

Treatment of urinary tract infections

Objectives:

- Recognize different groups of antibiotics used in UTIs.
- Describe their mechanism of action, pharmacokinetics properties and adverse effects.
- Describe the use of antibiotics and their rational of combination of different antibiotics.
- Describe the spectrum of various antibiotics.

To always give without expecting anything in return.



- Titles
- Very important
- Extra information
- Doctor's notes

Urinary tract infections (UTIs)

It's the infection that affect any part of the urinary tract including kidneys, ureters, bladder and urethra.

- It is the 2nd most common infection (After RTIs).
- It is often associated with some obstruction of the flow of urine.
- It is most common in **women** than men **Because of short urethra in females** (pathogens responsible for UTI are found in the colonic flora. Subsequent UTI is usually ascending, i.e. after perivaginal, perineal, and transurethral colonization, also immunity and other changes..)
- Incidence of UTI **increases in old age** (10% of men & 20% of women).
- ❖ It is be divided into:
 1. Upper urinary tract infection including kidneys and ureters e.g. *Pyelonephritis*.
 2. Lower urinary tract infection including bladder, urethra and prostate e.g. *Cystitis, Urethritis, and Prostatitis*.
- ❖ **Upper urinary tract infections are more serious than lower urinary tract infections.**

What are the causes of UTIs?!

Normally urine is sterile. Bacteria comes from digestive tract to the opening of the urethra.

- Obstruction of the flow of urine e.g. (Kidney stones)
- Enlargement of prostate gland in men. (Common cause)
- Catheters placed in urethra and bladder.
- **Not drinking enough fluids.** (Dehydration)
- Waiting too long to urinate.
- Large uterus in pregnant woman.
- Poor toilet habits (wiping back to front for women)
- Disorders that suppress the immune system e.g. diabetes and cancer chemotherapy.

Bacteria causing UTIs

- **Gram negative (most common):**
 1. Escherichia coli (E.coli approx. 80% of cases). **Live in colon (coli)**
 2. Proteus mirabilis.
 3. klebsiella.
 4. Pseudomonas aeruginosa (hospital acquired).
- **Gram positive:**
 1. Staphylococcus saprophyticus (approx. 20% of cases). **(Causes Honeymoon cystitis)**
 2. Mycoplasma, Chlamydia trachomatis and Neisseria gonorrhoea are **limited to urethra, and unlike E.coli they may be sexually transmitted.**

Urinary tract infection

Complicated

Infections **spread** to other part of the body and **resistant** to many antibiotics and more difficult to treat

Due to hospital acquired bacteria such as: E.coli, Klebsiella, Proteus, Pseudomonas, enterococci, staphylococci (can lead to kidney renal failure)

Simple

Infection **do not spread** to other body parts and go away readily with treatment

Due to E.coli in most cases

Treatment of UTI's

Mainly by **Antibiotics**:

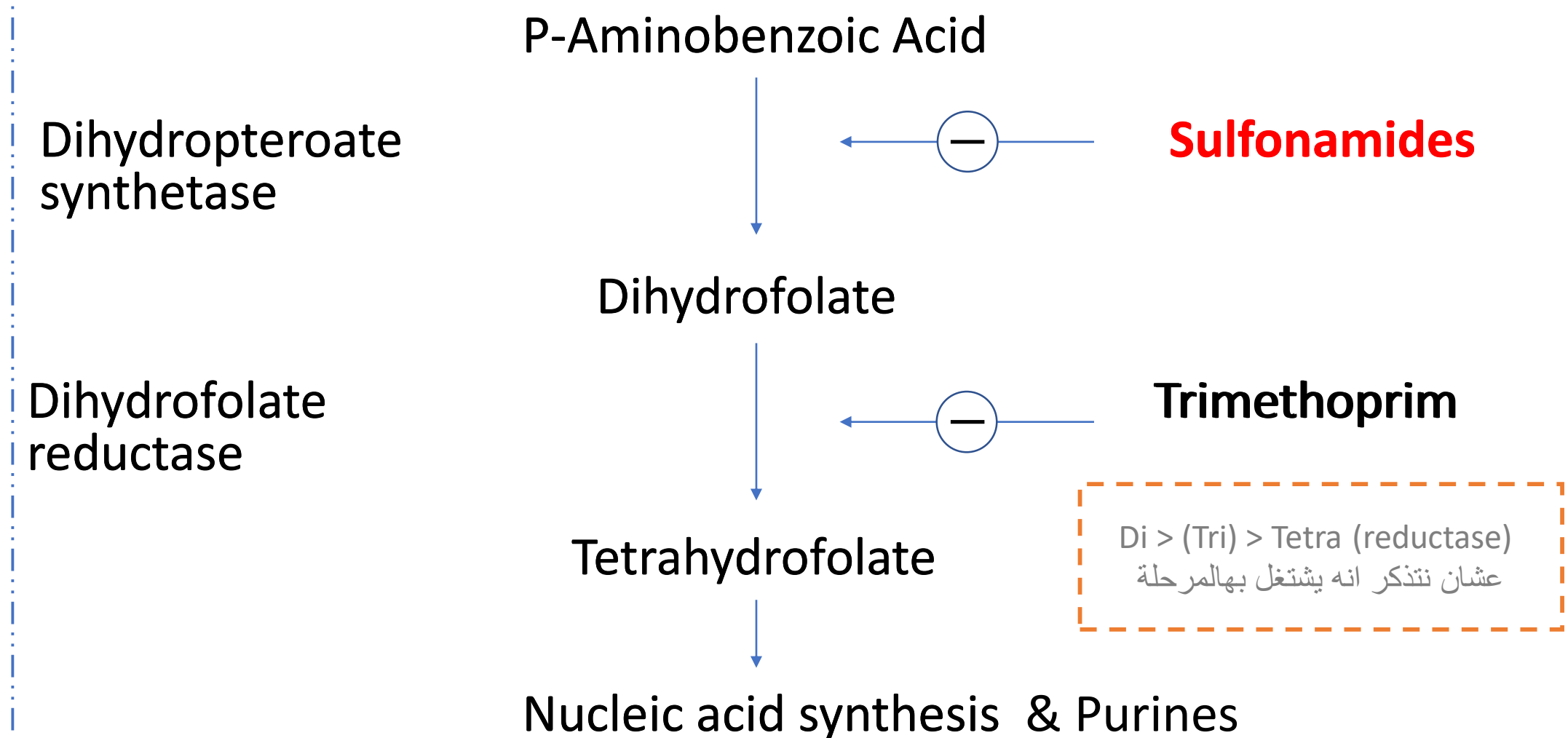
1. *Co-trimoxazole* (SMX/TMP) ,p.o. =Orally
2. *Nitrofurantoin*, p.o. =Orally
3. Tetracyclines, e.g. *Doxycycline*, p.o. =Orally
4. Aminoglycosides, e.g. *Gentamicin* i.v/i.m
5. Cephalosporins , e.g. *Ceftriaxone* & *Ceftazidime* IV
6. Quinolones, e.g. *Ciprofloxacin*,p.o. =Orally


Co-trimoxazole (Bactrim, Septra) Sulfamethoxazole- Trimethoprim (SMX) (TMP)

- Alone, each agent is **bacteriostatic**.
- Together they are **bactericidal** (**Synergism**).
- The optimal ratio of TMP to SMX in vivo is **1:20**.
(formulated 5(SMX):1(TMP); 800mg SMX+160mg TMP; 400 mg SMX+ 80 mg TMP; 40 mg SMX+8 mg TMP).
(the combination of these 2 drugs reduce the incidence of crystal urea that might be caused by sulfonamides)

عشان نتذكر ان هالدرق يشبه بالتركيب وانه يشتغل بهالمرحلة نقدر نقول (سولفوا لبأبا كيف صنعتوه) Synthetase

