

UTI

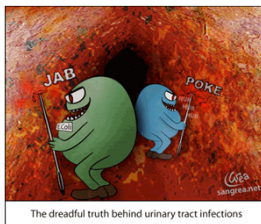
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Introduction

- Responsible for > 7 million consultations annually
- 15% of all antibiotic prescriptions
- 40% of all hospital acquired infections
- Significant burden on economy

Definition

- Presence and inflammatory response to a micro-organism infection of urine that can involve the upper or lower urinary tract



Uncomplicated UTI

Definition:

UTI without relevant structural and functional abnormalities within the urinary tract (uropathies), without relevant kidney disease (nephropathies), and without relevant comorbidities which can lead to more serious outcomes

- **Uncomplicated cystitis**
- **Uncomplicated pyelonephritis**

Antibiotic use

Antibiotic choice guided by:

- 1) Spectrum and susceptibility patterns of uropathogens
- 2) Efficacy for this indication
- 3) Tolerability
- 4) Collateral effects
- 5) Cost
- 6) Availability



Uncomplicated cystitis

- Empiric treatment
- Clinical success (cure and improvement) significantly more likely in women treated with antibiotics than those with placebo....
- Antibiotics more superior to placebo regarding cure, microbiological eradication at end of treatment, microbiological reinfection and relapse....
- More adverse events seen in antibiotic group

Bacterial spectrum

- Lack of data
- **Most common causative pathogen: E.coli (74.6%)**
- Other:
 - *Enterococcus faecalis* (4%)
 - *Staphylococcus saprophyticus* (3,6%)
 - *Klebsiella pneumoniae* (3,5%)
 - *Proteus mirabilis* (3,5%)

Antimicrobial susceptibility

- **E.coli:**
 - ✓ fosfomycin (98,1%)
 - ✓ mecillinam (95,8%)
 - ✓ nitrofurantoin(95,2%)
 - ✓ ciprofloxacin (91,8%)
- **Resistance pattern of E.coli strains varies in different countries**
 - ✓ amoxiclav (82,1%)
 - ✓ cefuroxime (82,5%)
 - ✓ nalidixic acid (82,5%)

Treatment of uncomplicated UTI

Short course:

Advantages

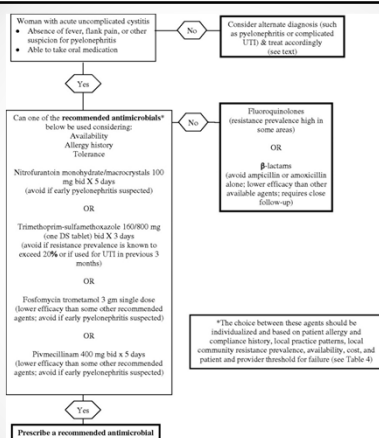
- Improved compliance
- Low cost
- Fewer adverse events

Disadvantages:

- Expense if treatment failure
- Psychological aspect

Recommended therapy

Substance	Daily dosage	Duration
Fosfomycin	3g single dose	1 day
Nitrofurantoin	50-100mg q 6 h	5-7 days
Pivmecillinam	400 mg bid	3 days
Ciprofloxacin	250 mg bid	3 days
Levofloxacin	250 mg qid	3 days
Norfloxacina	400 mg bid	3 days
Ofloxacin	200 mg bid	3 days
Cefpodoxime proxetil	100 mg bid	3 days
TMP-SMX	160/800 mg bid	3 days
Trimethoprim	200 mg bid	5 days



Follow up

- Routine post-treatment urinalysis in asymptomatic patient not indicated
- If symptoms do not resolve or recur within two weeks: urine culture and antimicrobial susceptibility
- Retreatment with a 7 day regimen using another agent

Acute uncomplicated pyelonephritis

- Flank pain
- N+V
- Fever
- Costovertebral angle tenderness
- With or without cystitis symptoms
- Bacterial spectrum similar to uncomplicated cystitis

