



# PHARMACOLOGY 2 & 3 LECTURES

## Treatment of UTIs

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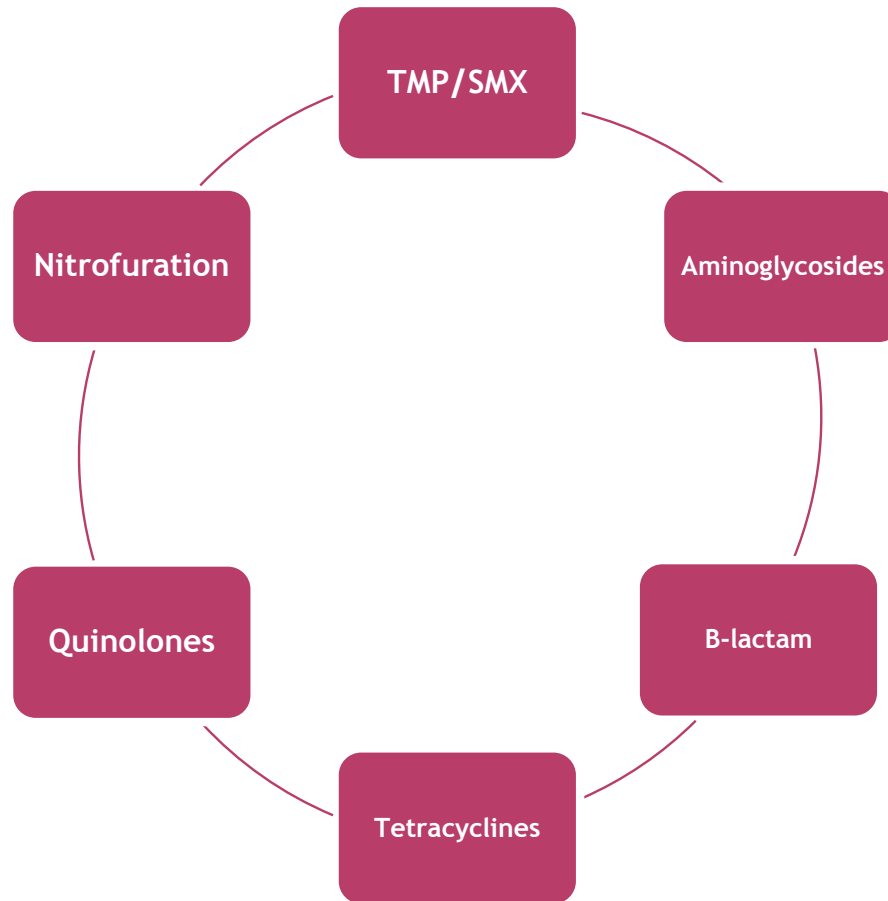
Revised by:

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There is no objectives

red	Important
purple	Extra note

# Treatment of uncomplicated and complicated UTI



Depending on similarity for the combination of drugs in UTI.

# co-trimoxazole = Sulfamethoxazole+Trimethoprim

Bacteriostatic + bacteriostatic = bactericidal (synergism). 'each one alone is a bacteriostatic'

Mechanism	Next Slide :”) it is consequential mechanism
Pharmacokinetics	<u>Sulfonamides+Trimethoprim</u> : ( <u>Bactrim, Septra</u> ) → Trade name <u>Sulfonamides</u> Orally and Rapidly absorbed from stomach and small intestine. Widely distributed < cross placenta >> contraindicated in pregnancy Protein bound, metabolized in liver by acetylation, eliminated in urine. <u>Trimethoprim</u> is given orally, well absorbed from gut, widely distributed, protein bound, more lipidic and 60% excreted in the urine and concentrates in the prostatic fluid.
Indication	Prostatitis ( acute/ chronic ) Acute urinary tract infections
<u>PARC</u>	Recurrent urinary tract infections especially in females Complicated urinary tract infections
Adverse Effect	Gastric upset, Allergy → because of both Hematologic: 1) <u>Acute hemolytic anemia</u> → mainly because of <u>Sulfonamides</u> : a) <u>Hypersensitivity from sulfa</u> b) <u>G6PD deficiency</u> 2) <u>Megaloblastic anemia</u> due to TMP “” cuz it reduce Folic acid”” Kernicterus ( Jaundice due to Displace bilirubin ) sulfa is high plasma protein bound molecule so it make the displacement of bilirubin to be free and go out making the Jaundice .
Contraindication	Pregnancy, Nursing mother, Infants under 6 weeks because they have immature enzymatic system called ( <u>glutathion instability</u> ) make them vulnerable to have Hemolytic anemia , Renal or hepatic failure because of the drug role of secretion , Blood disorders eg. Hemolytic anemia , megaloblastic anemia and G6PD deficiency .

