Upper GI predominates.
	Hepatitis	Primarily in pregnancy or the elderly.
	Renal (azotemia)	Tetracyclines have antianabolic effect and should be avoided in patients with ↓ renal function. Less problematic with doxycycline.
	Vestibular	Associated with minocycline, particularly high doses.

Antibiotic Adverse Effects and Toxicities (*Continued*)

Antibiotic	Side Effects	Comments
Vancomycin	Ototoxicity	Only with receipt of concomitant ototoxins such as aminoglycosides or macrolides.
	Nephrotoxicity	Nephrotoxic only with high doses or in combination with other nephrotoxins.
	Hypotension, flushing	Associated with rapid infusion of vancomycin. More common with increased doses.
	Phlebitis	Needs large volume dilution.
Dalfopristin/quinupristin	Phlebitis	Generally requires central line administration.
	Myalgia	Moderate to severe in many patients.
	Increased bilirubin	
Daptomycin	Myalgia	Primarily at high doses and reversible.
Linezolid	Thrombocytopenia, neutropenia, anemia, MAO inhibition, tongue discoloration	
Televancin	Renal toxicity, prolonged QT	
Sulfonamides	GI	Nausea, diarrhea.
	Hepatic	Cholestatic hepatitis, ↑ incidence in HIV.
	Rash	Exfoliative dermatitis, Stevens-Johnson syndrome. More common in HIV.
	Hyperkalemia	Only with trimethoprim (as a component of trimethoprim-sulfamethoxazole).
	Bone marrow	Neutropenia, thrombocytopenia. More common in HIV.
	Kernicterus	Caused by unbound drug in the neonate. Premature liver cannot conjugate bilirubin. Sulfonamide displaces bilirubin from protein, resulting in excessive free bilirubin and kernicterus.
Chloramphenicol	Anemia	Idiosyncratic irreversible aplastic anemia (rare). Reversible dose-related anemia.
	Gray syndrome	Caused by inability of neonates to conjugate chloramphenicol.
Quinolones	GI	Nausea, vomiting, diarrhea.
	Prolonged QT	Moxifloxacin; possibly all quinolones as a class.
	Drug interactions	↓ Oral bioavailability with multivalent cations.
	CNS	Altered mental status, confusion, seizures.
	Cartilage toxicity	Toxic in animal model. Despite this toxicity, appears safe in children including patients with cystic fibrosis.
	Tendonitis or tendon rupture	Common in elderly, renal failure, concomitant glucocorticoids.

Antimicrobial Dosing

Weight (low TI)

Site of infection

Anatomic and Physiologic Barriers

Patient age

Fever: increases and decreases blood flow to mesenteric, hepatic, and renal organ systems and can either increase or decrease drug clearance

Route of Elimination

- **B-lactam, AG, Vancomycin**
- **Azithromycin, clindamycin, metronidazol**

UCSF/Mt. Zion Medical Center Adult Antimicrobial Dosing Guidelines[a]

Approved by the Antibiotic Advisory Subcommittee and the Pharmacy and Therapeutics Committee 7/10
Department of Pharmaceutical Services

