Cephalosporins

By Dr Ayesha Jamil

Classify Cephalosporin's

Describe anti-bacterial spectrum of Cephalosporin's

Describe pharmacokinetics of Cephalosporin's with special emphasis on route of administration and excretion

Describe clinical uses of Cephalosporin's

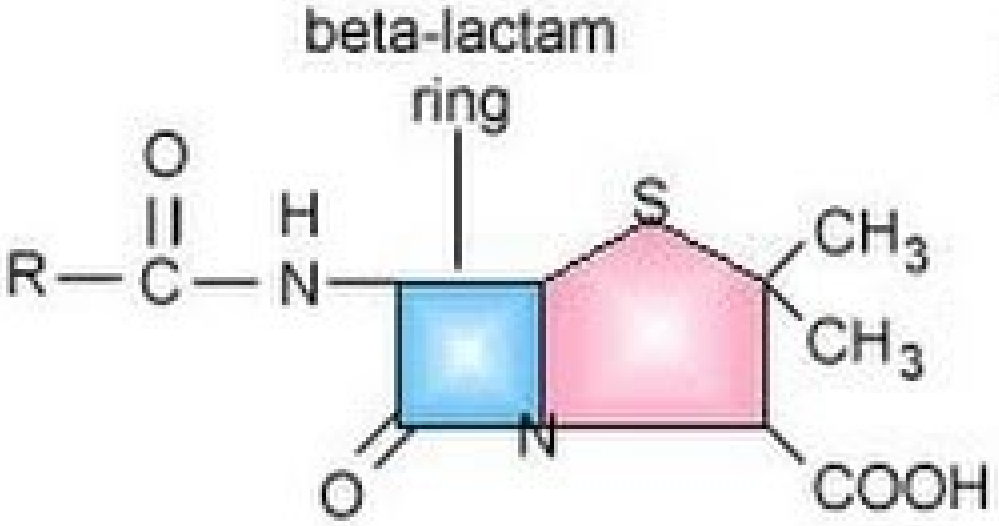
Describe the adverse effects of Cephalosporin's

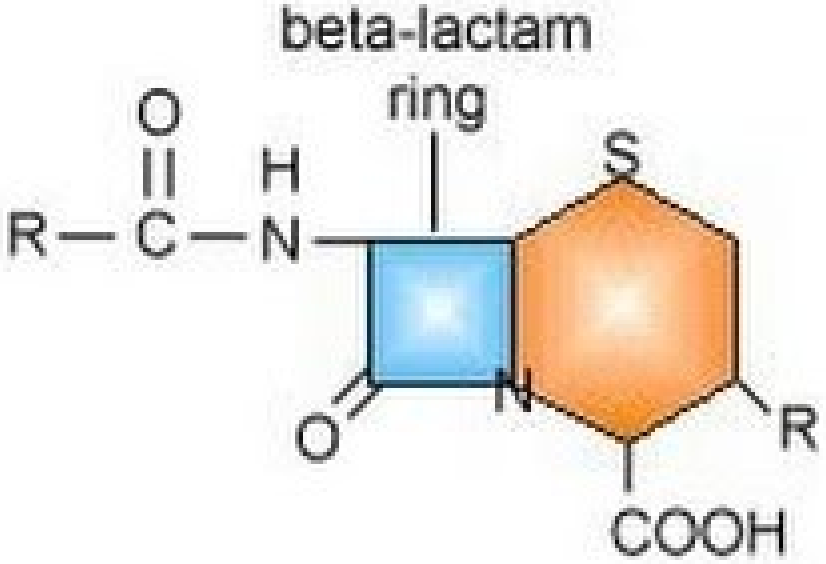
Describe drug interactions of Cephalosporin's with Ethanol

Describe the principal bacterial mechanism of resistance to Cephalosporin's

Relate pharmacokinetics and pharmacodynamics of Cephalosporin with their clinical applications / uses.

