Urinary tract infections

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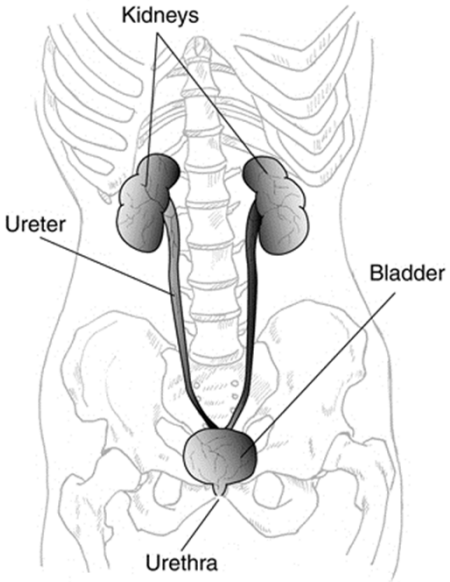
Urinary tract defined



Classification of UTI

- Based on origin of infection:
  - Community acquired UTI
  - Hospital acquired UTI (Nosocomial infection)
- Based on Part of UT that is infected
  - Pyelonephritis (Kidney)
  - Cystitis (Bladder)
  - Urethritis (Urethra)
  - Postatitis (Prostate)
- Generally only refer to Upper or Lower UTI (UUTI / LUTI)

Complicated UTIs

- Complicated (cUTI) *vs.* uncomplicated infection
- Anatomical and functional abnormalities
  - Outflow obstruction
  - Renal scarring
  - Foreign body (stone, tumour, catheter)
  - Pregnancy
- Metabolic abnormalities
  - Diabetes
  - Immunosuppression

Some definitions

- **UTI –** Detection of more than 10^5 organisms per mL of suitably collected urine
- **Recurrent UTI** – 3+ episodes of infections per year
- **Relapse** – Repeat infection re-occurs within 2 weeks with same strain of organism
- **Asymptomatic bacteriuria** is the presence of bacteria with no symptoms
  - Most often present in elderly patients

Aetiology

- Mostly bacteria but may be fungal (*Candida*) or viral
- Most often caused by gram-negative bacteria
  - *E. coli* (75% of bacterial UTIs)
  - *Klebsiella spp*
  - *Pseudomonas aeuriginosa*
  - *Enterobacter*
  - *Proteus mirabils*
- May also be gram-positive bacteria like *Staphylococcus saprophyticus*

Risk factors

Pre-menopausal

- Sexual intercourse
- Spermicidal creams containing antibiotics
- Previous UTI
- Maternal history of UTIs
- Non-secretor status

Post-menopausal

- Anatomical and functional defects (incontinence, post-void residual)
- Loss of lactobacilli from vaginal flora
- Cystocele
- Previous UTI
- Non-secretor status

Clinical presentation

- Symptoms worsen as infection spreads from the LUT to the UUT
- LUT
  - Urgency
  - Frequency
  - Dysuria (burning sensation during urination) → good indication of urethritis
  - Pyuria (foul smelling, cloudy urine)
  - Possible abdominal pain → good indication of cystitis
  - Possible mild fever
  - Possible hematuria (blood in urine)
- UUT
  - High fever
  - Nausea and vomiting
  - Back / flank pain
  - Possible hematuria (blood in urine)

Objectives of treatment

- Prevent / treat systemic consequences of infection
- Eradicate pathogen
- Relieve symptoms
- Prevent recurrences
- Minimise treatment adverse effects

Treatment (antibiotic)

Empirical treatment

- Quinolones
  - **Ciprofloxacin**, **Norfloxacin**, **Ofloxacin**, **Nalidixic acid** (Avoid due to resistance)
  - Prevents bacterial DNA synthesis by inhibiting topoisomerase
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - High urinary tract tissue and urine concentrations

- **Ciprofloxacin** / **Ciprofloxacin SR**
  - Cystitis 250 mg bid / 500 mg od for 3 days
  - Pyelonephritis 500 mg bid / 1000 mg od for 7 days