Drug	CrCl > 50 mL/min	CrCl 10–50 mL/min	CrCl < 10 mL/min (ESRD not on HD)	Dialysis (HD or CRRT)
Acyclovir	*Herpes simplex infections* 5 mg/kg/dose IV every 8 hours *HSV encephalitis / Herpes zoster* 10 mg/kg/dose IV every 8 hours	5 mg/kg/dose IV every 12–24 hours 10 mg/kg/dose IV every 12–24 hours	2.5 mg/kg IV every 24 hours 5 mg/kg IV every 24 hours	HD: 2.5 mg/kg IV ×1 now then 2.5 mg/kg every evening (give after HD on HD days) CRRT: 5 mg/kg every 24 hours HD: 5 mg/kg IV ×1 now then 5 mg/kg every evening (give after HD on HD days) CRRT: 5–10 mg/kg every 12–24 hours
Amphotericin B	0.6–1.0 mg/kg IV every 24 hours	No Change	No Change	No Change
Dosage reductions in renal disease unnecessary; however, due to the drug's nephrotoxicity, consider reducing the dose or holding the drug in the setting of a rising SCr.				
AmBisome	*Invasive mold infections* 3–5 mg/kg IV every 24 hours Doses up to 10mg/kg have been used for invasive mucormycosis *Invasive yeast infections* 3 mg/kg IV every 24 hours *Prophylaxis (heme-onc)* 1 mg/kg IV every 24 hours	No Change	No Change	No Change
Amikacin	≥60 mL/min 15–20 mg/kg/dose IV every 24 hours	See Below	See Below	
Consultation with ID/ID pharmacy recommended before use. Dose is based on ideal body weight (IBW) except in obese patients or those under their ideal body weight. Use actual body weight if patient weight is less than IBW. Use adjusted body weight (ABW) in patients who are obese. Amikacin is generally used as a second-line aminoglycoside because of its increased cost and need to send out levels. The total daily dose of amikacin can be administered as a single daily dose in patients with normal renal function (CrCl ≥60 mL/min). Patients with decreased renal function or abnormal body composition should have doses adjusted according to the recommendations below. Turnaround time on amikacin levels is usually 2–4 days. Peak levels are not useful with this dosing regimen; trough levels are recommended and should be <5 mg/L.				
	40–60 mL/min 5–7.5 mg/kg IV every 12 hours	20–40 mL/min 5 mg/kg IV every 12–24 hours	<20 mL/min 5 mg/kg loading dose *(Consult pharmacy for maintenance dose)*	HD: 5 mg/kg ×1, then 3 mg/kg IV after HD CRRT: 5 mg/kg ×1, then 3 mg/kg IV every 24 hours
With traditional dosing of amikacin, peak (20–30 mg/L) and trough (<8mg/L) levels are recommended in patients anticipated to receive aminoglycosides for severe gram-negative infection. Those patients with CrCl <60 mL/min, obesity, or increased fluid volume should be monitored with serum amikacin levels.				
Ampicillin	1–2 g IV every 4–6 hours	1–1.5 g IV every 6 hours	1 g IV every 8–12 hours	HD: 1–2 g IV every 12 hours CRRT: 1–2 g IV every 6 hours
Ampicillin/ sulbactam	1.5–3 g IV every 6 hours	1.5 g IV every 6–8 hours	1.5 g IV every 12 hours	HD: 1.5 g IV every 12 hours CRRT: 1.5 g IV every 6 hours
Aztreonam	2 g IV every 8 hours	2 g IV every 12 hours	1 g IV every 12 hours	HD: 1 g IV ×1 now then 1 g every evening (give after HD on HD days) CRRT: 2 g IV every 12 hours

UCSF/Mt. Zion Medical Center Adult Antimicrobial Dosing Guidelines[a] (*Continued*)

Drug	CrCl > 50 mL/min	CrCl 10–50 mL/min	CrCl < 10 mL/min (ESRD not on HD)	Dialysis (HD or CRRT)
Cefazolin	1–2 g IV every 8 hours	1–2 g IV every 12 hours	1 g IV every 24 hours	HD: 2 g after HD only CRRT: 2 g IV every 12 hours
Caspofungin Severe hepatic dysfunction: 70 mg LD, then 35 mg IV daily	LD: 70 mg × 1, then 50 mg every 24 hours Increase maintenance dose to 70 mg when given with phenytoin, rifampin, carbamazapine, dexamethasone, nevirapine, efavirenz	No Change	No Change	No Change
Cefepime Febrile neutropenia, meningitis, pseudomonas infections, critically ill patients	>60 mL/min 2 g IV every 12 hours 2 g IV every 8 hours	30–60 mL/min 2 g IV every 24 hours 2 g IV every 12 hours	10–30 mL/min 1 g IV every 24 hours 2 g IV every 24 hours	<10 mL/min 500 mg IV every 24 hours 1 g IV every 24 hours	HD: 2 g after HD only CRRT: 2 g IV every 12 hours
Ceftazidime	2 g IV every 8 hours	2 g IV every 12–24 hours	0.5 g IV every 24 hours	HD: 1 g after HD only CRRT: 2 g IV every 12 hours
Ceftriaxone Meningitis: 2 g every 12 hours Endocarditis and osteomyelitis: 2 g every 24 hours	1 g IV every 24 hours	No Change	No Change	No Change
Ciprofloxacin[IV-PO] Pseudomonas infections	400 mg IV every 12 hours 500–750 mg PO every 12 hours 400 mg IV every 8 hours 750 mg PO every 12 hours	30–50 mL/min No Change No Change	10–30 mL/min 200–400 mg IV every 12 hours 250–500 mg PO every 12 hours	200 IV every 12 hours 250 mg PO every 12 hours	HD: 400 mg IV every 24 hours or 500 mg PO every 24 hours CRRT: 400 mg IV every 12 hours
Clindamycin	600–900 mg IV every 8 hours	No Change	No Change	No Change
Colistin Consultation with ID pharmacy recommended	2.5 mg/kg IV every 12 hours	2.5 mg/kg IV every 12–24 hours	1.5 mg/kg IV every 24 hours	HD: 1.5 mg/kg every 24 hours CRRT: 1.5 mg/kg every 24 hours
Daptomycin Dose on total body weight	4–10 mg/kg IV every 24 hours Dose depends on indication	<30 mL/min 4–10 mg/kg IV every 48 hours		HD: 4–10 mg/kg IV every 48 hours CRRT: 4–10 mg/kg IV every 48 hours
Doxycycline[IV-PO]	100 mg IV/PO every 12 hours	No Change	No Change	No Change

