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
- In 2019, there were 405 million UTI cases worldwide, with 273,000 deaths reported.

Epidemiology

- One of the most common community-acquired infections in practice – accounting for 10–20% of all community-acquired infections
  - Nearly 40% of all hospital-acquired infections
  - 12% of men
  - 40–50% of women experience at least one incident in their lifetime
  - 1–3% of girls and 1% of boys within the first five years of life; up to 7% of febrile children
  - Beyond the first year of life, UTIs are 20–50 times more frequent in girls than in boys
  - The second most common bacterial infection in children after respiratory tract infections
  - Men over the age of 65 reach the same incidence level as older women
  - Up to 22–35% of women aged 20–40 years

UTI

- The incidence of UTI depends on the interaction between:
  defensive factors of the body
  and virulence microorganisms

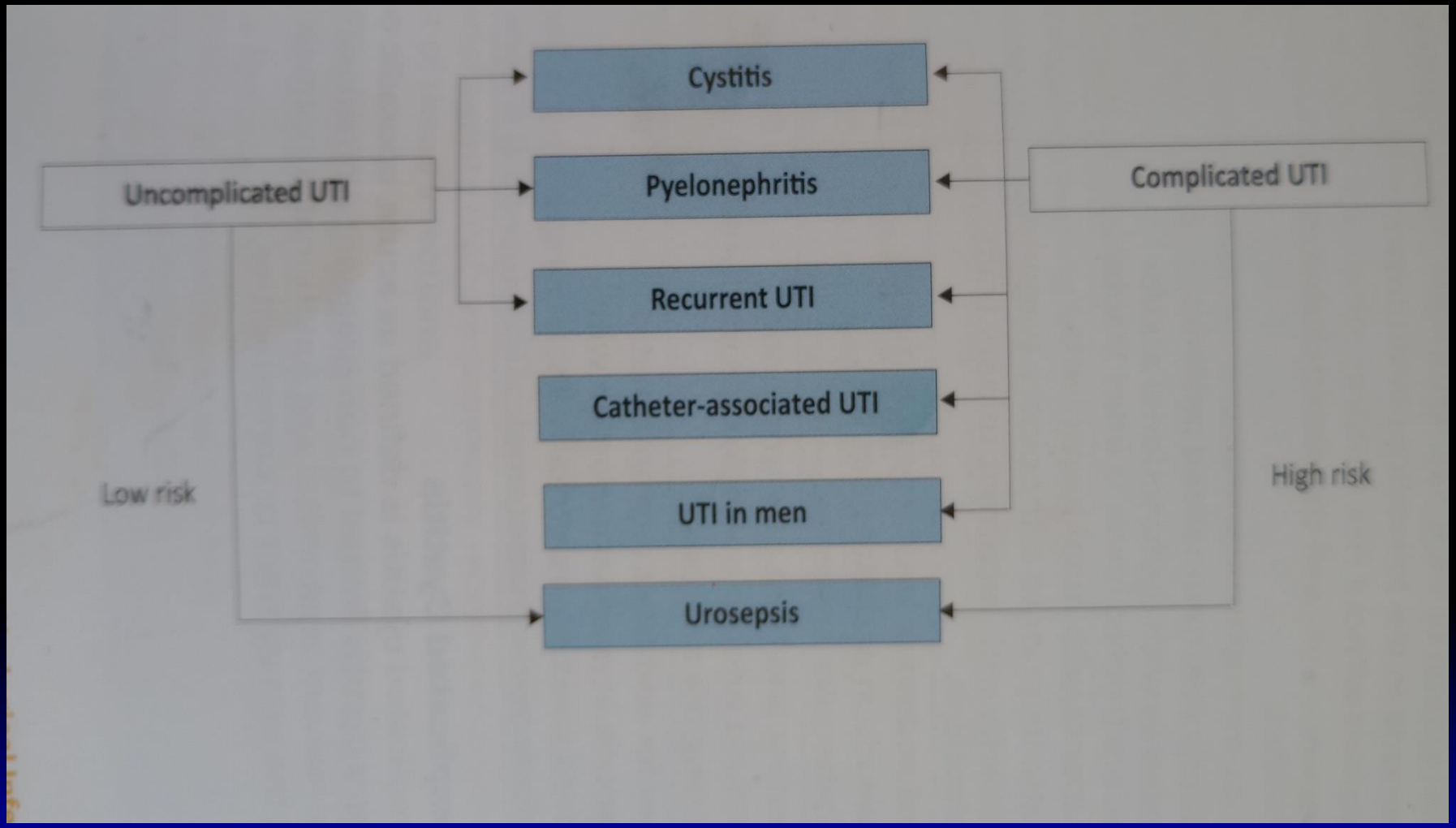
Classification of UTIs

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

  uncomplicated

  complicated

  sepsis


Cystitis
Uncomplicated UTI
Pyelonephritis
Complicated UTI
Recurrent UTI
Catheter-associated UTI
Low risk
High risk
UTI in men
Urosepsis

