URINARY TRACT INFECTIONS (UTI) IN PRIMARY CARE

UTI

- Urinary tract infections (UTIs) are among the most prevalent infectious diseases
- In Europe, there are no good data regarding the prevalence of various types of UTIs and their impact on the quality of life of the affected population
- In the USA, UTIs are responsible for over 7 million physician visits annually, including more than 2 million visits for cystitis

Epidemiology

- One of the most common community-acquired infections in practice
  12% of men,
  40-50% of women have one incident in the life
  1-3% of girls and 1% of boys in the first 5 years of life have UTI
- in children up to 7% of febrile have UTI
  Second in children with bacterial infections after respiratory infections
  UTI have even 22 - 35% of women aged 20 - 40 years

Classification of UTIs

- Traditionally, UTIs are classified based on clinical symptoms, laboratory data and microbiological findings.
- Practically UTIs have been divided in:

  uncomplicated

  complicated

  sepsis

Risk factors in UTI

- Healthy premenopausal women
- RF of recurrent UTI, but no risk of severe outcome

- Sexual behavior and contraceptive devices
- Hormonal deficiency in post menopause
- Secretary type of certain blood groups
- Controlled diabetes mellitus

- Extra-urogenital RF, with risk or more severe outcome

- Pregnancy
- Male gender
- Badly controlled diabets mellitus
- Relevant immunosuppression*
- Connective tissue diseases*
- Prematurity, new-born

- Nephropathic disease, with risk of more severe outcome

- Relevant renal insufficiency*
- Polycystic nephropathy

Risk factors in UTI

- Urological RF, with risk or more severe outcome, which can be resolved during therapy

- Ureteral obstruction (i.e. stone, stricture)
- Transient short-term urinary tract catheter
- Asymptomatic Bacteriuria
- Controlled neurogenic bladder dysfunction
- Urological surgery
- Permanent urinary Catheter and non resolvable

- urological RF, with risk of more severe outcome

- Long-term urinary tract catheter treatment
- Non resolvable urinary obstruction
- Badly controlled neurogenic bladder

Additive parameters of UTI classification and severity assessment

- Clinical presentation

UR: Urethritis
CY: Cystitis
PN: Pyelonephritis
US: Urosepsis
MA: Male genital glands

- Grade of severity

1: Low, cystitis
2: PN, moderate
3: PN, severe, established
4: US: SIRS
5: US: Organ dysfunction
6: US: Organ failure

- Risk factors ORENUC

O: No RF
R: Recurrent UTI RF
E: Extra urogenital RF
N: Nephropathic RF
U: Urological RF
C: Catheter RF

- Pathogens Species
- Susceptibility grade

• Susceptible
• Reduced susceptibility
• Multi-resistant

The laboratory tests
Microbiological urine culture

- significant bacteriuria

the following bacterial counts are clinically relevant:

- > 103 cfu/mL of uropathogens in a mid-stream sample of urine (MSU) in acute uncomplicated cystitis in women.
- > 104 cfu/mL of uropathogens in an MSU in acute uncomplicated pyelonephritis in women.
- > 105 cfu/mL of uropathogens in an MSU in women, or > 104 cfu/mL uropathogens in an MSU in men, or in straight catheter urine in women, in a complicated UTI.

In a suprapubic bladder puncture specimen, any count of bacteria is relevant

Diagnosis of urinary tract infections

- In clinical routine assessment, a number of basic criteria must be looked at before a diagnosis can be established, including:
- • clinical symptoms;
- • results of selected laboratory tests (blood, urine)
- • evidence of the presence of microorganisms by culturing or other specific tests;

Uncomplicated UTIs in adults

- Acute, uncomplicated UTIs in adults include episodes of acute cystitis and acute pyelonephritis in otherwise healthy individuals. These UTIs are seen mostly in women without structural and functional abnormalities within the urinary tract, kidney diseases, or comorbidity that could lead to more serious outcomes and therefore require additional attention

Aetiological spectrum

- The spectrum of etiological agents is similar in uncomplicated upper and lower UTIs
- *E. coli the* causative pathogen in 70-95% of cases
- *Staphylococcus saprophyticus in 5-10%.*
- *Occasionally, other* Enterobacteriaceae, such as *Proteus mirabilis and Klebsiella sp., are isolated*

Acute uncomplicated cystitis in premenopausal, non-pregnant women

- Clinical symptoms:

- urinary irritative symptoms: dysuria, urgency, frequency,
- suprapubic pain,
- no urinary symptoms in 4 weeks before this episode
- the absence of vaginal discharge or irritation,

Acute uncomplicated cystitis in premenopausal, non-pregnant women

- Laboratory test:
- Urinalysis > 10 WBC/mm3
- Urine dipstick testing, as opposed to urinary microscopy, is a reasonable alternative
- Urine cultures > 103 cfu/mL*are recommended for those with:
- -suspected acute pyelonephritis;

  - symptoms that do not resolve or recur within 2-4 weeks after the completion of treatment;

  - those women who present with atypical symptoms

Therapy of acute cystitis-empirical

Table 3.1: Recommended antimicrobial therapy in acute uncomplicated cystitis in otherwise healthy premenopausal women

Antibiotics	Daily dose	Duration of therapy
Fosfomycin trometamol°	3 g SD	1 day
Nitrofurantoin	50 mg q6h	7 days
Nitrofurantoin macrocrystal	100 mg bid	5-7 days
Pivmecillinam*	400 mg bid	3 days
Pivmecillinam*	200 mg bid	7 days
Alternatives		
Ciprofloxacin	250 mg bid	3 days
Levofloxacin	250 mg qd	3 days
Norfloxacin	400 mg bid	3 days
Ofloxacin	200 mg bid	3 days
Cefpodoxime proxetil	100 mg bid	3 days
If local resistance pattern is known (E. coli resistance < 20%):		
Trimethoprim-sulphamethoxazole	160/800mg bid	3 days
Trimethoprim	200 mg bid	5 days

°not available in all countries.
**available only in Scandinavia, the Netherlands, Austria, and Canada.*

Follow-up

- Routine post-treatment urinalysis or urine cultures in asymptomatic patients are not indicated
- In women whose symptoms do not resolve by the end of treatment, and in those whose symptoms resolve but recur within 2 weeks, urine culture and antimicrobial susceptibility tests should be performed
- For therapy in this situation, one should assume that the infecting organism is not susceptible to the agent originally used. Retreatment with a 7-day regimen using another agent should be considered

Acute uncomplicated pyelonephritis in premenopausal, non-pregnant women

- Clinical symptoms:
- Fever (> 38°C), chills, flank pain; nausea and vomiting, or costovertebral angle tenderness,
- It can occur in the absence of symptoms of cystitis

- Other diagnoses excluded;
- No history or clinical evidence of urological abnormalities (ultrasonography,radiography

Acute uncomplicated pyelonephritis in premenopausal, non-pregnant women

- Laboratory test:

- Urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrites, is recommended for routine diagnosis
- Colony counts > 104 cfu/mL of uropathogens are considered to be indicative of clinically relevant bacteriuria

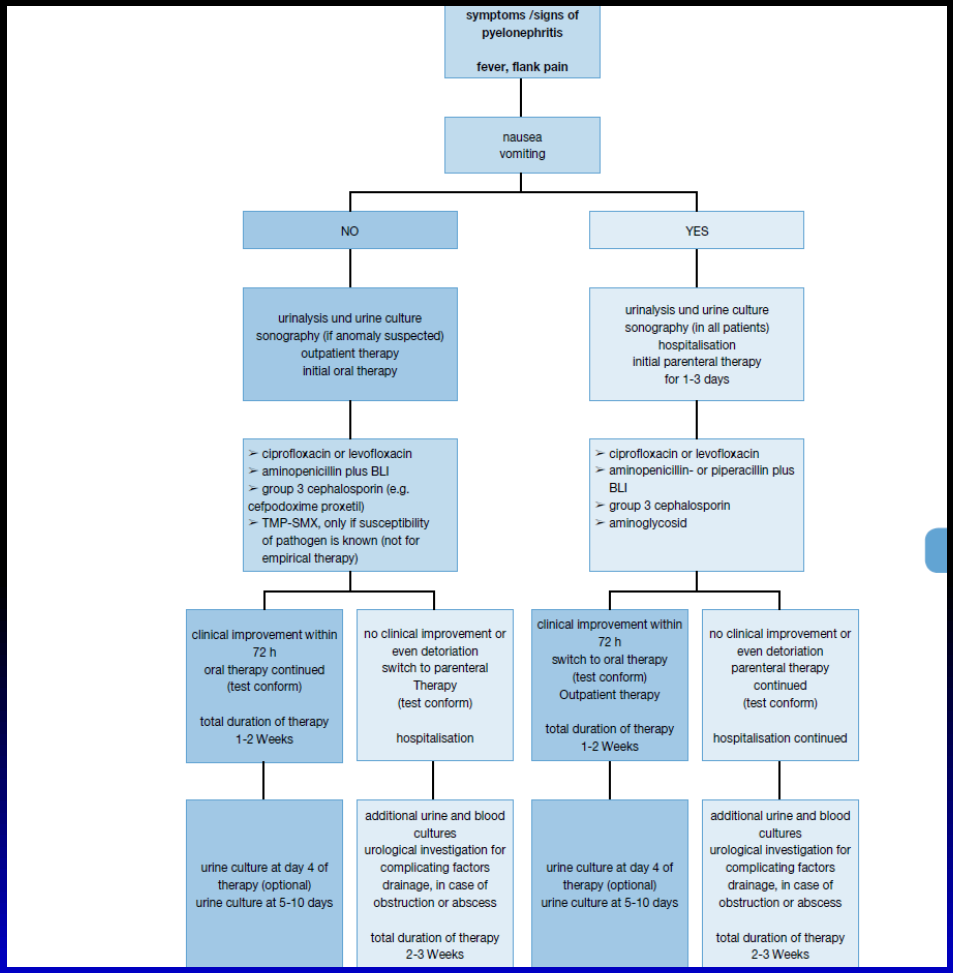
Acute uncomplicated pyelonephritis in premenopausal, non-pregnant women