# The normal Enzymes

Dihydropter  
oate  
synthetase

Dihydrofolat  
e  
reductase

P-Aminobenzoic  
Acid

Dihydrofolate

Tetrahydrofolate

Nucleic acid  
synthesis

Sulfonamide  
s

Trimethoprim

Each drug inhibit a specific  
step

# Nitrofurantoin (it is called urinary antiseptic drug)

Work on gram - but mainly Effective against E. coli but not P- aeruginosa ,gram + cocci are susceptible

<b>Mechanism</b>	Changed by <u>bacteria</u> to an active agent that inhibits various enzymes and <u>damages bacterial DNA (bacteriocidal )</u>
<b>Pharmacokinetics</b>	<ul style="list-style-type: none"><li>*Absorbed orally , <b>Well concentrated in the urine &gt;&gt; <u>Turns urine to harmless dark orange- brown</u></b></li><li>*75%of the dose is rapidly metabolized by the liver , 25%(200 micro gram per ml) is excreted in the urine unchanged → this small amount is enough to be bacteriocidal and work as antiseptic in urine .</li><li>*Drug &amp; its metabolites are excreted in the urine</li><li>*Given with food</li><li>*Keep urinary pH below 5.5 ( <u>acidic urine</u> augment drug antibacterial activity)</li><li>*prodrug</li><li>* <b>Poor systemic effect(not used in prostatitis ) .</b></li></ul>
<b>Indication</b>	<ul style="list-style-type: none"><li>*urinary antiseptics but has little or no systemic antibacterial effect.</li><li>*<b><u>Its usefulness is limited to lower UTI's.</u></b></li></ul>
<b>Adverse Effect</b>	<ul style="list-style-type: none"><li>*GIT disturbances: nausea, vomiting, diarrhea &amp; gastric <b>bleeding (<u>must be taken with food</u> )</b>.</li><li>*Headache and nystagmus.</li><li>*Hemolytic anemia</li><li>*Pulmonary fibrosis ( on chronic use )</li></ul>
<b>Contraindication</b>	<ul style="list-style-type: none"><li>*Patients with G 6PD deficiency &gt; <b>Hemolytic anemia</b></li><li>*Neonates ( babies up to the age of one month ) because they have immature enzymatic system called(glutathion instability) make them Vulnerable to have Hemolytic anemia</li><li>*<b>Pregnant women ( after 38 weeks of pregnancy )</b></li><li>*Hepatic and renal impairment cause the liver is the metabolism rout and the renal is the excreted rout</li></ul>

# Tetracyclines

Broad spectrum antibiotic >> Bacteriostatic : Doxycycline Tetracycline

Mechanism	Inhibit protein synthesis by binding <u>reversibly</u> to 30 s ribosomal subunit “Irreversible means it is Bactericidal”	
Pharmacokinetics	<ul style="list-style-type: none"><li>*Long acting tetracycline</li><li>*Usually given orally once daily</li><li>*Protein binding 40-80 %</li><li>*<u>Distributed well, including prostatic tissues</u> &gt;&gt; placenta and excreted in milk</li><li>*Metabolized in liver</li><li>•Excreted through <b>non renal</b> route ( through bile so its good for renal impairment )</li><li>*more systemic.</li></ul>	<p>Absorption is impaired :</p> <ol style="list-style-type: none"><li>1- divalent cations ( Ca, Mg, Fe )</li><li>2- milk and its products</li><li>3- antacids ( aluminium hydroxide gel, sodium bicarbonate)</li></ol>
Indication	<ul style="list-style-type: none"><li>*<u>UTI's due to Mycoplasma &amp; Chlamydia.</u></li><li>*<b>Prostatitis ( acute IV and chronic orally )</b></li></ul>	
Adverse Effect	<ul style="list-style-type: none"><li>❖ Nausea, vomiting, epigastric pain and diarrhea</li><li>❖ <u>Thrombophlebitis ( inflammation because of i.v route )</u></li><li>❖ Hepatic toxicity ( prolonged therapy with high dose )</li><li>❖ <b>Brown discoloration &amp; deformity of teeth ( children) due to its work on calcium</b></li><li>❖ Deformity or growth inhibition of bones( children)</li><li>❖ Vertigo in inner ear.</li><li>❖ Superinfections &gt;&gt; enhance the growth of GIT flora</li><li>❖ Severe diarrhea .</li><li>❖ Mouth ulceration</li><li>❖ Fever</li><li>❖ Phototoxicity ( patient shouldn't exposure to sun light ) .</li></ul>	
Contraindication	Pregnancy Breast feeding Children ( below 10 years )	