- Structurally and functionally they are related to penicillins.
- Most of the cephalosporins are produced semisynthetically by addition of chemical chain at 7-aminocephalosporanic acid.
- Their mode of action and the way bacteria develop resistance against it is the same as that of penicillins.
- But when cephalosporins become resistant to β-lactamases, this resistance is much more stronger than that offered by penicillins against β-lactamases.


beta-lactam
ring
Penicillin
O
H
R
C
N
S
CH3
CH3
N
O
COOH


beta-lactam
ring
Cephalosporin
O
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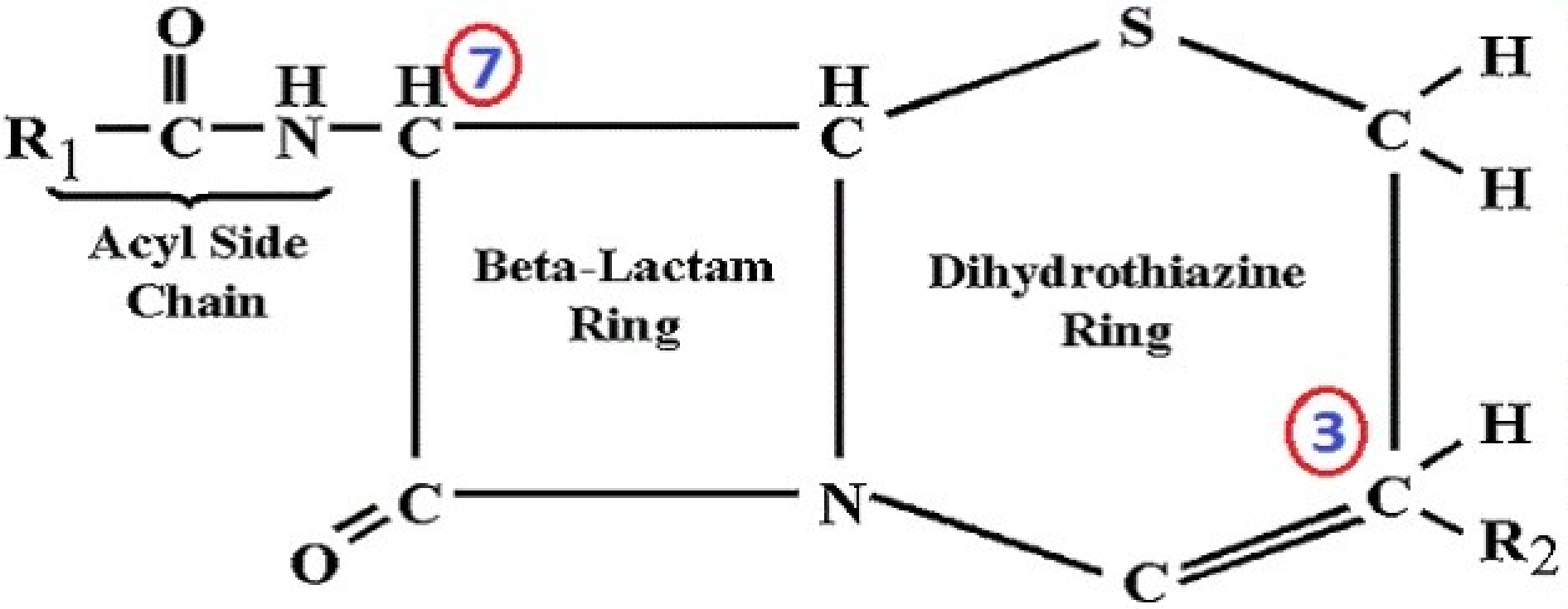


General Structure of Cephalosporins

BY ADDITION OF DIFFERENT SIDE CHAINS:

- *AT POSITION 7 (beta-lactam ring) antibacterial spectrum against specific organisms can be altered.*
- *At position 3 of dihydrothiazine ring , pharmacokinetics can be altered as required.*

Antibacterial spectrum

- Cephalosporins have been divided into 4 generations. This classification is based upon the
- Anti-microbial spectrum
- And resistance of the drug to β-lactamases (cephalosporinases) Cephalosporins are ineffective against MRSA, L. monocytogenes , Clostridium difficile , and the enterococci.

