PHARMACOLOGY

Lectures 2,3: treatment of Urinary tract infections (UTI's)

OBJECTIVES:

At the end of the two lectures the students will be able to:

- Recognize different groups of antibiotics used urinary tract.
- Describe their mechanism of action, pharmacokinetic properties and adverse effects.
- Describe the use of antibiotics and their rational of combination of different antibiotics.
- Describe the spectrum of various antibiotics

Team's note:
It is very advisable to study the pathology and microbiology lectures regarding UTI before studying this lecture.

Abbreviations:
od = once a day.
bd = twice a day.
p.o. = orally

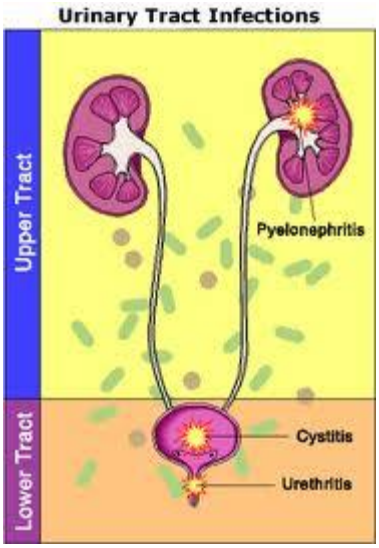
PHARMACOLOGY 435

- Important.
- Extra notes.
- Mnemonics

Introduction to UTI

Urinary tract infections are divided into:

- **Upper** urinary tract (kidney &ureters) infections: pyelonephritis
- **Lower** urinary tract (bladder, urethra & prostate): cystitis, urethritis & prostatitis.
  *Upper urinary tract infections are more serious.
- UTI is the 2nd most common infection (after RTI's).
- It is often associated with some **obstruction of the flow of urine**.
- It is **more common in women** more than men (30:1)
- Incidence of UTI **increases in old age** (10% of men & 20% of women).



Causes of UTI's:

Normally urine is sterile. Bacteria most commonly comes from digestive tract to enter through the opening of the urethra, in the presence of some predisposing factors.

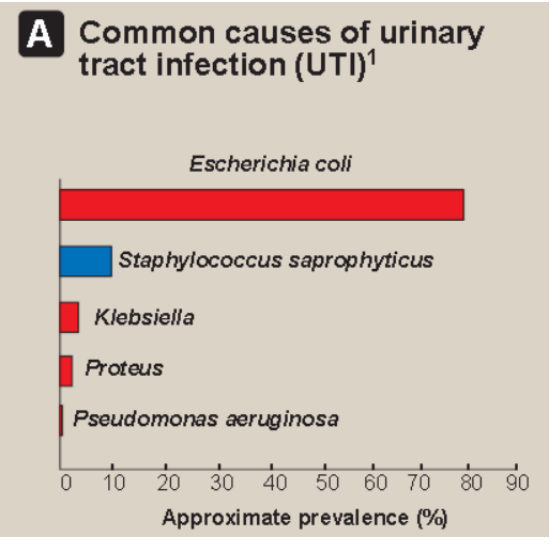
1. **Obstruction** of the flow of urine (e.g. kidney stone).
2. Enlargement of **prostate** gland in men (common cause).
3. **Catheters** placed in urethra and bladder.
4. Not drinking enough fluids (**Dehydration**).
5. Waiting too long to urinate.
6. Large uterus in **pregnant** women.
7. Poor toilet habits (wiping back to front for women)
8. Disorders that **suppress the immune system** (diabetes & cancer chemotherapy).

Bacteria responsible of UTI:

- **Gm- bacteria (most common):**
  E.coli (80% of cases), Proteus mirabilis, Klebsiella & Pseudomonas aeruginosa

- **Gm+ bacteria:**
  Staphylococcus Saprophyticus (Approx. 20%)

- **Mycoplasma, Chlamydia trachomatis & N. gonorrhea**
  Limited to urethra, may be sexually transmitted (unlike E.coli)



Treatment of UTI

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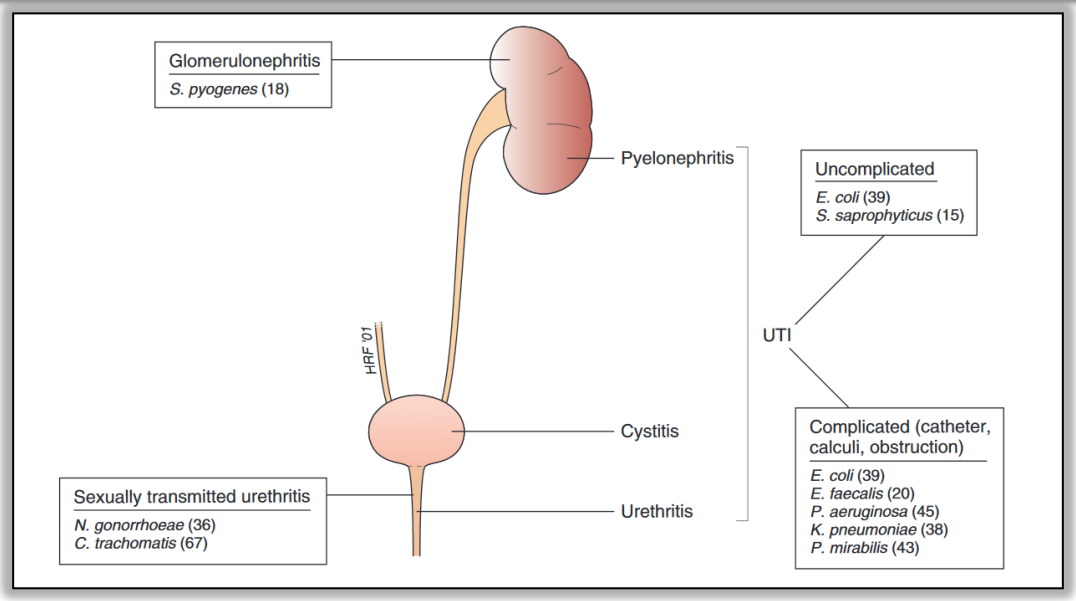


Urinary tract infections can be:

Simple:

Infections do not spread to other parts of the body and go away readily with treatment (Due to E.coli in most cases).

