URINARY TRACT INFECTION

1ST YR MEDICINE
KSU

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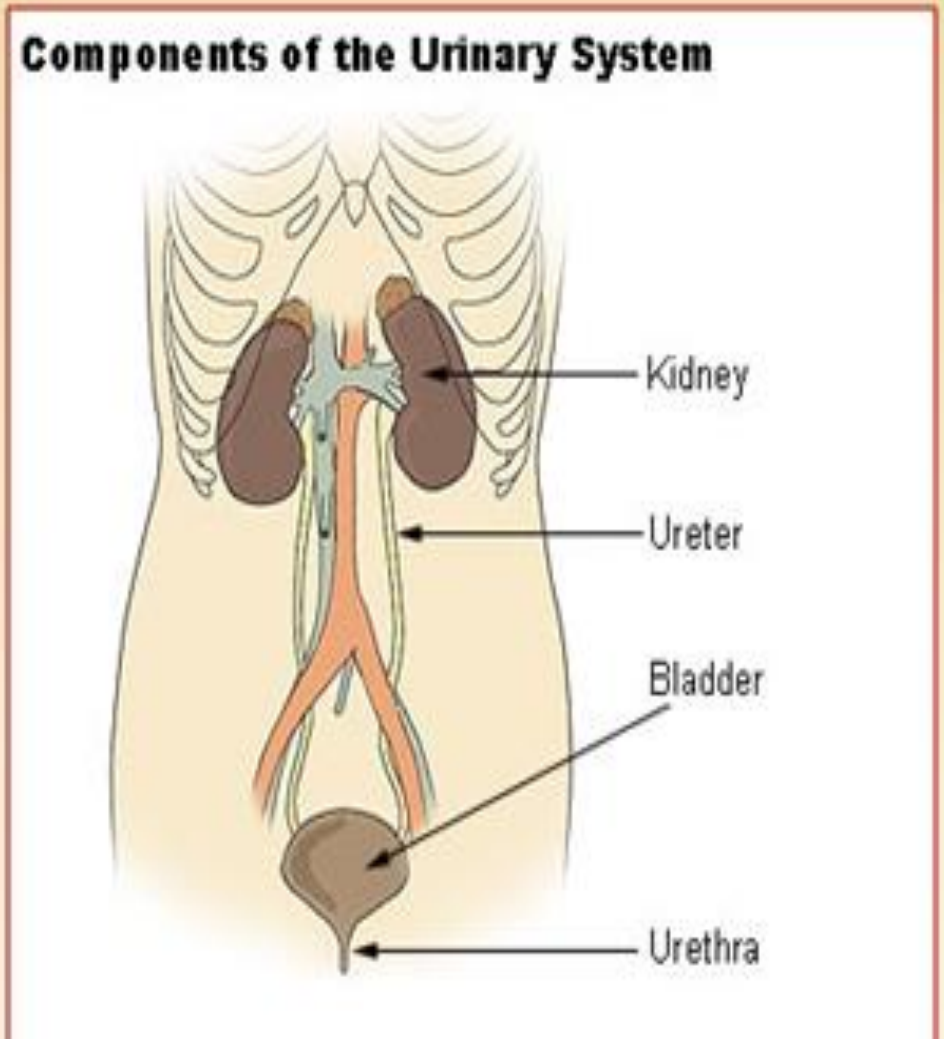
Urinary Tract System



Urinary tract infections (UTIs)

1. Upper urinary tract (kidney & ureters) infections: pyelonephritis

2. Lower urinary tract (bladder, urethra & prostate): cystitis, urethritis & prostatitis (more common).

**** Upper urinary tract infections are more serious.**

UTI

- It is the 2nd most common infection (after RTIs)
- It is often associated with some obstruction of the flow of urine
- It is more common in women more than men 30:1 (Why ?)
- Incidence of UTI increases in old age (10% of men & 20% of women).