Classification

CEPHALOSPORINS

FIRST GENERATION

ORAL	PARENTERAL
CEPHALEXIN CEPHRADINE CEFADROXIL	CEPHALOTHIN CEFAZOLIN

SECOND GENERATION

ORAL	PARENTERAL
CEFACLOR CEFUROXIME-AXETIL CEFPROZIL	CEFUROXIME CEFOXITIN

THIRD GENERATION

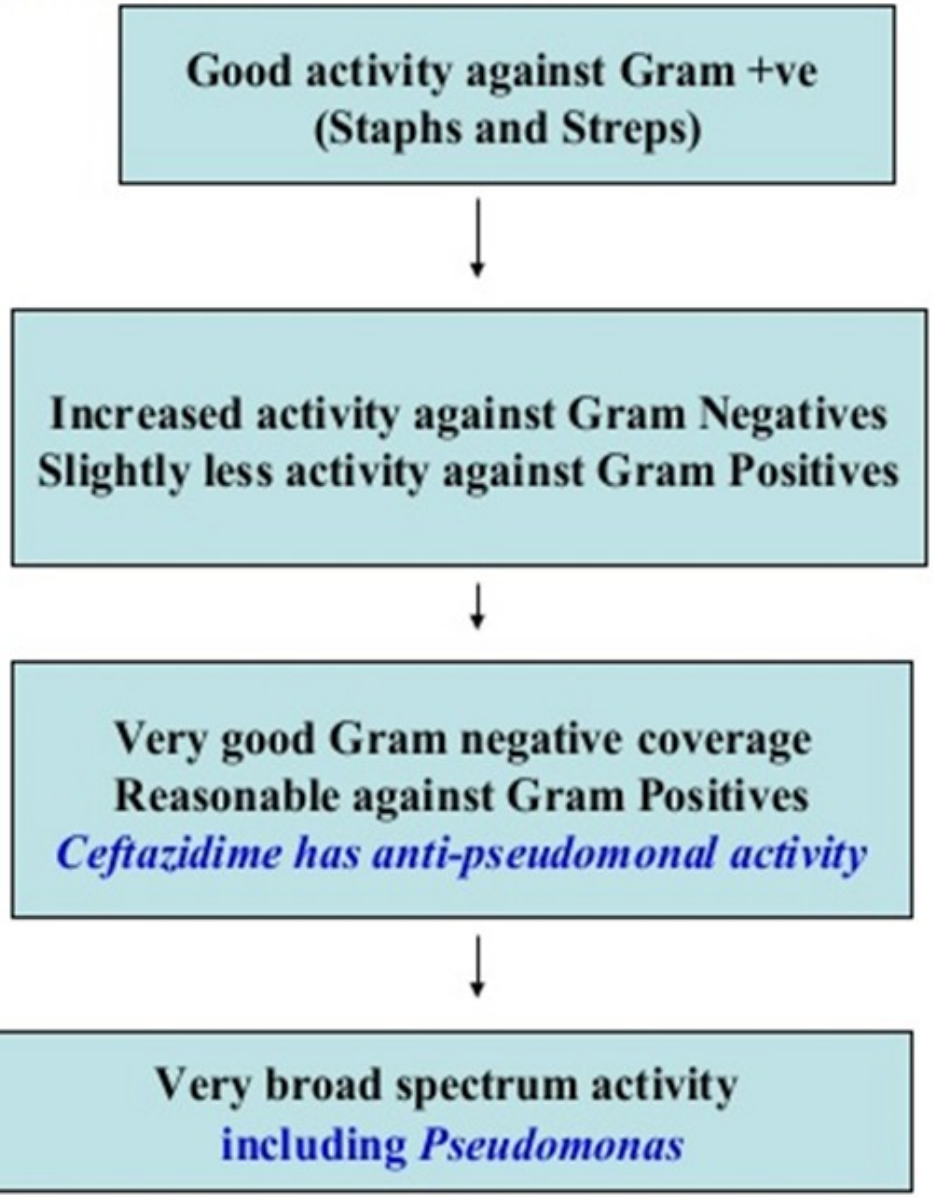
ORAL	PARENTERAL
CEFIXIME CEFDINIR CEFTIBUTEN CEFPODOXIME-PROXETIL CEFTAMET PIVOXIL	CEFOTAXIME CEFTIZOXIME CEFTRIAXONE CEFTAZIDIME CEFOPERAZO-NE