Treatment

- Oral therapy for 10-14 days
- Fluoroquinolones first-line therapy
- Alternative: cefpodoxime proxetil
- Cotrimoxazole not suitable
- Susceptibility testing

Follow up

- Routine urinalysis not recommended
- If symptoms do not improve within 3 days, or resolve and recur within 2 weeks, further investigations are indicated
- Treat with another agent for 2 weeks

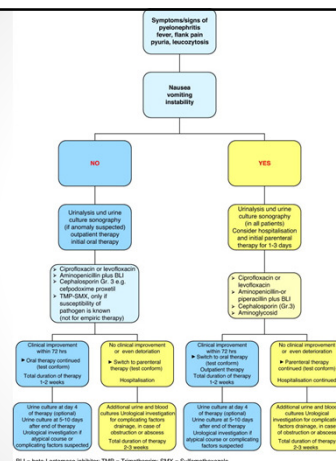
Further investigations

- Upper tract UTI
- Failure to respond to antibiotics
- Recurrent infection
- Complicated UTI
- Pregnancy



Severe pyelonephritis

- Parenteral fluoroquinolone
- 3rd generation cephalosporin
- Aminopenicillin plus beta lactamase inhibitor
- Aminoglycoside or carbapenem if resistant cases
- Hospital admission
- Switch to oral therapy if improvement
- Further investigations



Recurrent UTI in women

Definition

- More than 2 infections in 6 months
- 3 infections within 12 months

Risk factors

- Spermicide use
- New sex partner
- First UTI before 15 years of age
- Mother with history of UTI
- Post menopausal women

Prevention strategies

- Increase fluid intake
- Double voiding
- Omit bath products
- Voiding after sexual intercourse
- Avoidance of spermicide
- Topical oestrogen cream

Antimicrobial prophylaxis

- Continuous prophylaxis
- Post-coital prophylaxis
- Intermittent self-treatment
- **Previous UTI must be eradicated!!!!**

Continuous prophylaxis

- Decreases number of recurrent UTI
- Administer for 6 months
- Norfloxacin, ciprofloxacin, nitrofurantoin, trimethoprim-sulfamethoxazole, cephalexin, cefaclor, perfloracin
- SE: vaginal and oral candidiasis, GIT

Post-coital prophylaxis

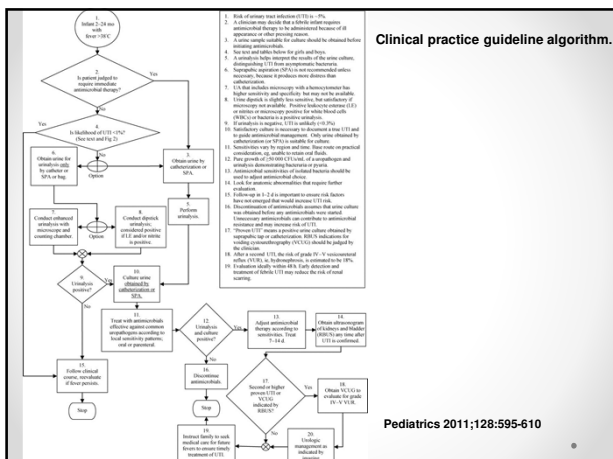
- Single dose
- TMP-SMX, nitrofurantoin, cephalexin, ciprofloxacin, norfloxacin, ofloxacin

UTI in children

New guidelines

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Empiric AB for oral therapy in children


Substance	Dosage
Amoxicillin-clavulanate	20-40 mg/kg/d in 3 doses
Trimethoprim- sulfamethoxazole	6-12 mg/kg T, 30-60 mg/kg S/d in 2 doses
Cefixime	8 mg/kg/d one dose
Cefpodoxime	10 mg/kg/d in 2 doses
Cefprozil	30 mg/kg/d in 2 doses
Cefuroxime axetil	20-30 mg/kg/d in 2 doses
Cephalexin	50-100 mg/kg/d in 4 doses