Gentamicin	≥60 mL/min 5 mg/kg/dose IV every 24 hours	See Below	See Below	

Dose is based on ideal body weight (IBW) except in obese patients or those under their ideal body weight. Use actual body weight if patient weight is less than IBW. Use adjusted body weight (ABW) in patients who are obese. The total daily dose of gentamicin can be administered as a single daily dose in patients with normal renal function (CrCl ≥60 mL/min). Peak levels are not useful in this regimen; however, trough levels are recommended and in most cases will be undetectable. Patients with decreased renal function or abnormal body composition should have doses adjusted according to the recommendations below.

Alternative: 1.6 mg/kg iv every 8 hours (total 5 mg/kg/day) for clinically tenuous patients or patients with changing volume status	40–60 mL/min 1.2–1.5 mg/kg IV every 12 hours	20–40 mL/min 1.2–1.5 mg/kg IV every 12–24 hours	<20 mL/min 2 mg/kg loading dose *(Consult pharmacy for maintenance dose)*	HD: 2 mg/kg ×1, then 1 mg/kg IV after HD CRRT: 2 mg/kg ×1, then 1.5 mg/kg IV every 24 hours

With traditional dosing of gentamicin, peak (5–8 mg/L) and trough (<2 mg/L) levels are recommended for patients receiving aminoglycosides for severe gram-negative infection. Lower doses (1 mg/kg/dose every 8 hours) are suggested when aminoglycosides are used synergistically in gram-positive infections. Those patients with CrCl <60 mL/min, obesity, or increased fluid volume should be monitored with serum gentamicin levels. Goals for gram-positive synergy dosing peak (3–4 mg/L) and trough (<1 mg/L)

Imipenem	500 mg IV every 6–8 hours *max 50 mg/kg/d*	500 mg IV every 8 hours	<20 mL/min 250–500 mg IV every 12 hours	HD: 250 mg IV every 12 hours CRRT: 500 mg IV every 8 hours
Isoniazid	300 mg PO every 24 hours	No Change	No Change	No Change
Levofloxacin[IV-PO] Nosocomial pneumonia/ Pseudomonas infections	250–500 mg IV/PO every 24 hours 750 mg IV/PO every 24 hours	500 mg ×1, then 250 mg IV/PO every 24 hours 750 mg ×1; then 750 IV/PO every 48 hours	500 mg ×1, then 250 mg IV/PO every 48 hours 750 mg ×1, then 500 mg IV/PO every 48 hours	HD: 500 mg ×1, then 250 mg every 48 hours CRRT: 500 mg ×1, then 250–500 mg every 24 hours
Linezolid[IV-PO]	600 mg IV/PO every 12 hours	No Change	No Change	No Change