- *Imaging diagnosis*
- Evaluation of the upper urinary tract with ultrasound should be performed to rule out urinary obstruction or renal stone disease.
- Additional investigations, such as an unenhanced helical computed tomography (CT), excretory urography, or dimercaptosuccinic acid (DMSA) scanning, should be considered if the patients remain febrile after 72 h of treatment in hospital

Recommended initial empirical antimicrobial therapy in acute uncomplicated pyelonephritis in otherwise healthy premenopausal women

- In mild and moderate cases of acute uncomplicated pyelonephritis, oral therapy of 10-14 days is usually sufficient
- A fluoroquinolone for 7-10 days can be recommended as first-line therapy if the resistance rate of *E. coli is still < 10%*
- If the fluoroquinolone dose is increased, the treatment can probably be reduced to 5 days
- A third-generation oral cephalosporin, such as cefpodoxime proxetil or ceftibuten, could be analternative 10 days
- Co-amoxiclav is not recommended as a drug of first choice for empirical oral therapy of acute pyelonephritis It is recommended when susceptibility testing shows a susceptible Gram-positive organism for 14 days
- cotrimoxazole is not suitable for empirical therapy in most areas, 960 mg2x 14 days

Clinical management of acute pyelonephritis



Recurrent (uncomplicated) UTIs in women

- Recurrent UTIs are common among young, healthy women, even though they generally have anatomically and physiologically normal urinary tracts
- Recurrent UTIs need to be diagnosed by urine culture.
- Excretory urography, cystography and cystoscopy are not routinely recommended for evaluation of women with recurrent UTIs

Prevention of UTI Antimicrobial prophylaxis

- **Continuous antimicrobial prophylaxis regimens for women with recurrent UTIs**

- TMP-SMX* 40/200 mg once daily
- TMP-SMX 40/200 mg thrice weekly
- Trimethoprim 100 mg once daily
- Nitrofurantoin 50 mg once daily
- Nitrofurantoin 100 mg once daily
- Cefaclor 250 mg once daily
- Cephalexin 125 mg once daily
- Cephalexin 250 mg once daily
- Norfloxacin 200 mg once daily
- Ciprofloxacin 125 mg once daily
- Fosfomycin 3 g every 10 days

- **Postcoital antimicrobial prophylaxis regimens for women with recurrent UTIs**

- TMP-SMX* 40/200 mg
- TMP-SMX 80/400 mg
- Nitrofurantoin 50 or 100 mg
- Cephalexin 250 mg
- Ciprofloxacin 125 mg
- Norfloxacin 200 mg
- Ofloxacin 100 mg

Prevention of UTI

- Immunoactive prophylaxis

  OM-89 (Uro-Vaxom) is sufficiently well-documented and has been shown to be more effective than placebo in several randomised trials.