What are the causes of UTI

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

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

Bacteria responsible of UTIs

Gm-ve bacteria (most common):

- E. coli (approx. 80% of cases)
- Proteus mirabilis
- Klebsiella
- Pseudomonas aeruginosa

Gm+ve bacteria (less common):

- Staphylococcus saprophyticus (Approx. 20%)
- Mycoplasma, Chlamydia trachomatis & Neisseria gonorrhea (**limited to urethra, unlike E. coli may be sexually transmitted**).

UTI can be:

- **Simple:**

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

- **Complicated:**

Infections spread to other parts of the body & resistant to many antibiotics, thus more difficult to cure. **{Due to hospital- acquired bacteria (E. coli, Klebsiella, Proteus, Pseudomonas, enterococci, staphylococci)}.**

Treatment of UTI

Antibiotics:

1- Co-trimoxazole (SMX + TMP), p.o.

2- Nitrofurantoin, p.o.

3- Tetracyclines, e.g. Doxycycline, p.o.

4- Aminoglycosides, e.g. Gentamicin

5- Cephalosporins (e.g. Ceftriaxone & Ceftazidime)

6- Quinolones, e.g. Ciprofloxacin, p.o.

Co-trimoxazole (Bactrim, Septra)

Sulfamethoxazole-Trimethoprim

(SMX) (TMP)

Alone, each agent is bacteriostatic

Together they are bactericidals (synergism)

The optimal ratio of TMP to SMX in vivo is 1:20.

(formulated 1(TMP): 5(SMX); 160 mg TMP + 800 mg SMX;

80 mg TMP + 400 mg SMX; 8 mg TMP + 40 mg SMX).

MECHANISM OF ACTION

P-Aminobenzoic Acid (PABA)

↓

Dihydropteroate synthetase ⊣ **Sulfonamides***

Dihydrofolate

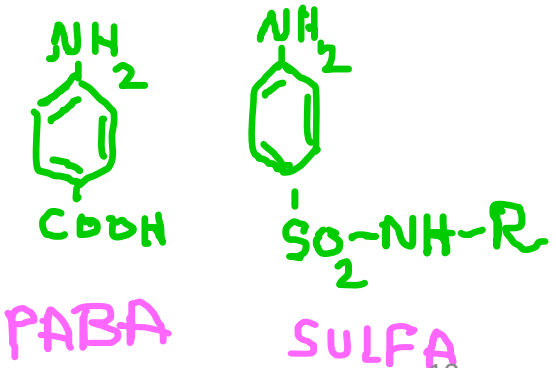
↓

Dihydrofolate reductase ⊣ **Trimethoprim***

Tetrahydrofolate

↓

Purines & DNA synthesis



* Inhibit gm-ve & gm+ve bacteria

Absorption, metabolism & Excretion (PK):

Sulfonamides

- Mainly given po/ (or IV)

- Rapidly absorbed from stomach & small intestine

- Widely distributed to tissues & body fluids (including CNS, CSF), placenta & fetus

- Absorbed sulfonamides bind to serum protein (approx. 70%)

- Metabolized in the liver by the process of acetylation

- Eliminated in the urine, partly as such & partly as acetylated derivative.

PK

TMP

- Usually given orally/ IV, 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
- It’s a weak base, concentrates in the prostatic & vaginal fluids (> acidic than plasma).

ADVERSE EFFECTS (TMP+SMX)

1. GIT- Nausea, vomiting

2. Allergy

3. Hematologic

    a) Acute hemolytic anemia

        a. hypersensitivity b. G6PD deficiency

    b) Megaloblastic anemia due to TMP.

Drug interactions

Displace bilirubin- if severe – kernicterus

Potentiate warfarin, oral sulfonylurea hypoglycemics.

CONTRAINDICATIONS (TMP+SMX)

1. Pregnancy
2. Nursing mother
3. Infants under 6 weeks
4. Renal or hepatic failure
5. Blood disorders.

Nitrofurantoin

Antibacterial Spectrum:

- Bactericidal for gm-ve & gm+ve bacteria

- Effective against E. coli & Staph. saprophyticus, but other common UT gm-ve bacteria may be resistant.