Ciprofloxacin

Adverse effects

- NB! Contra-indicated for children and during pregnancy
- Tendonitis and tendon rupture (↑ risk with corticosteroids)

Interactions

- Inhibits CYP3A4 - may cause elevated levels of:
  - Statins, medazolam, quinidine, progesterone, propranolol, lidocaine
- CYP1A2 substrate - may cause elevated levels of:
  - Warfarin, ropivacaine
- Significant interactions
  - Risk of seizures when used with NSAIDS
    - ↓ levels of pheytoin - further increases risk of seizures

Treatment (antibiotic)

Empirical treatment options in pregnancy

- Cephalosporins
  - **Cefixime** or **Cefpodoxime** (3rd generation) **Cefipime** (4th generation)
  - Disrupts peptidoglycan synthesis of bacterial cell walls
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - 5% cross-reactivity in patients with penicillin allergy

- **Cefpodoxime**
  - Cystitis 1000 mg bid for 3 days
  - Pyelonephritis 200 mg bid for 10 days

Cefpodoxime

Adverse effects

- Neurotoxicity @ high doses / renal impairment

Interactions

- May interfere with Vit K metabolism → warfarin
- May interfere with aldehyde dehydrogenase → disulfiram-like reactions

Treatment (antibiotic)

Second line treatment options in pregnancy

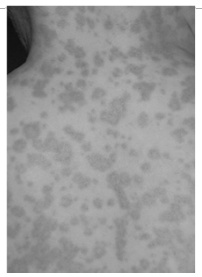
- Penicillins
  - **Amoxicillin / Clavulanic acid**
  - Disrupts peptidoglycan synthesis of bacterial cell walls
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - Do not use in patients with penicillin allergy

- **Amoxicillin**
  - Cystitis 375 mg bid for 3 days
  - Pyelonephritis 200 mg bid for 10 days

Amoxicillin

Adverse effects

- Hypersensistivity
- Amoxicillin-induced morbilliform rash



Interactions

- Oral contraceptives
- Warfarin

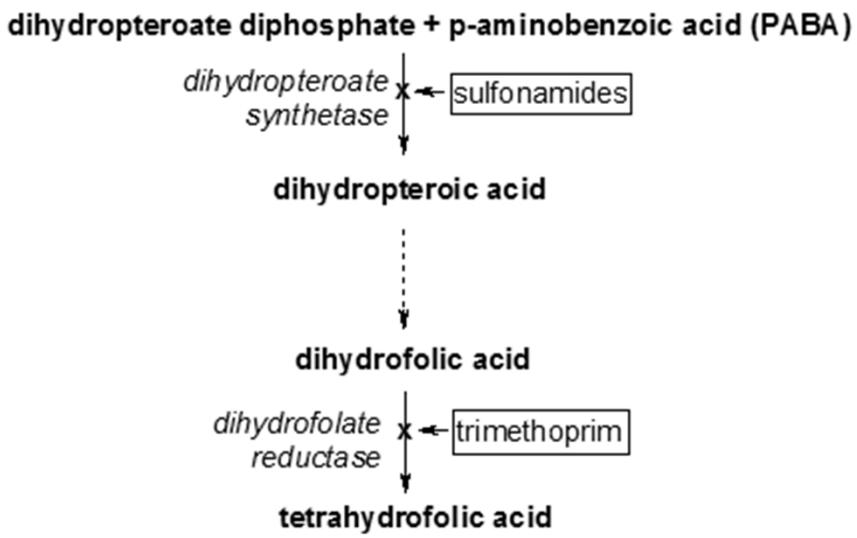
Treatment (antibiotic)

Alternative therapy options in penicillin allegry

- **Trimethoprim / Sulfamethoxazole (Co-trimoxazole)**
  - Bacteriostatic
  - Prevents formation of tetrahydofolate by
    - inhibiting dihydrofolate reductase Trimethoprim
    - Interfrese with PABA incopration Sulfamethoxazole
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - High urinary tract tissue and urine concentrations
  - Resistance

- **Co-trimoxazole**
  - Cystitis 160/800 mg bid for 5-7 days
  - Pyelonephritis 160/800 mg bid for 14 days