Complicated:

Infections Spread to other parts of the body and resistant to many antibiotics and more difficult to cure.
Due to hospital-acquired bacteria (E.coli, Klebsiella, Proteus, Pseudomonas, enterococci, staphylococci)

Antibiotic treatment of UTI's:

1. **Co-trimoxazole (SMX/TMP)**
2. **Nitrofurantoin.**
3. **Tetracyclines e.g. Doxycycline.**
4. **Aminoglycosides, e.g. gentamicin**
5. **Cephalosporins e.g. ceftriaxone & ceftazidime.**
6. **Quinolones, e.g. ciprofloxacin**

Route of Administration:

p.o. (orally)

Parentally

Treatment strategies: at slide 14

1. Co-trimoxazole (Sulfamethoxazole + Trimethoprim)

Co-trimoxazole (Sulfamethoxazole+ Trimethoprim)

Overview

- Alone, each agent is bacteriostatic but Together they are bactericidal, which we call: synergism.

- The optimal ratio of TMP to SMX in vivo is 1:20 (it means that the best ratio of TMP to SMX to kill the bacteria in the blood is 1:20).
Formulated as: 5(SMX):1(TMP); 800mg SMX+160mg TMP; 400 mg SMX+ 80 mg TMP; 40 mg SMX+8 mg TMP (in all of these values if we divided the value of TMP on the value of SMX we will get 1:5 ratio)

Mechanism of action:

Enzymes requiring folate-derived cofactors are essential for the synthesis of purines and pyrimidines (precursors of RNA and DNA) and other compounds necessary for cellular growth and replication. Therefore, in the absence of folate, cells cannot grow or divide. And that is the mechanism of THE FOLATE ANTAGONISTS (*Sulfamethoxazole + trimethoprim).*
The synergistic antimicrobial activity of *cotrimoxazole* results from its inhibition of two sequential steps in the synthesis of tetrahydrofolic acid. *Sulfamethoxazole* inhibits the incorporation of PABA into dihydrofolic acid precursors, and *trimethoprim* prevents reduction of dihydrofolate to tetrahydrofolate (Figure 40.7).

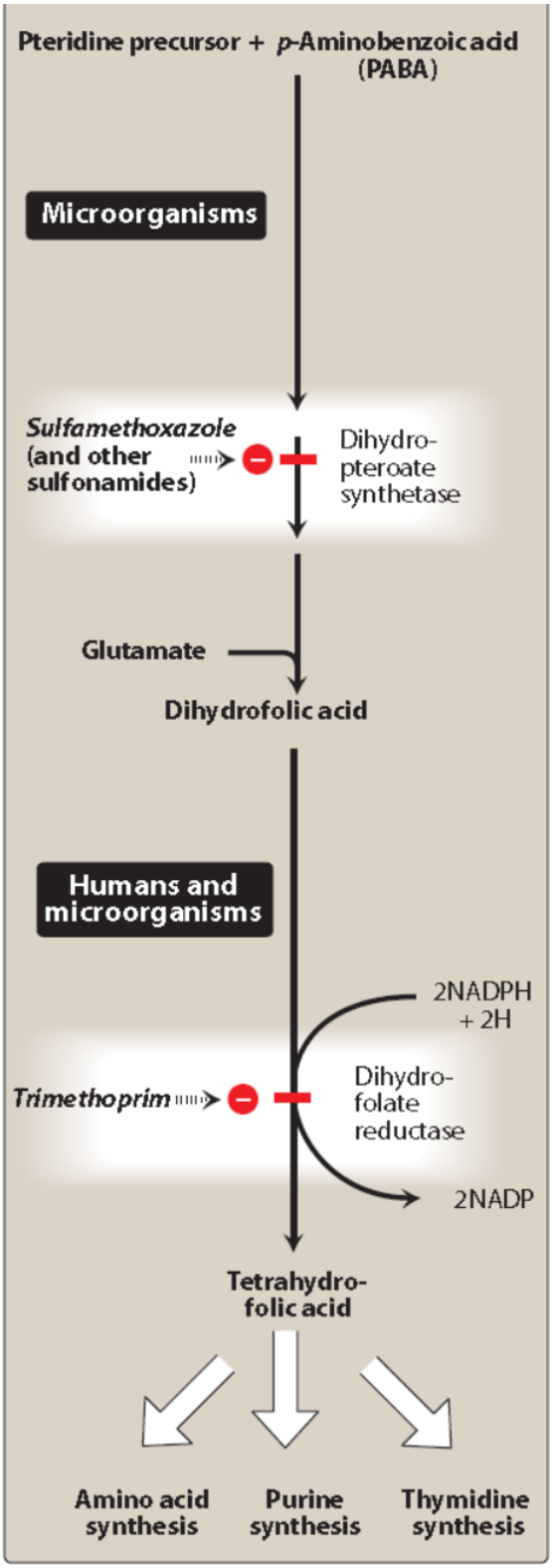
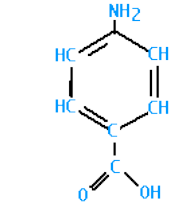
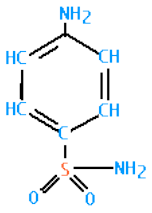


Figure 40.7
Inhibition of tetrahydrofolate synthesis by sulfonamides and *trimethoprim*.

YouTube **Cotrimoxazole mechanism (sulfamethoxazole/trimethylprim)**

Co-trimoxazole (Sulfamethoxazole + Trimethoprim (cont.))