- ## Indications for parenteral antibacterial medication
- New-borns and young infants (4-6 months)
 - Clinical suspicion of urosepsis
 - Critically ill condition
 - Refusal of fluids/ food/oral meds
 - Vomiting and diarrhoea
 - Non compliance
 - Complicated pyelonephritis (urinary obstruction)

Empiric AB for parenteral therapy in children

Substance	Dosage
Ceftriaxone	75 mg/kg every 24 hours
Cefotaxime	150 mg/kg/d divided every 6-8 hours
Ceftazidime	100-150 mg/kg/d divided every 8 hours
Gentamycin	7.5 mg/kg/d divided every 8 hours
Tobramycin	5 mg/kg/d divided every 8 hours
Piperacillin	300 mg/kg/

- ## Complicated UTI
- Male sex
 - Hospital acquired infection
 - Pregnancy
 - Indwelling catheter
 - Recent intervention
 - Functional/anatomic abnormality of urinary tract
 - Diabetes mellitus
 - Immunosuppression

- ## UTI in pregnancy
- Bladder displaced anteriorly and superiorly by uterus
 - Poor urinary flow and bladder emptying
 - Dilatation of upper tracts caused by mechanical obstruction and smooth muscle relaxation due to progesterone
 - Treat immediately
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UTI in men

- Bacterial prostatitis: 6 weeks course with quinolone
- Epididymo-orchitis: quinolone
- Doxycycline to cover *Chlamydia trachomatis*

Fosfomycin

- Inhibits cell wall synthesis, with different mechanism than beta lactam AB
- 40% oral bioavailability
- Excreted unchanged in urine
- Low incidence of *E. coli* resistant strains
- Active against quinolone-resistant strains *E. coli*



Nitrofurantoin

- Interferes with carbohydrate metabolism
- 90% bioavailable
- 40% excreted in urine
- Less effective against *Klebsiella* and *Enterobacter*
- Not active against *Proteus* or *Pseudomonas*
- Long term side effects include lung and hepatotoxicity

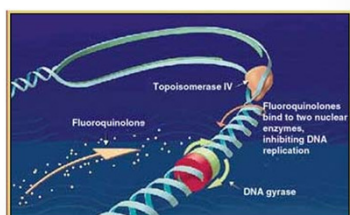


Pivmecillinam

- Beta lactam
- Interacts with penicillin-binding protein
- 60-75% bioavailable
- 45% excreted in urine
- Level of resistance low

Mechanism of action

- Inhibits bacterial DNA gyrase
- Responsible for cutting and supercoiling DNA
- Post AB effect against gram negative and positive organisms



Kinetics

- 80% systemic available after oral dose
- Bioavailability decreased by antacids
- Large volume of distribution: including eye, lungs, prostatic fluid, CSF, bone and cartilage
- Entero-hepatic cycle: AB in urine 5 days after stopping Rx
- Rx less often than $t_{1/2}$ (post AB effect)
- Removed by glomerular filtration and tubular secretion
- High urinary excretion with levofloxacin, lomefloxacin, and ofloxacin
- Less active in acidic urine

Side effects

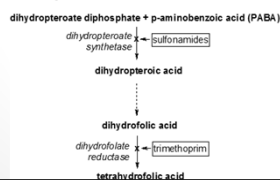
- GIT
- CNS
- Hypersensitivity
- QT prolongation/ torsades de pointes
- Liver and renal damage
- Reversible arthralgia
- Tendonitis/ tendon rupture
- Drug interactions

Aminoglycosides

- Alter bacterial protein synthesis
- Water soluble
- Excreted exclusively in urine by glomerular filtration
- Suitable for treatment of pyelonephritis
- Ototoxic: mild high-frequency impairment, to profound hearing loss, to vestibular disturbances

Cotrimoxazole

- Combination of trimethoprim (TMP) and sulfamethoxazole (SMX)
- Inhibit different steps in folic acid synthesis pathway
- Used more than 30 years for UTI
- High resistance rates
- Not active against *Pseudomonas*



Side effects

- Hypersensitivity reaction
- Steven Johnson's
- Aplastic/ hemolytic anaemia
- CI: newborn, porphyria, G6PD deficiency