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

The laboratory tests in UTI

- Urinalysis
  The presence of leukocytes -leukocuturia
  answer urothelium to bacterial invasion
  Rolls leukocyte in PN
  Haematuria 40% of women with bladder inflammation
- Blood tests
  Leukocytosis, CRP in PN
  Blood culture in sepsis, procalcitonin
  Assessment of renal function- creatinine, GFR

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

Other useful tests

- Ultrasound is indicated in complicated UTI and women with PN in the absence of improvement after standard treatment
  Ultrasound of the urinary tract can detect abnormalities of the urinary tract defects, urinary retention, kidney cysts, stones, renal abscess, flare
- CT is indicated for the detection of renal abscess, focal inflammation of the kidneys
- Urography can detect abnormalities of the ureters, pelvis, renal calyx

- In Children also using voiding cystourethrography (VCU), renal scintigraphy

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

Etiology – Hospital-Acquired and Complicated UTIs

- **Escherichia coli** – 40–70%
- **Klebsiella spp.** – 10–15% (multidrug-resistant strains, ESBL, virulent, New Delhi)
- **Proteus spp.** – associated with urine alkalization and urolithiasis
- **Enterobacter spp.** – up to 20%, catheter-associated UTIs
- **Pseudomonas spp.** – up to 10%, including *Acinetobacter baumannii*
- **Staphylococcus aureus** – catheter-associated UTIs, patients with diabetes
- **Anaerobic bacteria**
- Higher rates of infections involving multiple pathogens and antibiotic-resistant bacteria
- **Fungi**: *Candida spp.*

Etiology – Community-Acquired and Uncomplicated UTIs

- **Uropathogenic bacteria**:
  - *Escherichia coli* – 85% (75–95% of uncomplicated cases – mostly uropathogenic strains, UPEC)
  - *Staphylococcus saprophyticus* (10–15%)
  - *Enterococcus spp. – E. faecalis*
  - *Proteus spp.* and *P. mirabilis* (10–15%)
  - *Klebsiella spp.* (5–10%)
  - **Not detectable with standard methods**:
  - *Chlamydia trachomatis*, *Neisseria gonorrhoeae*
  - **Fungi**:
  - *Candida spp.*, *Aspergillus*, *Cryptococcus*
  - **Viruses**:
  - Adenovirus, Herpes.

Uncomplicated UTIs in adults

- Acute uncomplicated cystitis in premenopausal, non-pregnant women
- Acute uncomplicated pyelonephritis in premenopausal, non-pregnant women
- Recurrent (uncomplicated) UTIs in women
- UTIs in pregnancy
- UTIs in postmenopausal women
- Acute uncomplicated UTIs in young men
- Asymptomatic bacteriuria

Uncomplicated Cystitis

Uncomplicated cystitis is defined as acute, sporadic or recurrent cystitis limited to non-pregnant women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.

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,

Uncomplicated Cystitis – Symptoms

- **Dysuria** – burning and pain during urination.
- **Increased urinary frequency**.
- **Urgency to urinate**.
- **Suprapubic pain**.
- **Hematuria** – observed in 40% of cases (viral cystitis caused by adenoviruses).

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

Recommendations for the diagnostic evaluation of uncomplicated cystitis	Strength rating
Diagnose uncomplicated cystitis in women who have no other risk factors for complicated urinary tract infections based on: • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge.	Strong
Use urine dipstick testing for diagnosis of acute uncomplicated cystitis.	Weak
Urine cultures should be done in the following situations: • suspected acute pyelonephritis; • symptoms that do not resolve or recur within four weeks after the completion of treatment; • women who present with atypical symptoms; • pregnant women.	Strong

Uncomplicated Cystitis – Treatment

- **Antimicrobial therapy**: administered orally for 3–5 days.
- **General management**: high fluid intake, pain relief, and antipyretics such as paracetamol.
- **Prognosis**: good; in asymptomatic patients after treatment, routine urine culture and sensitivity tests are not recommended.
- **Fluoroquinolones are not recommended** due to induction of cross-resistance and adverse effects.
- **Aminopenicillins combined with β-lactamase inhibitors are not recommended** because of high antibiotic resistance in *E. coli*.