	Specific mechanism of each drug:
Sulfamethoxazole (SMX)	sulfonamides currently in clinical use are synthetic analogs of PABA. Because of their structural similarity to PABA (see chemical structure), the sulfonamides compete with this substrate for the bacterial enzyme, dihydropteroate synthetase. They thus inhibit the synthesis of bacterial dihydrofolic acid and, thereby, the formation of its essential cofactor forms.  Para-aminobenzoic Acid (PABA)  Sulfanilamide
Trimethoprim (TMP)	The active form of folate is the tetrahydro derivative that is formed through reduction of dihydrofolic acid by dihydrofolate reductase. This enzymatic reaction is inhibited by *trimethoprim*, leading to a decreased availability of the tetrahydrofolate cofactors required for bacterial DNA.

		Sulfamethoxazole (SMX) (Sulfonamides)	Trimethoprim (TMP)
Pharmacokinetic	Admin.	- Mainly given orally - Rapidly absorbed **from stomach and small intestine.**	- Usually given orally alone or in combination with SMX - Well absorbed from the gut
	Distribution	- Widely distributed in in body fluids & tissues (including CNS, CSF, placenta and fetus).	• Widely distributed in body fluids & tissues (including CSF) More lipid soluble than SMX • TMP concentrates in the prostatic fluid. Because the drug is a weak base, higher concentrations of *trimethoprim* are achieved in the relatively acidic prostatic and vaginal fluids.
	Protein binding	(approx.70%)	(approx.40 %)
	Metabolism & excretion	- Metabolized in the liver by the process of acetylation. The acetylated product retains the toxic potential to precipitate at neutral or acidic pH. This causes crystalluria "stone formation". - Eliminated in the urine, partly as such (unchanged) and partly as acetylated derivative.	- Metabolized in the liver by the process of O-demethylation -Elimination: 60% of TMP (unchanged) or its metabolite is excreted in the urine

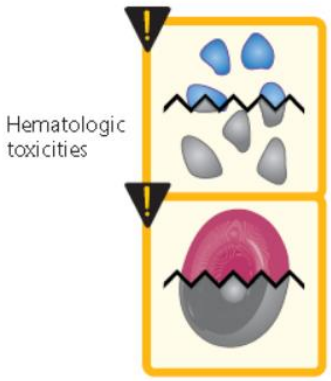
Co-trimoxazole (Sulfamethoxazole + Trimethoprim (cont.))

	Sulfamethoxazole (SMX) (Sulfonamides)	Trimethoprim (TMP)
ADVERSE EFFECTS	Adverse effects for the combination of Co-trimoxazole: 1.Gastrointestinal adverse effects: (Nausea, vomiting) 2. Allergy (Reactions involving the skin are very common) 3. Hematologic toxicities. The hematologic effects may be reversed by the concurrent administration of folinic acid, which protects the patient and does not enter the microorganism.	
	More specific for SMX: • Hematologic disorders: Acute hemolytic anemia, due to: 1) hypersensitivity reaction 2) G6PD deficiency • Drug interactions: 1) Displace bilirubin from binding sites on serum albumin. . The bilirubin is then free to pass into the CNS, because the blood–brain barrier is not fully developed (in neonates) or in severe displacement. This may lead to kernicterus (AKA Bilirubin encephalopathy) 2) Potentiate warfarin & oral hypoglycemic drugs.	More specific for TMP: • Hematologic disorders: Megaloblastic anemia, especially in pregnant patients and those having very poor diets (deficiency of folate).
CONTRA-INDICATIONS	Pregnancy, Nursing mother, Infants under 6 weeks, Renal or hepatic failure, Blood disorders	

= kernicterus

Allergy

Nausea, vomiting



- Acute hemolytic anemia
- Megaloblastic anemia

2. Antiseptic drugs: Nitrofurantoin

urinary antiseptic: **Nitrofurantoin**	
Anti-bacterial spectrum	Effective against: • **E. coli,** but other common UT gram -ve bacteria may resistant. • Gm +: **Staph. saprophyticus**,
Mechanism of action	Sensitive bacteria reduce the drug to active agent that **inhibits various enzymes and damages DNA.** **(i.e. the drug is activated by the bacteria its self .** Prodrug > active when find bacteria > starts working)
Pharmaco-kinetics & Therapeuti c Uses	1. complete Absorption **Orally** 2. Metabolized (75%) in liver 3. excreted so rapidly that no systemic antibacterial action is achieved. Thus cannot be used for upper UTI or systemic infections. Its usefulness is limited to lower UTI's. 4. Dose: 50-100 mg, p.o. q 6h/7 days. Long acting: 100mg twice daily. cheep In price. 5. Concentrated in urine. (25% of the dose excreted unchanged) 6. Urinary pH is kept <5.5 (acidic) to enhance drug activity. Recall: lecture (renal excretion of drugs): ion trapping. Nitrofurantoin contains ammonium hydroxide in its structure (weak base), which is best EXCRETED in acidic urine. Since its site of action is the lower UT, excretion will induce its effect. 7. turns urine to a **dark orange-brown**
Adverse effects	**1. GI disturbances**: bleeding of the stomach, nausea, vomiting and diarrhea (thus must be taken with food). 2. Headache and nystagmus (rapid involuntary movements of the eyes. See) 3. Hemolytic anemia (in patients with G6PD deficiency). Just like sulfonamides .
Contra-indications	1. Patients with G6PD deficiency (to avoid hemolytic anemia) 2. Neonates 3. Pregnant women (after 38 weeks of pregnancy)

2. Antiseptic drugs: Nitrofurantoin (cont.)

Amazing work by team pharmacology 434:

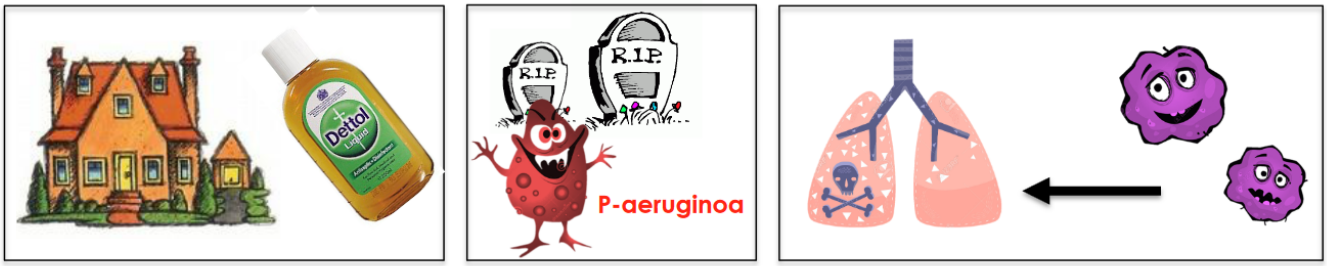
سوبر نايترو بيقضي على الأعداء !