Co-trimoxazole



Trimethoprim

Adverse effects

- Disulfiram-like reactions
- Hyperkalemia
  - Binds same receptor as Amiloride in the distal tubule of the nephrone

Interactions

- Oral contraceptives
- ↑ digoxin levels

Sulfamethoxazole

Adverse effects

- Rash and hives
- Steven Johnson Syndrome
- HIV patients more susceptible to hypersensitivity reactions
- Pseudomembranous colitis

Interactions

- Warfarin
- ↑ digoxin levels

Treatment (antibiotic)

Alternative treatments

- **Fosfomycin**
  - Single dose → compliance
  - Inhibits cell wall synthesis
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - High urinary tract tissue and urine concentrations
  - Resistance develops quickly

- **Fosfomycin**
  - Cystitis 3000 mg single dose
  - Pyelonephritis Not indicated

Fosfomycin

Adverse effects

- GIT disturbances
- Rash

Interactions

- None

Treatment (antibiotic)

Alternative treatments

- **Nitrofurantoin**
  - Single dose → compliance
  - Inhibits cell wall synthesis
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - High urinary tract tissue and urine concentrations
  - Resistance develops quickly
  - **NB! Do not use in pregnancy**

- **Nitrofurantoin**
  - Cystitis 100 mg tid for 7 days
  - Pyelonephritis Not indicated
  - Prophylaxis 100 mg once daily @ night

Nitrofurantoin

Adverse effects

- Pulmonary side-effects
  - Acute reactions - hypersensitivity type symptoms
  - Chronic reactions - fibrosis (especially in the elderly)

Interactions

- Levlonumide (Used for rheumatoid arthritis)
  - May cause drug-induced liver injury

Treatment (antibiotic)

cUTI and nosocomial UTIs

- **Aminoglycosides (Gentamicin, Tobramycin, Amikacin)**
  - Can be used in combination with β-lactam-type antibiotics (synergistic effect)
  - Inhibits protein synthesis
  - Broad spectrum, active against both G(+) and G(-) bacteria
  - High urine concentrations
  - Reserved for multidrug resistant bacterial UITs
  - **NB! Do not use in pregnancy (affects development of the 8th cranial nerve)**

- **Gentamycin**
  - Cystitis 5 mg/kg iv single dose
  - Pyelonephritis 5 mg/kg iv single dose

Gentamicin

Adverse effects

- Hypersensitivity reactions

Interactions

- Tenofovir / emtricitibine
- Vaccines
- Loop diuretics
  - ► Nephrotoxicity

Treatment (antibiotic)

cUTI and nosocomial UTIs

- **Imipenem / cilastatin, Piperacillin / tazobactam**
  - Can be used in combination with β-lactam-type antibiotics (synergistic effect)
  - Inhibits cell wall synthesis
  - Very broad spectrum, active against both G(+) and G(-) bacteria
  - High urine concentrations
- **Imipenem**
  - Cystitis 500 mg tid for 7 days
  - Pyelonephritis 500 mg tid for 7 days

Imipenem/cilastatin

Adverse effects

- Palpatations
- Pulmonary side-effects

Interactions

- Tramadol
- Valproic acid
- Bupropion
- Fluoroquinolones
- **Risk of seizures**

Non-pharmacological therapy

- Urinary alkalinisers
  - Helps for dysuria
- Urinary analgesics
  - Helps for dysuria
- Hormonal therapy
  - Only for post-menopausal woman
- Cranberry juice
  - Decreases the incidence of UTIs - prophylaxis
  - May cause kidney stones in predisposed individuals
- Increased water intake
  - 'Flushes' the urinary tract

Urinary alkalinisers & antibiotics

- Avoid the use during antibiotic therapy of UTIs
  - May affect urine concentrations of drugs
  - May influence the efficacy of drugs
- Be sure to inform the patient of this

Avoiding UTIs

- Drink plenty of water every day
- Don't resist the urge to urinate
- Take showers instead of baths

Additional advice for women:

- Wipe from front to back following urination
- Clean the genital area before sexual intercourse
- Urinate and clean the genital area after sex