FOURTH GENERATION

PARENTERAL
CEFEPIME CEFPIROME

Classification of Cephalosporins

- **First Generation**
  - Cephazolin
- **Second Generation**
  - Cefuroxime
  - Cefaclor
  - Cefoxitin (cephamycin)
- **Third Generation**
  - Ceftriaxone, Cefotaxime
  - Ceftazidime
- **Fourth Generation**
  - Cefipime



1st generation cephalosporins

- They act as a substitute for Penicillin G.
- They are effective against staphlococcocal infections (resistant to cephalosporinase produced by *staph*.)
- It also shows activity against
- Proteus mirabillis
- E.coli
- Klebsiela

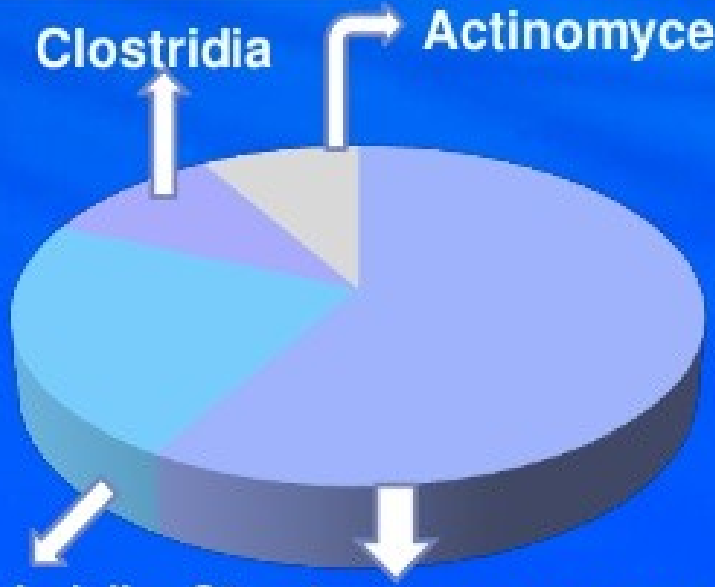
Not effective against salmonella and pseudomonas

CHARACTERISTICS AND ACTIONS:

CEFAZOLIN

- *Prototype first generation cephalosporin.*
- *Mainly used as penicillin G substitute.*
- *Long plasma half –life (2 hours) , longer duration of action, hence used for surgical prophylaxis.*
- *Dose :0.25g 8hourly(mild cases) i.m. / i.v.*

  1g 6hourly(severe cases) i.m. / i.v.




1st Generation - Common Trade Names
Cefazoline
(Parentral)
Cefadroxil
(Oral)
1 VIAL
ZINOL
500 mg
BROAD SPECTRUM
ANTIBIOTIC
CURISAFF
Biodroxil 500 mg
SANDOZ
CAPSULES
500 mg
DURICEF
12 Capsules
SB


SB
1 Vial 1 gm
VELOSEF
Sterile Cephradine
for injection
SB


12 Capsules
SQUIBB
500 mg.
VELOSEF
Cephradine U.S.P. Capsules


VELOSEF
Cephradine
Powder
For Oral
Suspension
250mg / 5ml
www.gardeniapharmacy.com
SB

2nd generation cephalosporins

- They have a broader anti-microbial spectrum.
- In addition to the coverage which is also given by 1st gen it also covers three gram –ive organisms.