نايتروفيرنتوين شخص طبيعي جدا، ولكن عندما يرى الإي كولاي عدوه اللدود يتحول إلى أكتف إيجنت ويصبح اسمه سوبر نايتروفيرنتوين، فيصبح قويا جدا ويعصر الإي كولاي مثل العصير ويقضي على الدي ان اي تبعه فيصبح لون الإي كولاي غامق عندما ينخنق (Dark urine)!

سوبر نايتروفيرنتوين لديه أعداء آخرون أيضاً !

فهو يقضي على قرام (−) جميعهم ما عدا رئيسهم سودوموناس أرجينوسا، ويخافوا منه قرام (+)، فعندما يجي سوبر نايترو في المكان يخافوا منه وينكتم نفسهم فيسبب لهم pulmonary fibrosis.

الناس دائما يستعينون بسوبر نايترو لكي يقيهم من الأعداء (prophylaxis) ولكي يطهر بيوتهم (anti-septic).



Recall: lecture (renal excretion of drugs) slide 5: active tubular secretion of drugs – competition.

❖ **Therapeutic <u>disadvantages</u> of competition:**

❑ probenecid & nitrofurantoin

- Inhibition of nitrofurantoin secretion by probenecid → decreased efficacy of nitrofurantoin in treatment of UTIs.

Nitrofurantoin is an antibiotic used for treating UTIs. So the drug's site of action is the urinary tract. Thus we need the drug to be more excreted rather than remaining in the plasma. But When Probenecid inhibits its excretion by binding to the carrier transporter, nitrofurantoin will remain more in plasma instead of being excreted, its action is reduced.

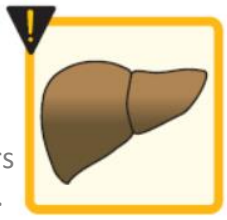
3. Tetracyclines (e.g. Doxycycline)

Doxycycline

Mechanism	**Inhibit protein synthesis** by binding reversibly to 30 s subunit
Pharmaco-kinetics	• Usually given **orally,** long acting. • Absorption is 90-100% in the upper small intestine. • best given in the absence of food , because Food, di & tri-valent cations (Ca, Mg, Fe, AL) impair its absorption. They Form insoluble product, excreted in stool. • Protein binding 40-80 % • Distributed well, including CSF • **Cross placenta and excreted in milk** • Largely metabolized in the liver. In renaly compromised patients, *doxycycline* is preferred, as it is primarily eliminated via the bile into the feces.
Side effects	1. nausea, vomiting ,diarrhea & epigastric pain (in this case, has to be given with food (other than dairy products) although it will decease its absorption) 2. Thrombophlebitis (if given i.v for a long time) 3. Hepatic toxicity (prolonged therapy with high dose) 4. **Brown discoloration of teeth – children** 5. Deformity/ or growth inhibition of bones in **children** Deposition in the bone and primary dentition occurs during the calcification process in growing **children**. This may cause discoloration and hypoplasia of teeth and a temporary stunting of growth. Thus the use of tetracyclines is limited in pediatrics. 6. Phototoxicity. Patients should be advised to wear adequate sun protection. 7. Vertigo. It concentrates in the endolymph of the ear and affects function. *Doxycycline* may also cause vestibular dysfunction. 8. Superinfections. because it is broad spectrum so it kills normal flora & allows other organisms to enter the body.