Mechanism of action of nitrofurantoin

Sensitive bacteria reduce the drug to an active agent (by bacterial reductase) that inhibits various enzymes & damages DNA.

PK of nitrofurantoin

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

Adverse effects of nitrofurantoin

- **GI disturbances**: bleeding of the stomach, nausea, vomiting & diarrhea (must be taken with food)
- Headache and nystagmus
- Hemolysis in patients with G6PD deficiency

Contraindications:

- Patients with G6PD deficiency >>> anemia
- Neonates
- Pregnant women (after 38 wks of pregnancy).

Therapeutic Uses of nitrofurantoin

It is used as urinary antiseptic.

Its usefulness is limited to lower uncomplicated UTI's & cannot be used for upper UT or systemic infections.

Dose: 50-100 mg, po q 6h/7 days

Long acting: 100 mg twice daily.

Tetracyclines
(e.g. Doxycycline)

It is a long-acting tetracycline

Mechanism of action

Bacteriostatic, Inhibits protein synthesis by binding reversibly to bacterial 30S ribosomal subunits.

Against gm+ve & gm-ve bacteria.

Doxycycline (Cont.')

PK

- Usually given po
- Absorption is 90-100%
- Absorbed in the upper s. intestine & best in absence of food
- Food & di & tri-valent cations (Ca^{2+}, Mg^{2+}, Fe^{2+}, AL^{3+}) impair drug absorption & reduce its effectiveness
- Protein binding 40-80 %
- Distributed well, including CSF
- Cross placenta & excreted in milk
- Largely metabolized in the liver.

Doxycycline (Cont'.)

Side effects

1. GIT: nausea, vomiting , diarrhea & epigastric pain (give with food)
2. Thrombophlebitis – i.v
3. Hepatic toxicity (prolonged therapy with high dose)
4. Brown discolouration of **teeth** – children
5. Deformity or growth inhibition of **bones** – children
6. Phototoxicity (sensitivity to sunlight)
7. Vertigo
8. Superinfections (alter the intestinal flora due to broad spectrum activity).

Contraindications of doxycycline

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

Therapeutic Uses of Doxycycline

- Treatment of UTI's due to many gm-ve & gm+ve bacteria including **Mycoplasma** & **Chlamydia**, 100 mg p.o bid for 7 days
- Prostatitis.

Aminoglycosides

e.g. GENTAMICIN, i.m, i.v.

- Bactericidal antibiotics
- Inhibits protein synthesis by binding to 30S bacterial ribosomal subunits
- Active against **gm-ve aerobic** organisms
- Poorly absorbed orally
- Cross placenta.

Gentamicin (CONT')

- Excreted unchanged in urine
- More active in alkaline medium

Adverse effects :

- Ototoxicity
- Nerve damage (e.g. vestibular nerve)
- Nephrotoxicity
- Neuromuscular blocking effect.

Gentamicin (CONT')

Therapeutic uses in UTI's

Severe infections caused by gm-ve organisms

(pseudomonas or enterobacter) infection.

Cephalosporins, (Detail was explained in respiratory lec.)

3rd generation cephalosporins

Ceftriaxone & Ceftazidime

- Mainly effective against gm-ve bacteria
- Acts by inhibition of cell wall synthesis
- Bactericidal
- They are given parenterally
- Given in severe / complicated UTIs
- & acute prostatitis.

Fluoroquinolones

(Detail was explained in respiratory lec.)

e.g. Ciprofloxacin

Active against gm-ve aerobic organisms

Mechanism of action

Inhibits bacterial DNA gyrase enzyme & cell division resulting in bacterial cell death

Clinical use

- UTI caused by multidrug resistance organisms as pseudomonas
- Prostatitis (acute/ chronic).

Ciprofloxacin ….Adverse effects

- GIT: Nausea, vomiting, diarrhea
- CNS effects: confusion, insomnia, headache, anxiety
- Damage of growing cartilage (reversible arthropathy)
- Photosensitivity (avoid excessive sunlight).


Thank you