MECHANISM OF ACTION



Sulfonamides	Trimethoprim (TMP)
<p>Absorption, Metabolism and Excretion</p>	<ul style="list-style-type: none"> • Usually given orally, alone or in combination with SMX. • Well absorbed from the gut. • Widely distributed in body fluids & tissues (including CSF). • More lipid soluble than SMX. • Protein bound (approx.40 %). • 60% of TMP or its metabolite is excreted in the urine. • TMP concentrates in the prostatic fluid.
<p>ADVERSE EFFECTS</p>	<ul style="list-style-type: none"> • Gastrointestinal- Nausea, vomiting • Allergic reactions. • Hematologic: <ul style="list-style-type: none"> A. Megaloblastic anemia due to <u>TMP</u>. B. Acute hemolytic anemia: <ul style="list-style-type: none"> I. Hypersensitivity II. G6PD deficiency. <i>Could be genetically acquired</i> • Drug interactions • Displace bilirubin -if severe- kernicterus • Potentiate warfarin, oral hypoglycemic. <p><i>حاول مثل ما قالوا (Tri \ Meth \ megal)</i></p> <p><i>Severe elevation of bilirubin may cause nerve cell damage</i></p> <p><i>من كثر ما سولفوا (Sulfonamide) فوق راسي فقعوا مرارتي (Displace bilirubin) حتى وصلت لمخي (Kernicterus)</i></p> <p><i>روبن (biliRUBIN) بون بي تحب تسولف كثير (Sulfo)</i></p> 
<p>CONTRAINDICATIONS</p>	<ul style="list-style-type: none"> • Pregnancy because of kernicterus • Nursing mother. because it may be excreted in milk • Infants under 6 weeks. liver isn't mature • Renal or hepatic failure. drug metabolized by liver and excreted by kidney • Blood disorders. "TMP could lead to hemolytic anemia"

Nitrofurantoin	Tetracyclines (e.g. Doxycycline)
<p>Mechanism of action</p>	<ul style="list-style-type: none"> • long acting bacteriostatic against gram +ve and –ve. ❖ Bacteriostatic against gram +ve and –ve, Inhibit protein synthesis by binding reversibly to 30s subunit. <i>In mycoplasma & chlamydia infections. (sexually transmitted)</i>
<p>Pharmacokinetics</p>	<ul style="list-style-type: none"> • Usually given orally. • Absorption is 90-100%. • Absorbed in the upper small intestine & best in absence of food. should be taken on an empty stomach • Food & di & tri-valent cations (Ca, Mg, Fe, AL) impair absorption. Example: milk • Protein binding 40-80%. • Well distributed, it can cross the BBB and placenta and excreted in milk. • Largely metabolized in the liver.
<p>Therapeutic Uses</p>	<ul style="list-style-type: none"> • Treatment of UTI's due to Mycoplasma & Chlamydia, 100 mg p.o bid for 7 days. • Prostatitis. (limited for urethra) first choice.

- Sensitive bacteria reduce the drug to an active agent (by bacterial reductase) that inhibits various enzymes and damages DNA. “it’s a prodrug and should be activated”
- Bactericidal against gram +ve and –ve bacteria.

- Absorption is complete after oral use.
- Metabolized (75%)& excreted so rapidly that **no systemic antibacterial action is achieved.**

ممکن نقرأ اسم الدرق نيتروجين في اليورن فدائيركت وجهته هناك مايروح للجسم كله Nitro f uran

ممکن نقرأ اول مقطع من اسم الدرق No travel to systemic = Ni trof

- Concentrated in the urine(25% of the dose excreted unchanged).
- Urinary pH is kept <5.5(acidic) to enhance drug activity.
- It turns urine to a dark **orange-brown.** (harmless side effect)

نقدر نقول (Nitro) نظروا (انتظروا) فوران (furan) الميه ع النار ، والنار يجي لونها (orange)

Although it’s normal, you should tell the patient about it

Dose: 50-100 mg, po q 6h/7 days. *Girls’ Dr. said “I don’t ask about doses”*

- ❖ Long acting: 100mg twice daily.