2nd generation cephalosporins

- In addition to this there are two other drugs in this group
- ***Cefotetan***
- ***Cefoxitin***

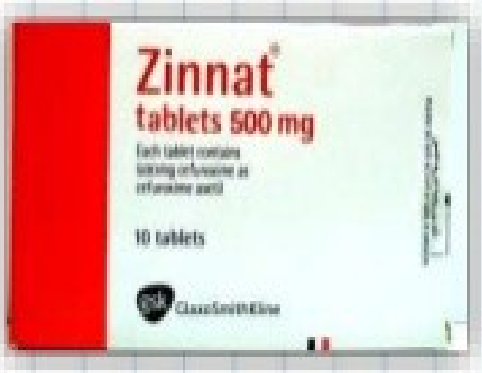
that also cover anaerobs *(Bacteroides Fragalis)*,but they are the not the first choice drugs due to increasing prevalence of resistance in *B.fragalis.*

so the coverage offered by 2nd gen

Staph aureus (MSSA)		neisseria . Gonor	**gm –iv cocci**
Strep. Pnem			
Strep. pyog	**g+ive**	enterobacter	
Anaerobic .strep		E.coli,H. inf,	**gm –ive rods**
		klebsiella , proteus	

2nd Generation - Common Trade Names

Cefuroxime axetil (Oral)



Cefaclor (Oral)

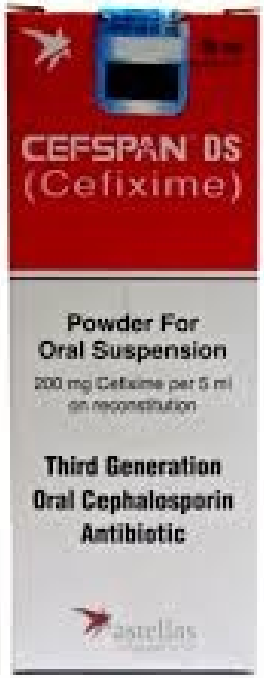
3rd generation cephalosporins

- These cephalosporins have an important role in the treatment of infectious disease. Although inferior to first-generation cephalosporins in regard to their activity against gram-positive cocci, the third-generation cephalosporins have enhanced activity against gramnegative bacilli, including those mentioned for the 2nd gen, as well as most other enteric organisms plus Serratia marcescens .
- ***Ceftriaxone or cefotaxime*** *have become* agents of choice in the treatment of meningitis.
- ***Ceftazidime activity against P.*** **aeruginosa** . The problem of resistance is increasing day by day against it . Therefore careful and very much recommended use is preffered.


Claforan®
(Cefotaxime Sodium)
1g
For I.V. or I.M. Injection
1 Vial of dry substance
+1 Amp. of 4ml water for injection
sanofi aventis


Rocephin®
(Ceftriaxone)
1g i.v.
1 vial with 1g active ingredient
+1 ampoule with 10 ml solvent
Martin Dow


CEFSPAN®
(Cefixime)
Powder For Oral Suspension
Third Generation Oral Cephalosporin Antibiotic
astellas


CEFSPAN DS
(Cefixime)
Powder For Oral Suspension
200 mg Cefixime per 5 ml on reconstitution
Third Generation Oral Cephalosporin Antibiotic
astellas