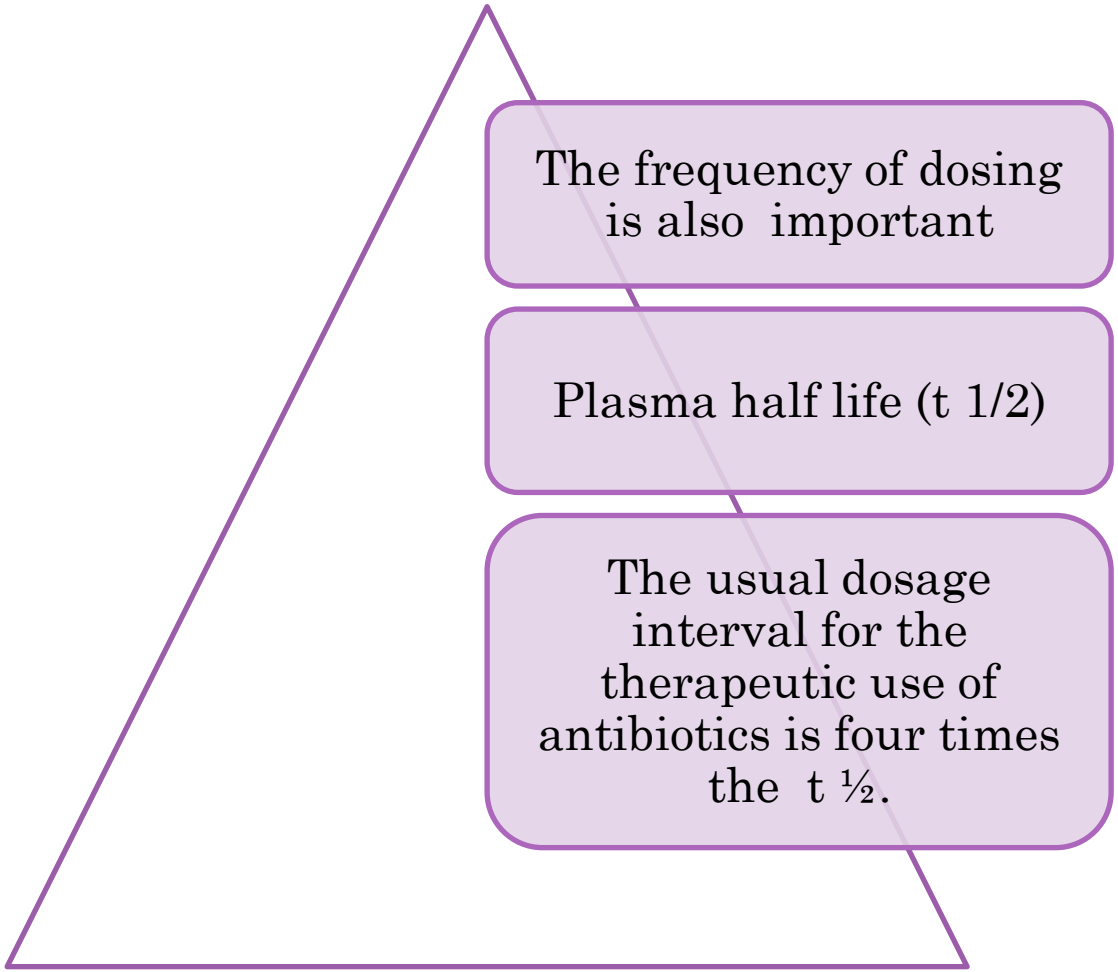
Meropenem		25–50 mL/min	10–25 mL/min		
Meningitis/documented or suspected *Pseudomonas* infections or critically ill	0.5–1 g IV every 8 hours 2 g IV every 8 hours	0.5–1 g IV every 12 hours 2 g IV every 12 hours	0.5 g IV every 12 hours 1 g IV every 12 hours	0.5 g IV every 24 hours 1 g IV every 24 hours	HD: 500 mg IV ×1 now then 500 mg every evening (give after HD on HD days) CRRT: 1 g IV every 12 hours

Metronidazole[IV-PO]	500 mg IV/PO every 8 hours	500 mg IV/PO every 8 hours	500 mg IV/PO every 12 hours ESRD not on HD	500 mg IV/PO every 8 hours
Moxifloxacin[IV-PO]	400 mg IV/PO every 24 hours	No Change	No Change	No Change
Nafcillin	1–2 g IV every 4–6 hours	No Change	No Change	No Change
Penicillin G	2–3 MU IV every 4–6 hours	1–2 MU IV every 4–6 hours	1 MU IV every 6 hours	HD: 1 MU IV every 6 hours CRRT: 2 MU IV every 4–6 hours

TABLE 51–5 Antimicrobial agents that require dosage adjustment or are contraindicated in patients with renal or hepatic impairment.