# Aminoglycosides(gentamicin)

Mechanism	<p>bactericidal ,Inhibits protein synthesis by binding to <u>30S</u> ribosomal subunits</p> <p>Bactericidal antibiotics.</p> <p>*irreversible</p> <p>Narrow spectrum; work on aerobic and gram - bacteria.</p> <p>has Curary action (neuromuscular blocking effect )</p>
Pharmacokinetics	<p>Poorly absorbed orally</p> <p>Given I.M, I.V.,</p> <p>cross placenta</p> <p>Most active in alkaline meduim</p> <p>Excreted unchanged in urine</p>
Indication	<p>Sever UTI caused by gram negative aerobic organism(pusedomonas)</p>
Adverse effects	<p>Ototoxicity up to deafness</p> <p>Nephrotoxicity up to failure</p> <p>Neuromuscular blocking effect up to paralysis</p>
Contraindication	<p>Renal dysfunction</p> <p>Pregnancy , breast feeding → might make the baby deaf</p> <p>Patients with hearing problem (Diminished hearing )</p> <p>Myasthenia gravis</p> <p>Don't given to patient before surgery because might develop respiratory paralysis.</p>



# B-LACTAM (AUGMENTINE IS A COMBINATION OF AMOXCILLINE AND CLAULANIC ACIDE )

	( A) Extended- spectrum penicillins	(B )3 <sup>rd</sup> generation cephalosporins
E.g	Amoxicillin / clavulanic acid or <b>piperacillin</b> inhibit (gram - . gram + and P-areginosa)	Ceftriaxone & Ceftazidime
Mechanism	Inhibit bacterial cell wall synthesis Bactericidal.	Mainly effective against gram negative
Pharmacokintics		They are given parenterally
Indication	<b>Piperacillin:- Effective against pseudomonas aeruginosa &amp; .Enterobacter</b> Penicillinase sensitive Can be given in comination with-b-lactmase inhibter as clavulanic acid,sulbactam,tazobactam	Sever or complicated UTIs and acute prostatitis
Advers effects	Hypersensitivity , gastric upset	

# FLUROQUINOLONES

(CIPROFLOXACIN & LEVOFLOXACIN)

Mechanism	Inhibits DNA gyrase enzyme (bacteriocidal). inhibit gram - . gram + and P-areginosa/
Indication	UTIs caused by multidrug resistance organisms as <i>pseudomonas</i> . <i>prerotatitidis</i>
Adverse effects	Orthopathy
Contraindication	Children below 18 year → damage of growing cartilage (artheropathy)

# Treatment Of Prostatitis

## • Acute

Non catheter or catheter associated usually due to gm- (e.coli or klebsiella)



## • Chronic

Due to e. coli , klebsiella and proteus



**Non- catheter:** Antibiotics used:

**TMP/SMX (IV) cephalosporin or ciprofloxacin.**

**Catheter associated :** Antibiotics used:

**ciprofloxacin or ceftriaxone.**

**Antibiotics used:**

**ciprofloxacin**

# NOTE

- ◉ Always remember what for pregnant women same as what is for breast feeding women .
- ◉ If its not mention psudomonas aregenosa in the drug indication that's mean it doesn't work on it
- ◉ It is very important to know drugs work on **p-aregenosa because it is high resistant organism** .
- ◉ 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins → Simple UTIs .
- ◉ 3<sup>rd</sup> generation cephalosporins → sever UTIs, Chronic or acute depend on dose,
- ◉ rout and duration .
- ◉ if u want to change urine to be more acidic , give amonium chloride.

QS

\* What is the drug of choice to treat a patient with acute prostatitis ?

- a. Gentamicin
- b. Ciprofloxacin
- c. Aspirin

\*\*Which one is a side effect of nitrofurantoin ?

- a. Bone deformity
- b. Pulmonary fibrosis
- c. Ototoxicity

\*\*\*which one of the following caused arthropathy (Joints problems)?

- a. Gentamicin
- b. nitrofurantoin
- c. Fluoroquinolones



\*b  
\*\*b  
\*\*\*c

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