GI disturbance


Deposition of drug in bones and teeth


Liver failure


Phototoxicity

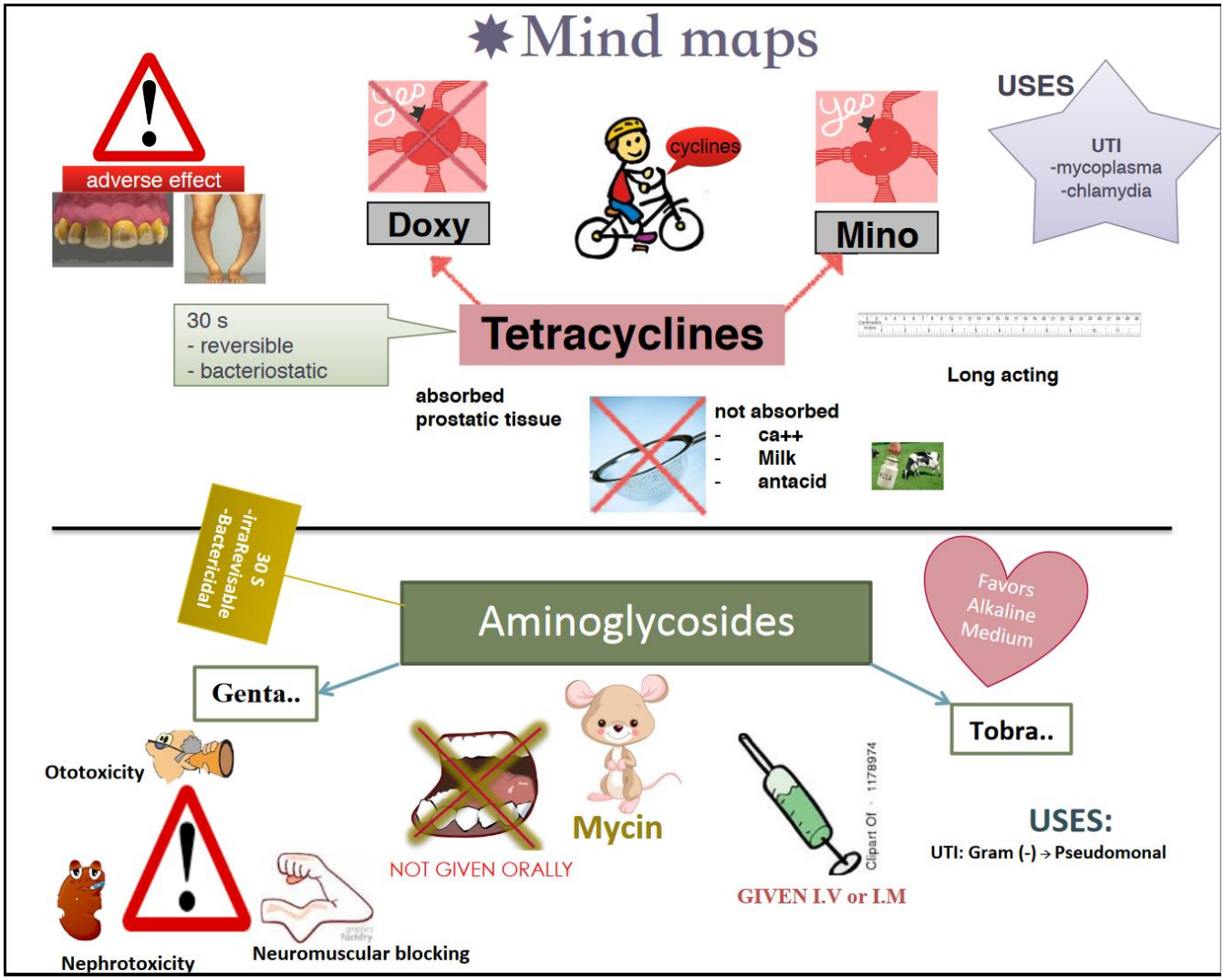

Vertigo


Avoid in pregnancy

3. Tetracyclines (e.g. Doxycycline). (cont.)

Doxycycline	
Contra-indications	• Pregnancy • Breast feeding • Children (below 10 yrs), due to its effect on growing bone and teeth.
Therapeutic Uses	• Treatment of UTI's due to: ✓ **Mycoplasma** (there is usually co-infection with Neisseria gonorrhoeae) ✓ **Chlamydia** (100 mg p.o. bid for 7 days). • **Prostatitis**

Amazing work by team pharmacology 434:



4. Aminoglycosides (e.g. gentamicin)

GENTAMICIN

Route of administration	• Intravenous (IV) or Intramuscular (IM) • Poorly absorbed orally (highly charged) The highly polar, polycationic structure of the aminoglycosides prevents adequate absorption after oral administration. Thus not given orally except in case of GIT infections or for preparing GIT for surgery. Therefore, all aminoglycosides (except *neomycin)* must be given parenterally to achieve adequate **serum** levels.
Pharmaco-kinetic	• Active against **(gram -ve)** aerobic organisms. • More active in **alkaline** medium • cross placenta • Excreted unchanged in urine
Mechanism of action	• **Inhibits protein synthesis** by binding to 30S ribosomal subunits irreversibly. • It is bactericidal. ! Although tetracycline and aminoglycosides have the same mechanism (binding with 30S ribosomal subunit), tetracyclines are bacteriostatic, and aminoglycosides are bactericidal. WHY? That is because tetracyclines bind reversibly, while aminoglycosides bind irreversibly.
Therapeutic uses	Severe infections caused by (gram -ve) organisms: (**Pseudomonas or Enterobacter**).
Adverse effects	• Ototoxicity. The antibiotic accumulates in the endolymph and perilymph of the inner ear. Deafness may be irreversible and has been known to affect developing fetuses. Patients simultaneously receiving concomitant ototoxic drugs, such as *cisplatin* or loop diuretics, are particularly at risk. • Nephrotoxicity. Retention of the aminoglycosides by the proximal tubular cells disrupts calcium-mediated transport processes. This results in kidney damage. • Neuromuscular blocking effect. This adverse effect is associated with a rapid increase in concentrations (for example, high doses infused over a short period.) or concurrent administration with neuromuscular blockers. Patients with myasthenia gravis are particularly at risk.

5. Cephalosporins

In the following 2 slides are some extra recalls from the lecture (treatment of RTIs) of respiratory block. (in gray)

Broad- spectrum Penicillins
(Act on both gram +ve & gram-ve microorganisms)

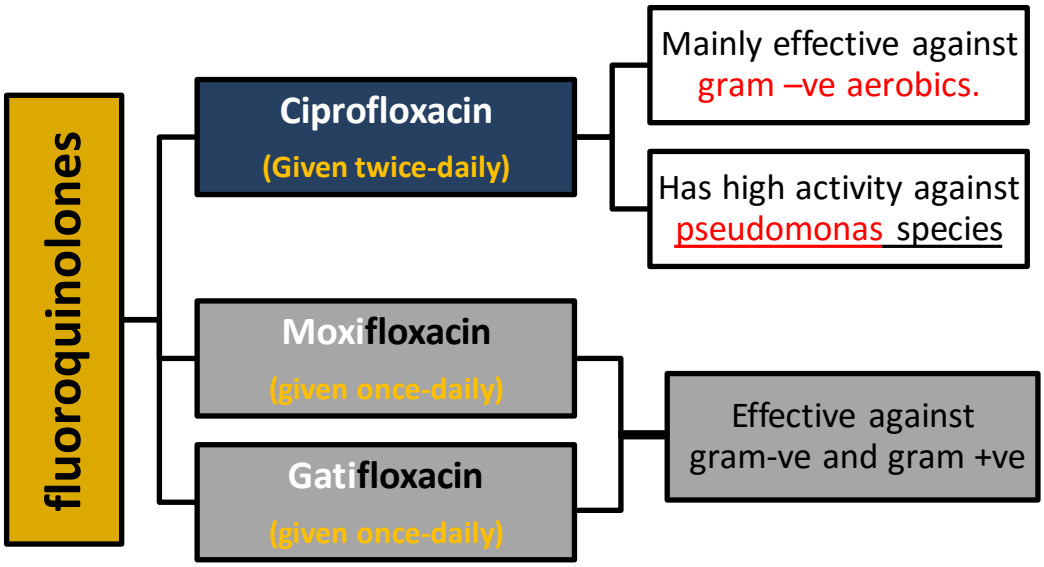
- **Amoxicillin - Clavulanic acid**
- **Ampicillin - Sulbactam**
- **Piperacillin - Tazobactam**