CEFSPAN®
(Cefixime)
Capsule
400 mg

4th generation cephalosporins

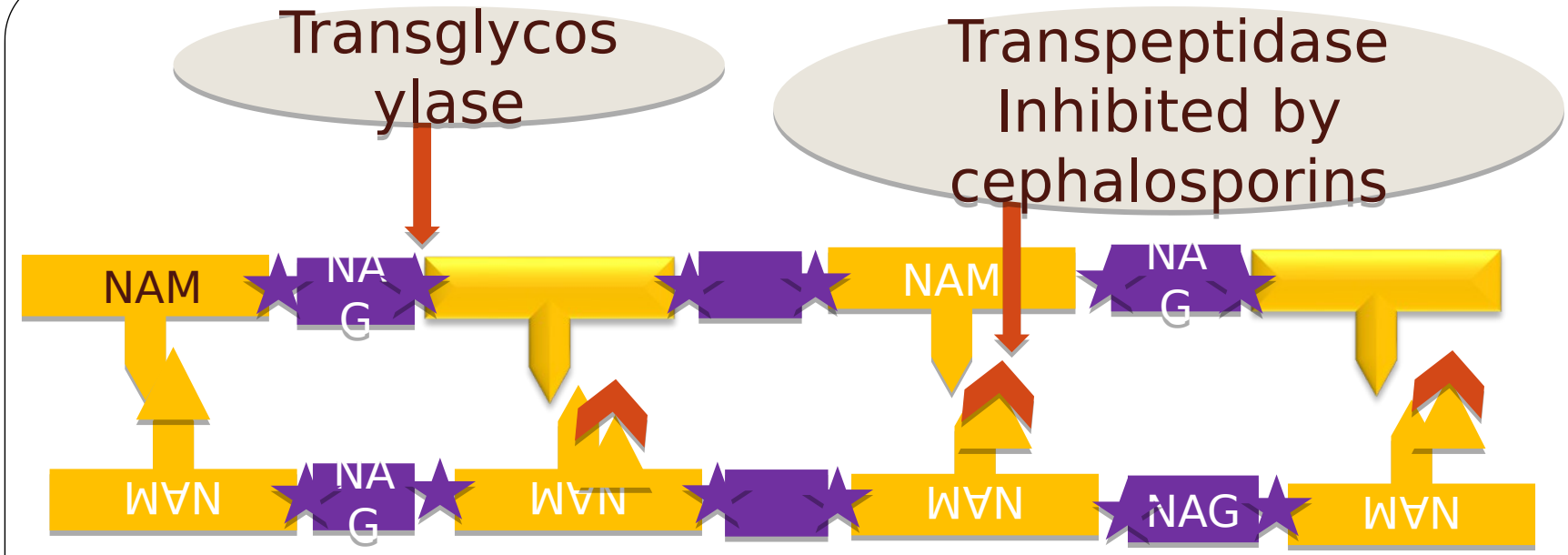
- ***Cefipime*** is included in this group.
- It is only used parentally.
- Has good gm+ive & gm-ive coverage.
- It is also very effective against ***P.Aurigenosa.*** The incidence of resistance is also not much associated with it .


1 VIAL
+ 2 Ampoules 5 ml water for injection
CEFEPIME 1g
CEFEPIME 1g
BROAD SPECTRUM
ANTIBIOTIC
Powder for solution
for I.M. or I.V. injection
PHARCO IS


CefStar™
(Cefepime)
سیف اسٹار
1000mg
IV/IM Injection
CefStar
(Cefepime)
سیف اسٹار
1000mg

Resistance

- Mechanisms of bacterial resistance to the cephalosporins are essentially the same as those described for the penicillins.
- However some of the gm-ive organism s produce extended spectrum β-lactamases(ESBL), thus showing resistance against cephalosporins.
- These gm-ive bacilli producing ESBL are
- *E-coli*
- *K- pneumonie*



Mechanism Of Action Of Cephalosporins

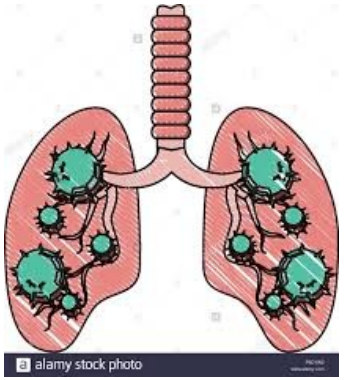
Therapeutic uses of first generation of cephalosporins

- Skin and soft tissues infections particularly those caused by staphylococci and streptococci.