نقدر نقول (Nitro) نظروا (انتظروا) فوران (furan) الميه ع النار عشان تتعقم وتتطهر

- It is used as urinary antiseptics.
- Its usefulness is **limited to lower UTIs** & cannot be used for upper UT or systemic infections. Nitro f uran which is stored in bladder in the lower UT
- Effective **against E.coli and staph.** Saprophyticus, but common UTI gram –ve bacteria may be resistant.

Nitrofurantoin

Tetracyclines (e.g. Doxycycline)

ADVERSE EFFECTS

- GI disturbances:
 - bleeding of the stomach.
 - nausea, vomiting and diarrhea (**must be taken with food**).

- Headache and nystagmus. نظرتهم حتى طلعت عيوني من مكانها

Nystagmus: Involuntary rapid movement of the eye

- Hemolytic anaemia (G6PD deficiency).

طاح الطفل من السيكل (cycline) وتوسخت أسنانه بالتراب (brown teeth) وتكسرت عظامه (deformity of bone)، وبعدين مع الجرح جته انفكشن (Superinfection)

1. nausea, vomiting ,diarrhea & epigastric pain (taken with food).
2. Thrombophlebitis. If given IV (it is an inflammatory process that causes a blood clot to form and block one or more veins, usually in the legs).
3. **Hepatic toxicity** (prolonged therapy with high dose).
4. **Brown discoloration of teeth** – children

5. Deformity or growth inhibition of bones-children.
6. **Photo toxicity.**
7. Vertigo.
8. Superinfections.

ليش طاح الطفل من السيكل (cycline)؟ عشان ضوء الشمس كان قوي عليه (Photo toxicity) فجته دوخة ودارت فيه الدنيا (Vertigo) وطاح

Binds to Ca in bones or teeth, and then it becomes yellow. Then it turns permanently to brown after being exposed to light

CONTRAINDICATIONS

- Patients with G6PD deficiency.
- Neonates.
- **Pregnant women** (after 38 weeks of pregnancy). Because it may cause hemolysis in new born babies since the glutathione system isn't mature.

- Pregnancy.
- Breast feeding.
- Children (below 10 years).

Aminoglycosides		Fluroquinolones (Detail was explained in respiratory lec.)	Cephalosporins
Example	e.g. GENTAMICIN, i.m, i.v (Not orally (not absorbed from GIT) جنتا (Gentamicin) معه اکتئاب وقرر ينتحر (Bactericidal)	e.g. <i>Ciprofloxacin</i>	3 rd generation Cephalosporins: * <i>Ceftriaxone & Ceftazidime</i> *Long t1/2 usually in used in ER
Type of action	All of them are Bactericidal antibiotics.		
Spectrum	Active against gram negative aerobic organisms.		Mainly effective against gram negative bacteria.
Mechanism of action	Inhibits protein synthesis by binding to 30S ribosomal subunits irreversibly.	Inhibits bacterial DNA gyrase enzyme & cell division resulting in bacterial cell death.	Acts by inhibition of cell wall synthesis.
Pharmacokinetic	<ul style="list-style-type: none"> Poorly absorbed orally (highly charged). Cross placenta. #pregnancy Excreted unchanged in urine. More active in alkaline medium. 	<p>منى (PseudoMONAs) بيغى لها صبر (Cipro) او منى صابر</p>	They are given parenterally. Not absorbed by GIT
Therapeutic uses	<ul style="list-style-type: none"> Severe infections caused by gram negative organisms (Pseudomonas or Enterobacter). <p>جنتل مان (Gentamicin) زوجته اسمها منى (pseudoMONAs)</p>	<ul style="list-style-type: none"> UTIs caused by multidrug resistance organisms as pseudomonas. Prostatitis (acute/chronic) <i>travelers diarrhea</i> <p>يا صبر منى زوجها عنده بروسنات</p>	
Adverse effects	<ul style="list-style-type: none"> Ototoxicity. (drug or chemical related damage to the inner ear) Nephrotoxicity (Very narrow therapeutic index). Neuromuscular blocking effect. <i>paralysis</i> (high doses). <p>لما الواحد ما يسمع زين وتقول له سالفه بيقول ها مين هو قلي (Amin o gly)</p> <p>شخص مريض وباقي من عمره قليل ، ندعي له الله يمد بعمره قولي آمين (Amin gly)</p> <p>Like Gentamicin = an Gentleman who built his muscles</p>	<ul style="list-style-type: none"> Nausea , vomiting , diarrhea. CNS effects (confusion, insomnia, headache, anxiety). Damage of growing cartilage (arthropathy). In <18 year Phototoxicity (avoid excessive sunlight). Alkalization in GI if taken with milk. 	<p>ما صفا (Cepha) لنا الا هالدرق اخر شيء</p> <p>Given in severe/complicated (upper) UTIs & acute prostatitis</p> <p>صفا (Cepha) زوجها عنده بروسنات</p>