- Formulation with **β-lactamase inhibitors** protects **Penicillins** from enzymatic hydrolysis (by the β-lactamase produced by bacteria) and extends their antimicrobial spectra.
- Antipseudomonal Penicillins (Ticarcillin, Piperacillin)

	Generations of Cephalosporins:		
	1st	2nd	3rd
Mechanism of action	**Inhibit cell wall synthesis,** so they are **bactericidal** (just like penicillin but more resistant to β-lactamase)		
Drugs	Cephalexin	Cefuroxime axetil Cefaclor	**Ceftriaxone** **Ceftazimide** Cefixime Cefotaxime
$T_{1/2}$	Short , but ceftriaxone is the longest (4-7H)		
administration	Orally		**parenterally** (Except cifixime orally)
Clinical uses	Gram+	Mainly Gram-	Mainly effective against Gram –ve. Used for severe /complicated UTIs & acute prostatitis
Adverse effects	1) Hypersensitivity reaction (avoid or use with caution in patient with penicillin allergy) 2) Thrombophlebitis (inflammation wall of vein) 3) Diarrhea 4) Superinfection		
Elimination	through tubular secretion and/or glomerular filtration One exception is ceftriaxone , which is excreted through the bile into the feces (employ it for renal insufficiency)		

6. Fluoroquinolones (e.g. ciprofloxacin)

Mechanism of action: **inhibits DNA gyrase enzyme, which is an enzyme involved in DNA supercoiling.**



Clinical uses:

- **UTIs caused by multidrug resistance organisms as pseudomonas**
- **Prostatitis (acute/chronic).** It concentrates in many tissues (kidney, prostate, lung, bones and joints), thus more likely effective in these tissues infections.

Adverse effects:

1. Nausea, vomiting and diarrhea.
2. CNS effects (confusion, insomnia, headache and anxiety)
3. Damage of growing cartilage (arthropathy)

Therefore, these agents should be avoided in pregnancy and lactation and in children under 18 .

4. Phototoxicity (use sunscreen & avoid excessive sun light)

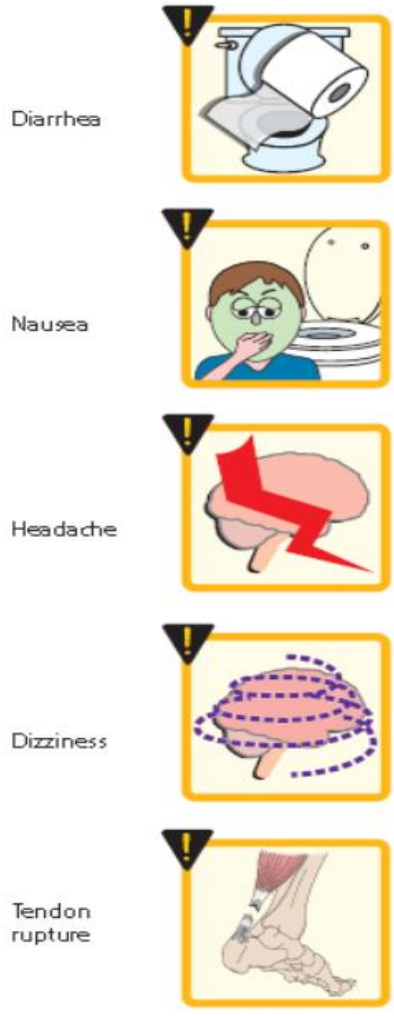


Figure 40.5
Some adverse reactions to fluoroquinolones.

Treatment strategies:

Uncomplicated lower UTI (e.g. cystitis)

For empirical therapy:

First line:

- **Trimethoprim 200mg bd (or co-trimoxazole 960mg bd). short-course (3 days)**
- ***Or* Nitrofurantoin 100mg bd (not in renal impairment). longer-course (7 – 10 days)**

After sensitivity testing results:

If second-line treatment is necessary, e.g. due to

- hypersensitivity reactions for the first-line drugs
- side effects / contraindications to the first-line drugs
- failure of first-line treatment,

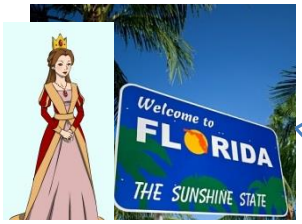
then, urine culture with sensitivity testing is recommended.