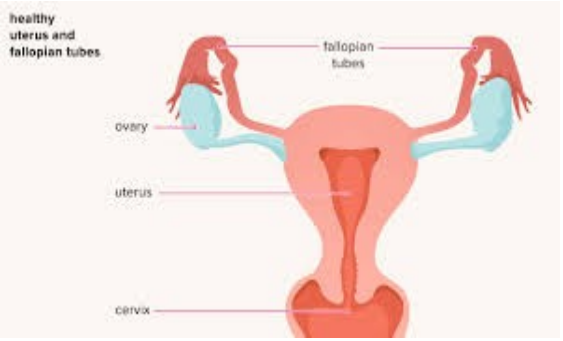
- ***Cefazolin*** is used before surgical procedures prophylactically due to its longer duration of action.

Therapeutic uses of second generation cephalosporins

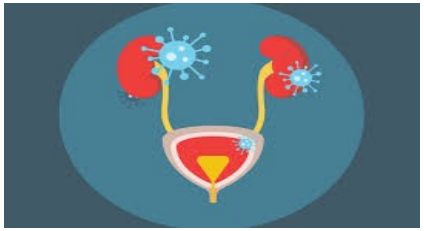
- ***Cefuroxime ZINACEF(sodium/ parenteral) & Cefuroxime (axetil/ oral):***
- Respiratory tract infections like otitis media, sinusitis, bronchitis.



- ***Cefotetan & cefoxitin*** are used for the treatment of pelvic and abdominal infections caused by anaerobic microbes & Gm-ive bacteria.



Therapeutic indications of third generation cephalosporins



- pyelonephritis due to gm-ve bacteria, ***Ceftrioxone:***
- Gonorrhea ***Ceftrioxone***

- Community acquired pneumonias ***Ceftrioxone:***
- Typhoid fever ***Ceftrioxone and cefaperazone***
- Meningitis caused by H-influenza & Neisseria meningitides by ***Ceftrioxone / cefotaxime.***
- nosocomial infections
- Infection by aerobic & anaerobic bacteria.
- Septicemia by gm-ive bacilli

Therapeutic indications for the fourth generation cephalosporins

- Same indications as those for third generation cephalosporins but they are reserved for serious hospital acquired infections

Relation of pharmacokinetics and pharmacodynamics of Cephalosporin with their clinical applications / uses

All cephalosporins distribute very well into body fluids

Adequate distribution and adequate therapeutic levels in the CSF, e.g, ceftriaxone or cefotaxime are achieved and are effective in the treatment of neonatal and childhood meningitis caused by H.
influenzae.