- Prophylaxis with probiotics

  Prevent bacterial vaginosis, a condition that increases the risk of UTI

- Prophylaxis with cranberry

  Cranberry (Vaccinium macrocarpon) is useful in reducing the rate of lower UTIs in women. The daily consumption of cranberry products, giving a minimum of 36 mg/day proanthocyanindin A (the active compound), is recommended.

UTIs in pregnancy

- UTIs are common during pregnancy.
- Most women acquire bacteriuria before pregnancy,
- 20-40% of women with asymptomatic bacteriuria develop pyelonephritis during pregnancy.
- Pregnant women should be screened for bacteriuria during the first trimester

Treatment regimens for asymptomatic bacteriuria and cystitis in pregnancy.

Antibiotics Duration of therapy Comments

- Nitrofurantoin (Macrobid®) 100 mg q12 h, 3-5 days Avoid in G6PD deficiency
- Amoxicillin 500 mg q8 h, 3-5 days Increasing resistance
- Co-amoxicillin/clavulanate 500 mg q12 h, 3-5 days
- Cephalexin (Keflex®) 500 mg q8 h, 3-5 days Increasing resistance
- Fosfomycin 3 g Single dose
- Trimethoprim-sulfamethoxazole q12 h, 3-5 days Avoid trimethoprim in first trimester/term and sulfamethoxazole in third trimester/term

UTIs in pregnancy

- ***Treatment of pyelonephritis or Complicated UTI in pregnency***
- Prolonged parenteral antibiotic therapy (7-10 days)
- Requiared referral to hospital
- When indicated, ultrasonography or magnetic resonance imaging (MRI) should be used preferentially to avoid radiation risk to the foetus

Asymptomatic bacteriuria

- Screening for and treatment of asymptomatic bacteriuria is recommended:
- For pregnant women
- Before an invasive genitourinary procedure for which there is a risk of mucosal bleeding.

Screening for or treatment of asymptomatic bacteriuria is not recommended for:

- Premenopausal, non-pregnant women
- Postmenopausal women
- Women with diabetes
- Healthy men
- Residents of long-term care facilities
- Patients with an indwelling urethral catheter
- Patients with nephrostomy tubes or ureteric stents
- Patients with spinal cord injury
- Patients with candiduria
- In renal transplant patients beyond the first 6 months

COMPLICATED UTIs DUE TO UROLOGICAL DISORDERS

Factors that suggest a potential complicated UTI

- The presence of an indwelling catheter, stent or splint (urethral, ureteral, renal) or the use of intermittent bladder catheterisation
- Post-void residual urine of > 100 mL
- An obstructive uropathy of any aetiology, e.g. bladder outlet obstruction (including neurogenic urinary bladder), stones and tumour
- Vesicoureteric reflux or other functional abnormalities
- Urinary tract modifications, such as an ileal loop or pouch
- Chemical or radiation injuries of the uroepithelium
- Peri- and postoperative UTI
- Renal insufficiency and transplantation, diabetes mellitus and immunodeficiency

Sepsis is a systemic response to infection Systematic inflammatory response syndrome (SIRS)

- This systemic response is manifested by two or more of the following conditions:
- - Temperature > 38°C or < 36°C
- - Heart rate > 90 bpm
- - Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mmHg (< 4.3 kPa)
- - WBC > 12,000 cells/mm3 or < 4,000 cells/mm3 or > 10% immature (band) forms

UTIs IN CHILDREN

- UTI in children is a frequent health problem, with the incidence only a little lower than that of upper respiratory and digestive infections.
- The incidence of UTI varies depending on age and sex. In the first year of life, mostly the first 3months, UTI is more common in boys (3.7%) than in girls (2%), after which the incidence changes, being 3% in girls and 1.1% in boys
- The risk of UTI during the first decade of life is 1% in males and 3% in females
- *E. coli is responsible* for 90% of UTI episodes Gram-positive bacteria (particularly enterococci and staphylococci) represent 5-7% of cases.
- Predisposes to UTI in children: Phimosis,labial adhesion , chronic constipation, variety of congenital urinary tract abnormalities: urethral valves, ureteropelvic junction obstruction, vesicoureteric reflux (VUR) and dysfunctional voiding, e.g. as caused by a neuropathic disorder.

UTIs IN CHILDREN

- Symptoms are non-specific, and vary with the age of the child and the severity of the disease
- UTI in neonates may be non-specific and with no localisation
- In small children,<2 y high fever UTI may present with gastrointestinal signs, such as vomiting and diarrhoea.
- Later on, when they are older than 2 years, frequent voiding, dysuria and suprapubic, abdominal or lumbar pain may appear with or without fever.