In uncomplicated cystitis a fluoroquinolone should only be used when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

Recommendations for antimicrobial therapy for uncomplicated cystitis	**Strength rating**
Prescribe fosfomycin trometamol, pivmecillinam or nitrofurantoin as first-line treatment for uncomplicated cystitis in women.	Strong

Do not use aminopenicillins or fluoroquinolones to treat uncomplicated cystitis.	Strong

Table 1: Suggested regimens for antimicrobial therapy in uncomplicated cystitis

Antimicrobial	Daily dose	Duration of therapy	Comments
First-line women			
Fosfomycin trometamol	3 g SD	1 day	First-line women Recommended only in women with uncomplicated cystitis.
Nitrofurantoin macrocrystal	50-100 mg four times a day	5 days	
Nitrofurantoin monohydrate/ macrocrystals	100 mg b.i.d	5 days	
Nitrofurantoin macrocrystal prolonged release	100 mg b.i.d	5 days	
Pivmecillinam	400 mg t.i.d	3-5 days	
Alternatives			
Cephalosporins (e.g. cefadroxil)	500 mg b.i.d	3 days	Or comparable
If the local resistance pattern for E. coli is < 20%			
Trimethoprim	200 mg b.i.d	5 days	Not in the first trimenon of pregnancy
Trimethoprim-sulphamethoxazole	160/800 mg b.i.d	3 days	Not in the last trimenon of pregnancy

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

Recommendations for the diagnostic evaluation of uncomplicated pyelonephritis	Strength rating
Perform urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrite, for routine diagnosis.	Strong
Perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis.	Strong
Perform imaging of the urinary tract to exclude urgent urological disorders.	Strong

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

Recommendations for the treatment of uncomplicated pyelonephritis	Strength rating
Treat patients with uncomplicated pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment.	Strong
Treat patients with uncomplicated pyelonephritis requiring hospitalisation with an intravenous antimicrobial regimen initially.	Strong
Switch patients initially treated with parenteral therapy, who improve clinically and can tolerate oral fluids, to oral antimicrobial therapy.	Strong
Do not use nitrofurantoin, oral fosfomycin, and pivmecillinam to treat uncomplicated pyelonephritis.	Strong

Table 2: Table 2: Suggested regimens for empirical oral antimicrobial therapy in uncomplicated pyelonephritis

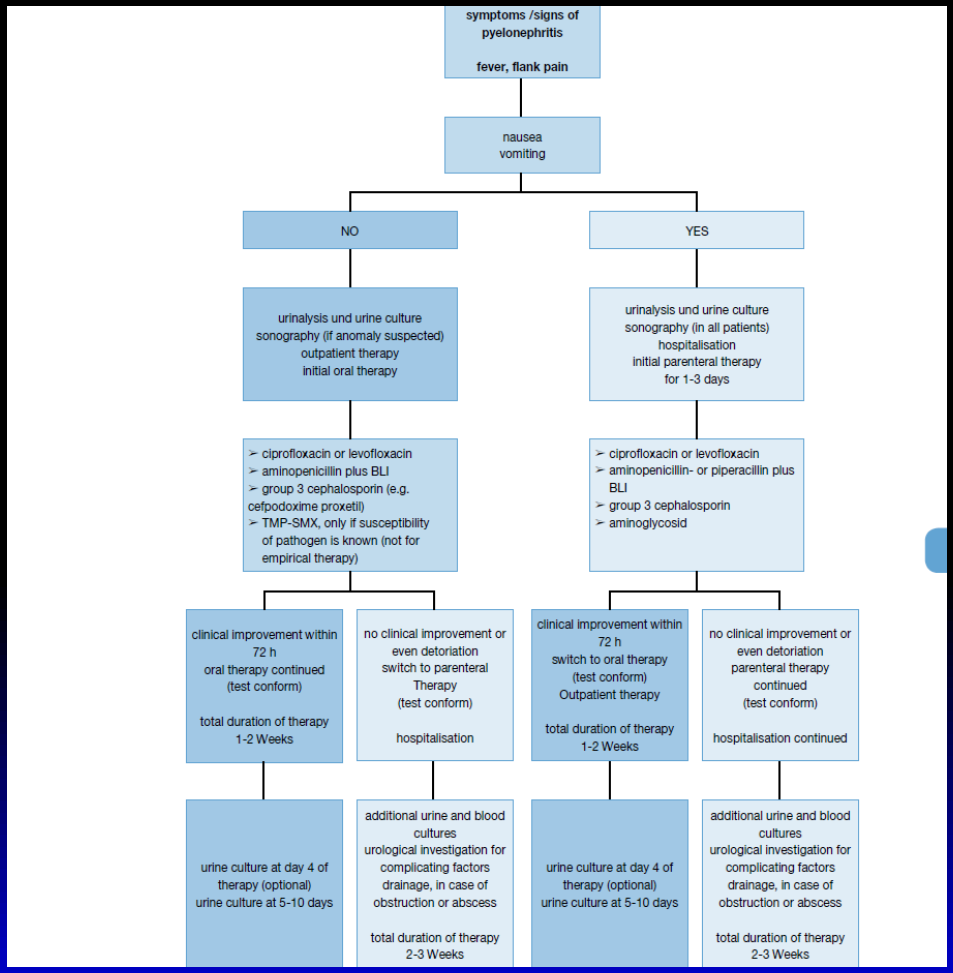
Antimicrobial	Daily dose	Duration of therapy	Comments
Ciprofloxacin	500-750 mg b.i.d	7 days	Fluoroquinolone resistance should be less than 10%.
Levofloxacin	750 mg q.d	5 days	
Trimethoprim sulphamethoxazol	160/800 mg b.i.d	14 days	If such agents are used empirically, an initial intravenous dose of a long-acting parenteral antimicrobial (e.g. ceftriaxone) should be administered.
Cefpodoxime	200 mg b.i.d	10 days	
Ceftibuten	400 mg q.d	10 days	