MCQ

1. A 22-year-old pregnant female presents with a 2-day history of dysuria with increased urinary frequency and urgency. She is diagnosed with (UTI) caused by E. coli. Which one of the following can be used ?
 - A. Ceftriaxone
 - B. Ciprofloxacin
 - C. Doxycycline
 - D. Gentamycin
2. Which of the following drugs is correctly matched with the appropriate adverse effect?
 - A. Ciprofloxacin—hyperkalemia.
 - B. Nitrofurantoin—Ototoxicity.
 - C. Trimethoprim —Megaloblastic anemia
 - D. Sulfonamides—nystagmus.
3. A 38 male came to the hospital with prostatitis . Which one of these is NOT indicated in his case?
 - A. Gentamycin
 - B. Ciprofloxacin
 - C. Doxycycline
 - D. Ceftriaxone
4. which of the following drugs could cause folate deficiency in pregnant woman?
 - A. ampicillin.
 - B. ceftriaxone.
 - C. Trimethoprim
 - D. sulfonamide
5. Damage of growing cartilage is an adverse effect of which of the following ?
 - A. Ceftriaxone
 - B. GENTAMICIN
 - C. Ciprofloxacin
 - D. Doxycycline
6. a 27 years old male patient was diagnosed with UTI, he mentioned in history that he traveled to al-Bahrain recently, which of the following bacteria is involved ? and which drug should be prescribed to him ?
 - A. Chlamydia - Doxycycline
 - B. Chlamydia - Nitrofurantoin
 - C. E.coli – Nitrofurantoin
 - D. E.coli - Doxycycline
7. which of the following statements is not correct ? .
 - A. TMP is widely distributed to tissues and body fluids including CNS, CSF.
 - B. Doxycycline interact with Food & di & tri-valent cations (Ca, Mg, Fe, AL) and impair the absorption.
 - C. Ciprofloxacin may cause Megaloblastic anemia.
 - D. Sulfonamides may cause Displace bilirubin.
8. Mechanism of action of Co-trimoxazole includes :
 - A. Sulfonamides inhibiting Dihydrofolate reductase
 - B. Trimethoprim inhibiting Dihydropteroate synthetase
 - C. Trimethoprim inhibiting Dihydrofolates.
 - D. Sulfonamides inhibiting Dihydropteroate synthetase
9. Patient in medication with Antibiotic, after 2 days he came to the emergency complaining from orange brown urine , the most likely antibiotic is :
 - A. Doxycycline.
 - B. Ciprofloxacin
 - C. GENTAMICIN
 - D. Nitrofurantoin
10. which of the following drugs should be avoided if given to children ?
 - A. Ceftriaxone.
 - B. GENTAMICIN.
 - C. Doxycycline
 - D. Nitrofurantoin

Answers:
1. A
2. C
3. A
4. C
5. C
6. A
7. C
8. B
9. D
10. D



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