Options:

- Fluoroquinolones: ciprofloxacin 500mg bd or levofloxacin 250mg od.
- **Oral** Cephalosporins (cefixime) often offer a useful **alternative**.
- Encourage high fluid intake, e.g. >2L/day

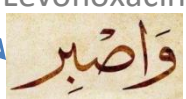
co-trimoxazole

nitrofurantoin



fluoroquinolones

A story that may help you remembering them in order:
A group of people lived an uncomplicated life (uncomplicated UTI), they liked trying (trimethoprim) new things together (co-trimoxazole). But one night (nitrofurantoin), they failed to find new things to do (failure of first line), so (second line) they went to Florida's queen (fluoroquinolones) and asked her to figure something out, she said: «اصبروا، وحبوا بعض» (ciprofloxacin/levofloxacin) . They tried to be patients, but they got bored quickly. They told her (oral):" بتشوفين لنا حل ولا بالسيف؟؟" (Cephalosporins). So she decided to fix (cefixime) something up and ended up saying:" have you ever tried to drink water?" (hydration)



Ciprofloxacin

Oral Cephalosporins: cefixime

Treatment strategies:

Complicated UTIs e.g. pyelonephritis

For empirical therapy:

- Fluoroquinolones: ciprofloxacin or levofloxacin
- Third generation cephalosporin (e.g. ceftriaxone) (i.v.)
  similar to second line of uncomplicated UTI, but choose a cephalosporin given by i.v. instead of orally (complicated UTI).
- Use additional single dose of aminoglycosides (**Gentamycin**) if needed
- **Rehydration** is very useful

After sensitivity testing results:

- Select the antibiotics as per culture sensitivity results
- Rehydration is very useful

Treatment In pregnancy:

Recommended:

(FIRST LINES)

- Penicillins: Ampicillin or amoxicillin
- Third generation cephalosporin: Ceftriaxone

Contraindicated/can be used with caution:

- Nitrofurantoin (caution in neonatal jaundice and kernicterus)
- Trimethoprim (use folate supplementation, avoid in folate deficiency)
- Short term **aminoglycosides** can also be used in **complicated** UTIs.

Treatment strategies:

prostatitis

- TMP/SMX (co-trimoxazole)
- 3rd Generation cephalosporin: Ceftriaxone
- Quinolones: Ciprofloxacin , levofloxacin
- Tetracyclines: Doxycycline

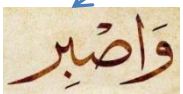
A story that may help you remembering them in order:
Three men (prostatitis) from the same group of co-trying-new things (co-trimoxazole), decided to get revenge of the queen. They held their swords سيف (cef) and three (tri) axes (axone) (Ceftriaxone). Florida's queen was frightened and again said «اصبروا نتفاهم ونحب بعض» . however they didn't listen this time. They surrounded (cycline) her mansion from all four (tetra) directions accompanied by their dogs (dox-ycycline)

co-trimoxazole

Ceftriaxone

fluoroquinolones

Tetracyclines: e.g. doxycycline



Ciprofloxacin

Levofloxacin

Summary

Co-trimoxazole		
drug	Sulfamethoxazole	Trimethoprim
Mechanism of action	inhibit Dihydropteroate synthetize	inhibit Dihydrofolate reductase
Pharmacokinetics	- given orally - Rapidly absorbed - Widely distributed in - Protein bound (approx.70%) - Metabolized by liver - Excreted by urine	- given orally - Well absorbed - Widely distributed in - Protein bound (approx.40 %) - Excreted in urine - Concentrated in prostatic fluid - More lipid soluble than TMP
Adverse effects	- Allergy - Nausea, vomiting - Anemia (hemolytic , Megaloblastic)	
Contraindications	- Pregnancy - Nursing mother - Infants under 6 weeks - Renal or hepatic failure - Blood disorders	
Therapeutic Uses	- Acute, Complicated and Recurrent urinary tract infections - Prostatitis (acute/ chronic)	
Drug interaction	-displace bilirubin , causes (kernicterus) -displace warfarin and hypoglycemic drugs	

drug	Nitrofurantoin (urinary antiseptic)	Tetracyclines e.g. Doxycycline
Spectrum	**E. coli and Staph. saprophyticus**	
Mechanism of action	**-Inhibits bacteria various enzymes and damages DNA.** **-Prodrug: active when find bacteria start work**	-Inhibit protein synthesis by binding reversibly to 30 s subunit
Pharmacokinetics	**-Oral complete Absorption** **-Metabolized (75%) in liver** **-excreted rapidly no systemic antibacterial** **-25% of the dose excreted unchanged** **-Urinary pH <5.5(acidic) to enhance drug activity.** **-turns urine to a dark orange-brown**	**-given orally long acting** **-Absorption is 90-100% in the upper s. intestine Food & di & tri-valent cations (Ca, Mg, Fe, AL) impair absorption** **-Protein binding 40-80 %** **-Distributed well, including CSF Cross placenta and excreted in milk** **-Largely metabolized in the liver**
Adverse effects	**-GI disturbances: bleeding of the stomach, nausea, vomiting and diarrhea (must be taken with food).** **-Headache and nystagmus** (rapid involuntary movements of the eyes.) **-Hemolytic anemia (G6PD deficiency)**	**-nausea, vomiting ,diarrhea & epigastric pain(give with food)** **-Thrombophlebitis i.v** **-Hepatic toxicity (prolonged therapy with high dose)** **-Brown discoloration of teeth (children)** **-Deformity or growth inhibition of bones (children)** **-Phototoxicity** **-Vertigo** **-Superinfections.**
Contraindications	**-Pts with G6PD deficiency** **-Neonates** **-Pregnant women(after 38 wks. of pregnancy)**	**-Pregnancy** **-Breast feeding** **-Children(below 10 yrs.)**
Therapeutic Uses	**Its usefulness is limited to lower UTI's & cannot be used for upper UT or systemic infection.** - Effective against **E. coli & Staph. saprophyticus**	**-Treatment of UTI's due to Mycoplasma (**Neisseria gonorrhoeae usually co-infection with Mycoplasma **) & Chlamydia 100 mg p.o. bid for 7 days.** **-Prostatitis**