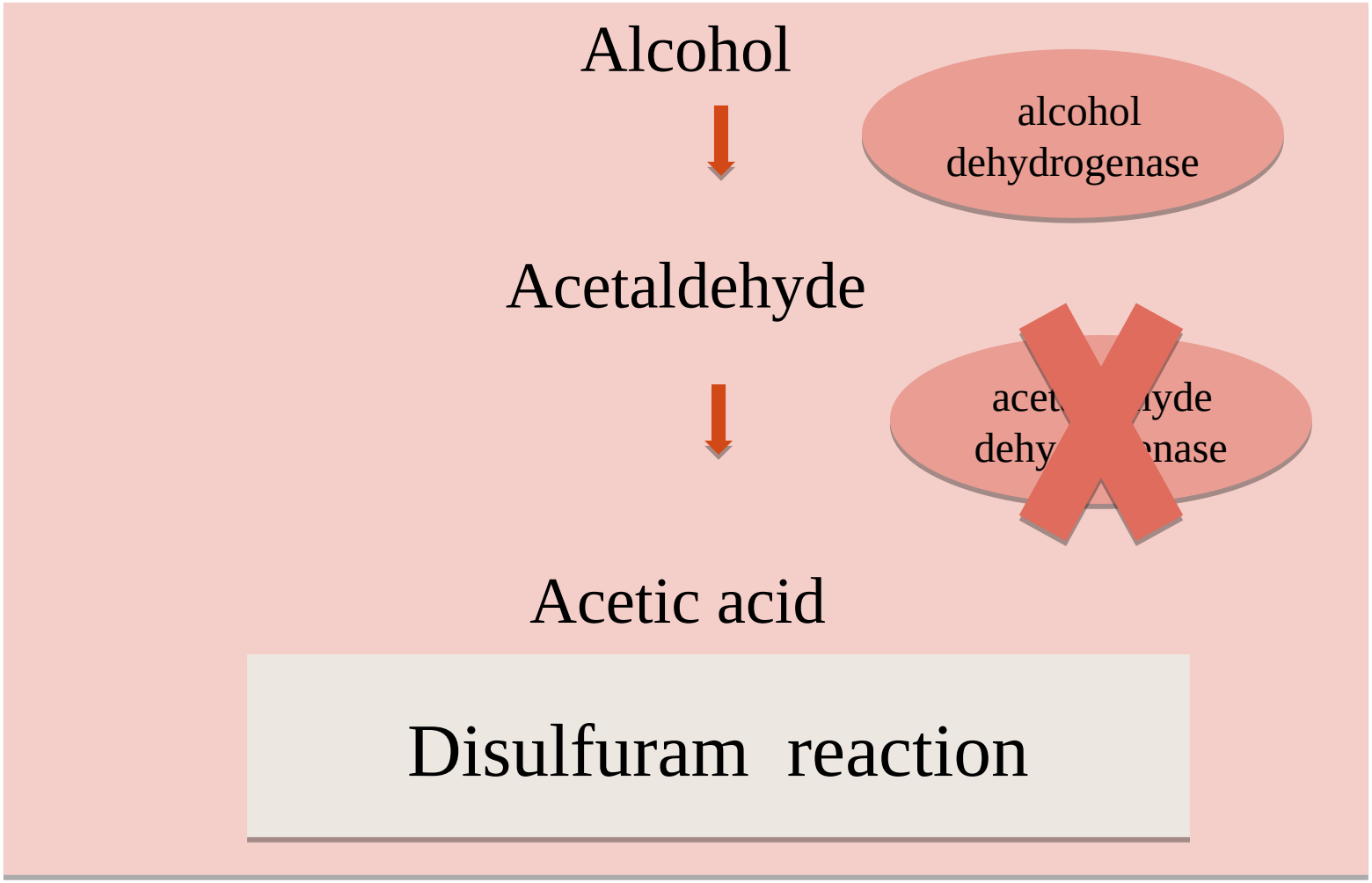
Cefazolin is used preoperatively as it distributes well in bone.

Elimination occurs through tubular secretion and/or glomerular filtration Therefore doses must be adjusted in cases of severe renal failure to guard against accumulation and toxicity. *Ceftriaxone* is excreted through the bile into the feces and, therefore, is frequently employed in patients with renal insufficiency

Adverse effects

- Hypersensitivity reactions
- GI disturbances
- Pain at the site of i/m inj , i/v inj can cause thromophlebitis.
- Nephrotoxity
- Disulfuram like reaction
- Hypoprothrombinemia/ thrombocytopenia/ platelet dyfunction may lead to severe bleeding .

Drug interaction of cephalosporin with Ethanol



Disulfuram reaction

Signs:
Vomiting, nausea, flushing, headache, sweating, chest pain, breathlessness, hypotension, hypoglycemia, confusion,shock and even death.


Thank
You