Dosage Adjustment Needed in Renal Impairment	Contraindicated in Renal Impairment	Dosage Adjustment Needed in Hepatic Impairment
Acyclovir, amantadine, aminoglycosides, aztreonam, carbapenems, cephalosporins,[1] clarithromycin, colistin, cycloserine, daptomycin, didanosine, emtricitabine, ethambutol, ethionamide, famciclovir, fluconazole, flucytosine, foscarnet, ganciclovir, lamivudine, penicillins,[3] pyrazinamide, quinolones,[4] rimantadine, stavudine, telavancin, telbivudine, telithromycin, tenofovir, terbinafine, trimethoprim-sulfamethoxazole, valacyclovir, vancomycin, zidovudine	Cidofovir, methenamine, nalidixic acid, nitrofurantoin, sulfonamides (long-acting), tetracyclines[2]	Amprenavir, atazanavir, chloramphenicol, clindamycin, erythromycin, fosamprenavir, indinavir, metronidazole, rimantadine, tigecycline

PROPER TIME-INTERVAL



Route of administration

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The intravenous route is preferred in the following situations:

(1) for critically ill patients

(2) for patients with bacterial meningitis or endocarditis

(3) for patients with nausea, vomiting, gastrectomy, or diseases that may impair oral absorption

(4) when giving antimicrobials that are poorly absorbed following oral administration(vancomycin, antipsudomonas penicillin).

many antimicrobials have similar pharmacokinetic properties when given orally or parenterally (**tetracycline, cotrimoxazole, quinolones, chloramphenicol, metronidazole, clindamycin).** In most cases, oral therapy with these drugs is equally effective, less costly and with fewer complications

ANTIMICROBIAL FAILURE

- Patient specific host factors
- Drug or dosage selection
- Concomitant disease states
- Drug resistance

Inappropriate Antibiotic Use

- Use of antibiotics with no clinical indication (eg, for viral infections)
- Use of broad spectrum antibiotics when not indicated
- Inappropriate choice of empiric antibiotics

MECHANISMS OF ANTIBACTERIAL RESISTANCE

Structurally modified antibiotic target site, resulting in:

- Reduced antibiotic binding

Altered uptake of antibiotics, resulting in:

- Decreased permeability
- Increased efflux

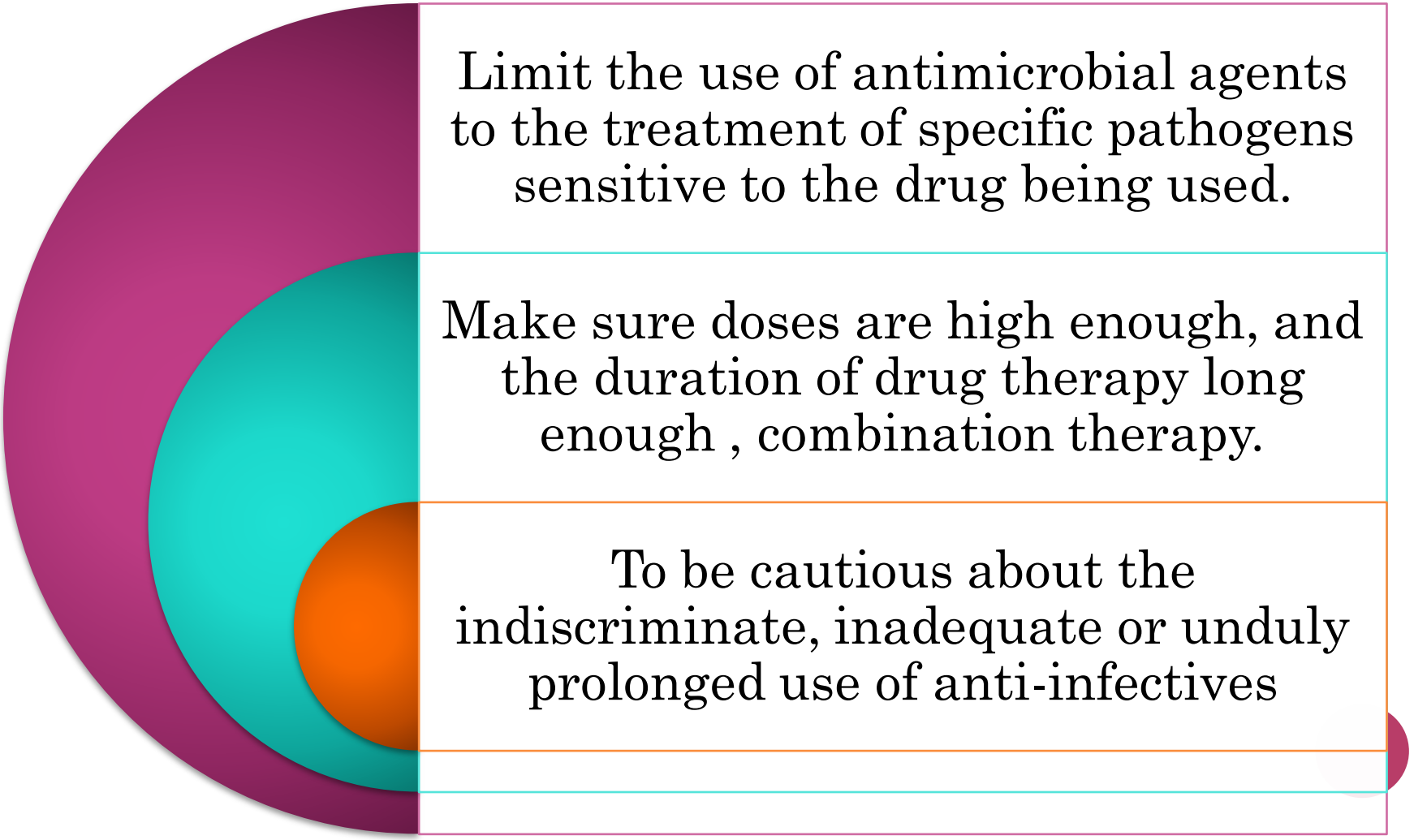
Antibiotic inactivation

- bacteria acquire genes encoding enzymes that inactivate antibiotics like β-lactamases, aminoglycoside-modifying enzymes, chloramphenicol acetyl transferase

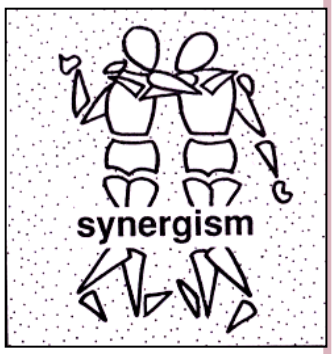
Antibiotic Resistance: importance

1. Financial loss
   - As a rule, second line drugs are more expensive
   - Emergence of resistance to the newer agent
   - Cost of laboratory tests, longer hospital stay
2. Increase morbidity
   - Adverse effects of more complicated regimen
   - Threatening other medical interventions
3. Increase mortality

Preventing Resistance to Drugs



Antibiotic drug-combination therapy -



Rationale

- Minimize the emergence of antibiotic-resistant microorganisms.
- To increase the certainty of a successful clinical outcome.
- To treat mixed bacterial infections & severe infections of unknown etiology.
- To prevent superinfection.
- To decrease toxicity without decreasing efficacy.

Indications :

- In the patients with life threatening sepsis of unknown etiology.
- When increased bactericidal effect against a specific organism is desired. e.g.: treatment of Enterococcus infection (penicillin & aminoglycoside)
- Prevention of rapid emergence of resistant bacteria . e.g.: Tuberculosis

Commonly used antimicrobial combinations:

1. **Penicillin and gentamycin are synergistic against S. especially S.viridans and enterococci.**
2. Antipseudomonas penicillins and aminoglycosides are synergistic.
3. Cephalosporins and aminoglycosides are synergistic against K. pneumoniae.
4. Sulfamethoxazole and trimethoprim are synergistic against some gram positive and negative organisms.
5. Penicillins and cephalosporins are potentiation with beta-lactamase inhibitors such as clavulanic acid and sulbactam.
6. Unique dug combination; imipenem-cilastatin. The enzyme inhibitor cilastatin prevents metabolic breakdown of imipenem by the kidney.

Antibiotics in pregnancy

CATE-GORY	DESCRIPTION	DRUG
A	No human fetal risk or remote possibility of fetal harm	
B	No controlled studies show human risk; animal studies suggest potential toxicity	β-Lactams β-Lactams with inhibitors Cephalosporins *Aztreonam* *Clindamycin* *Erythromycin* *Azithromycin* *Metronidazole* *Nitrofurantoin* Sulfonamides
C	Animal fetal toxicity demonstrated; human risk undefined	*Chloramphenicol* Fluoroquinolones *Clarithromycin* *Trimethoprim* *Vancomycin* *Gentamicin* *Trimethoprim-sulfa-methoxazole*
D	Human fetal risk present, but benefits may outweigh risks	Tetracyclines Aminoglycosides (except *genta-micin*)
X	Human fetal risk clearly outweighs benefits; contraindicated in pregnancy	


ANY
QUESTION