drug	Aminoglycosides e.g. GENTAMICIN	Cephalosporins			Fluoroquinolones -Ciprofloxacin -Moxifloxacin -Gatifloxacin
		1st	2ed	3ed	
Spectrum	-(gram -)aerobic organisms. -bactericidal	Gram+	Mainly Gram-	More effective on Gram-	-Ciprofloxacin gram –ve pseudomonas species - Moxifloxacin and Gatifloxacin gram-ve and gram +ve
Mechanism of action	Inhibits protein synthesis by binding to 30S irreversibly	Inhibit bacterial cell wall synthesis(bactericidal)			-inhibits DNA gyrase enzyme
Pharmacokinetics	-(IV) or (IM). Poorly absorbed orally -cross placenta -active in alkaline medium --Excreted unchanged in urine	Orally (cifixime)		I.V mostly	-orally or parentally. -Concentrates in many tissues (kidney, prostate, lung, bones and joints), -Excreted mainly trough the kidney -Has long half-life.
		Short T1/2 Elimination through tubular secretion and/or glomerular filtration			
Adverse effects	-Ototoxicity -Nephrotoxicity -Neuromuscular blocking effect	-Hypersensitivity reaction (avoid or use with caution in patient with penicillin allergy) -Thrombophilibitis (inflammation wall of vein) -Diarrhea -Superinfection			-Nausea, vomiting and diarrhea. -CNS effects (confusion, insomnia, headache and anxiety) -Damage of growing cartilage (arthropathy) -Phototoxicity
Contraindications	----------				-patients under 18 years. -Pregnancy -Breast-feeding Women
Therapeutic Uses	-Severe infections caused by (gram -) organisms (Pseudomonas or Enterobacter).	- 3rd generation: severe / complicated UTIs acute prostatitis			-UTIs caused by multidrug resistance organisms as pseudomonas -Prostatitis (acute/chronic)

Summary

drug	Mechanism	Therapeutic uses	Adverse effects
TMP-SMX	SMX: inhibit Dihydropteroate synthetase TMP: inhibit Dihydrofolate reductase	- **Acute, Complicated and Recurrent urinary tract infections** - **Prostatitis (acute/ chronic)**	- Allergy - Nausea, vomiting - Anemia (hemolytic , Megaloblastic) - Drug interactions (bilirubin, warfarin, hypoglycemic drugs)
Nitro furantoin	Inhibits bacteria various enzymes and damages DNA.	urinary antiseptic. Its usefulness is limited to lower UTI's & cannot be used for upper UT or systemic infections.	- GI disturbances: bleeding of the stomach, nausea, vomiting and diarrhea (must be taken with food). -Headache and nystagmus -Hemolytic anemia (G6PD deficiency)
Genta micin	Inhibits protein synthesis by binding to **30S irreversibly**	- Severe infections caused by (gram -) organisms: Pseudomonas or Enterobacter.	-Ototoxicity -Nephrotoxicity -Neuromuscular blocking effect
Doxycycline	Inhibit protein synthesis by binding **reversibly to 30 s** subunit	- Treatment of UTI's due to: Mycoplasma & Chlamydia -Prostatitis	- nausea, vomiting ,diarrhea & epigastric pain (give with food) -Thrombophlebitis (i.v) -Hepatic toxicity (prolonged therapy with high dose) -Brown discoloration of teeth (children) -Deformity or growth inhibition of bones (children) -Photo toxicity -Vertigo -Superinfections.
Cephalo-sporins 3rd generation	Inhibit bacterial cell wall synthesis (bactericidal)	- Gram –ve bacteria - severe/ complicated UTIs - acute prostatitis - **Effective in treatment of pneumonia produced by β-lactamase bacteria**	**-Hypersensitivity reaction** **-Thrombophlebitis** **-Diarrhea** **-Superinfection**
Cipro-floxacin	inhibits DNA gyrase enzyme	- Effective against Gm-aerobic bacteria. - UTIs caused by multidrug resistance organisms as pseudomonas - Prostatitis (acute/chronic)	-Nausea, vomiting and diarrhea. -CNS effects (confusion, insomnia, headache and anxiety) - arthropathy -Photo toxicity

Questions

Q1) a Patient came to the hospital with prostatitis . Which one of these is NOT indicated in his case?

1. Ciprofloxacin
2. TMP
3. Gentamicin
4. Doxycycline

Q2) which of the following drugs is effective against E. coli and Staph. Saprophyticus , but other gram –ve bacteria may be resistant:

1- Ciprofloxacin
2- Gentamicin
3- Doxycycline
4- Nitrofurantoin

Q3) a 35 pregnant women came to the ER complaining of pain during urination and increase the urgency for urination , the doctor will prescribe her …?

1-ceftrixzone
2-ciprofloxacin
3-doxacycline
4-gentamycin

Q4) Which one of the following is one of the adverse effects of fluoroquinolones?

1. Hypertension
2. Nephritis
3. Thrombophlebitis
4. Damage growing cartilage (arthropathy)

Q5) A 20 Year old female was diagnosed with cystitis, the doctor prescribed a medication , after 2 days she came to the emergency complaining from orange brown urine , the drug is most likely to be:

1-ampicillin
2-gentamycin
3-nitrofurantoin
4-TMP-SMX

5-3
4- 4
3- 1
2- 4
1- 3

Questions

Q6) The drug with no systemic effect :

1. Nitrofurnation
2. Cephtraxzone
3. Ampicilin
4. Gentamycin

Q7) a 12 year old male was diagnosed with complicated UTI, the proper empiric therapy will be:

1-ciprofloxacin
2-nitrofurnation
3-ampicillin
4-amoxacilin

Q8) a 7 year old was diagnosed with UTI , which drug should be completely excluded:

1-amoxacilin
2-gentamycin
3-doxycyclin
4-cephalosporins

Q9) we can acidify the urine to increase the excretion of:

1-ciprofloxacin
2-gentamicin
3-cephalosporin
4-nitrofurnayoin

Q10) patient with chronic kidney disease , complained of UTI , what drug should we avoid giving to this patient ?

1-amoxacilin
2-ciprofloxacin
3-gentamicin
4-TMP-SMS

Explanation: nephrotoxicity is a side effect of gentamycin.

6-1
7-1
8-3
9-2
10-3

THANK YOU FOR CHECKING OUR WORK

THE PHARMACOLOGY TEAM

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For any correction, suggestion or any useful information do not hesitate to contact us :Pharmacology.med435@gmail.com

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