UTIs IN CHILDREN

Clinical classification of UTIs in children

Severe UTI	Simple UTI
Fever > 39°C	Mild pyrexia
Persistent vomiting	Good fluid intake
Serious dehydration	Slight dehydration
Poor compliance	Good treatment

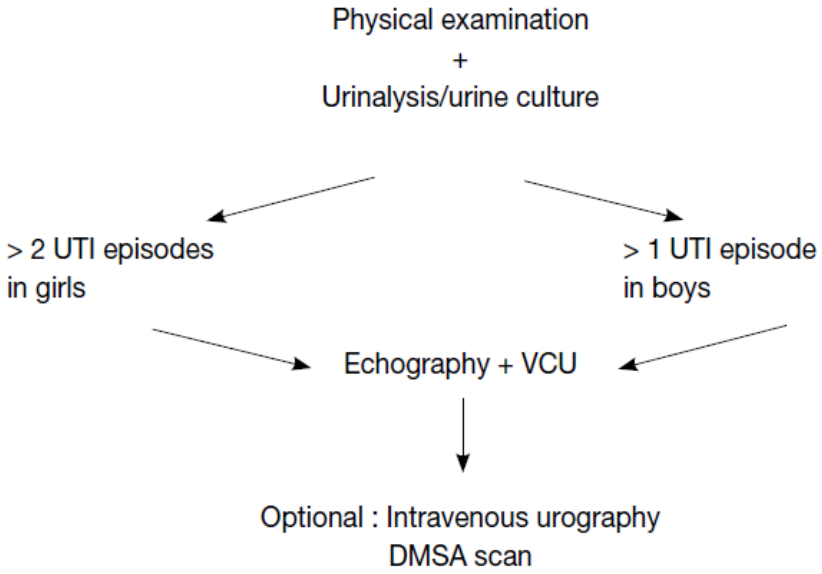
UTIs IN CHILDREN diagnosis

- ***Physical examination***

It is mandatory to look for phimosis, labial adhesion, signs of pyelonephritis, epididymo-orchitis, and stigmata of spina bifida, e.g. hairy patch on the sacral skin

- The definitive diagnosis of infection in children requires a positive urine culture significant bacteriuria of > 105 cfu/mL
- Plastic bag attached to the genitalia is no reccomended Prospective studies have shown a high incidence of false-positive results

Figure 7.1: Schedule of investigation of a UTI in a child



DMSA = dimercaptosuccinic acid; UTI = urinary tract infection; VCU = voiding cystourethrograp

UTIs IN CHILDREN

Treatment has four main goals:

- 1. elimination of symptoms and eradication of bacteriuria in the acute episode
- 2. prevention of renal scarring
- 3. prevention of a recurrent UTI
- 4. correction of associated urological lesions

- For treatment of UTI in children, short courses are not advised and therefore treatment is continued for 5-7 days and longer 10-14
- If the child is severely ill with vomiting and dehydration, hospital admission is required and parenteral antibiotics are given initially
- Oral empirical treatment with TMP, an oral cephalosporin or amoxycillin/clavulanate is recommended
- In children < 3 years of age all cases must treat like PN

URETHRITIS *Treatment*

gonorrhoeal urethritis

As first-choice treatment

- • cefixime, 400 mg orally as a single dose, or 400 mg by suspension (200 mg/5 mL)
- • ceftriaxone, 1 g intramuscularly (with local anaesthetic) as a single dose

Alternative regimens

- • ciprofloxacin, 500 mg orally as single dose
- • ofloxacin, 400 mg orally as single dose
- • levofloxacin, 250 mg orally as single dose.

non-gonorrhoeal urethritis

As first choice of treatment:

- azithromycin, 1 g orally as single dose
- doxycycline, 100 mg orally twice daily for 7 days

As second choice of treatment:

- erythromycin base, 500 mg orally four times daily for 14 days
- erythromycin ethylsuccinate, 800 mg orally four times daily for 7 days
- ofloxacin, 300 mg orally twice daily for 7 days
- levofloxacin, 500 mg orally once daily for 7 days

UTI summation

Figure 2.1. Traditional and improved classification of UTI as proposed by the EAU European Section of Infection in Urology (ESIU) (1)