b.i.d = twice daily; q.d = every day.

Therapy of severe cases of acute uncomplicated pyelonephritis

- Patients with severe pyelonephritis who cannot take oral medication because of systemic symptoms such as nausea and vomiting, have to be treated initially with one of the following parenteral antibiotics:
- a parenteral fluoroquinolone,
- a third-generation cephalosporin,
- an aminopenicillin plus a β-lactamase-inhibitor,
- an aminoglycoside or carbapenem
- Hospital admission should be considered if complicating factors cannot be ruled out by available diagnosticprocedures and/or the patient has clinical signs and symptoms of sepsis

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

Recurrent UTIs

Recurrent UTIs (rUTIs) are recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.

Recommendations for the diagnostic evaluation and treatment of rUTIs	Strength rating
Diagnose recurrent UTI by urine culture.	Strong
Do not perform an extensive routine workup (e.g cystoscopy, full abdominal ultrasound) in women younger than 40 years of age with recurrent UTI and no risk factors.	Weak
Advise pre-menopausal women regarding increased fluid intake as it might reduce the risk of recurrent UTI.	Weak
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI.	Strong
Use immunoactive prophylaxis to reduce recurrent UTI in all age groups.	Strong
Advise patients on the use of a local or oral probiotic containing strains of proven efficacy for vaginal flora regeneration to prevent UTIs.	Weak

Recurrent Cystitis

Etiology – In Women

- **Vestibular anomalies**.
- **Constipation**.
- **Gynecological infections**.
- **Undiagnosed diabetes mellitus**.

Treatment:

- The same as for uncomplicated cystitis, but for a longer duration of **7–14 days**.
- In cases of recurrence, performing a **urine culture** and treating according to the **antibiogram** is recommended.

Recurrent Cystitis

In patients with recurrent UTIs (rUTIs), potential risk factors for infection should be identified.

- **In young women and premenopausal women**:
  - Sexual intercourse,
  - Use of spermicide,
  - New sexual partner,
  - Mother with a history of UTIs,
  - History of UTIs in childhood.
- **In postmenopausal and older women**:
  - History of UTIs prior to menopause,
  - Urinary incontinence,
  - Atrophic vaginitis due to estrogen deficiency,
  - Post-void residual urine (urine retention after urination).

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

Advise patients on the use of cranberry products to reduce recurrent UTI episodes; however, patients should be informed that the quality of evidence underpinning this is low with contradictory findings.	Weak
Use D-mannose to reduce recurrent UTI episodes, but patients should be informed of the overall weak and contradictory evidence of its effectiveness.	Weak
Use methenamine hippurate to reduce recurrent UTI episodes in women without abnormalities of the urinary tract.	Strong
Use endovesical instillations of hyaluronic acid or a combination of hyaluronic acid and chondroitin sulphate to prevent recurrent UTIs in patients where less invasive preventive approaches have been unsuccessful. Patients should be informed that further studies are needed to confirm the results of initial trials.	Weak
Use continuous or post-coital antimicrobial prophylaxis to prevent recurrent UTI when non-antimicrobial interventions have failed. Counsel patients regarding possible side effects.	Strong
For patients with good compliance self-administered short-term antimicrobial therapy should be considered.	Strong

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

UTIs in pregnancy-*Definition of significant bacteriuria*

- in an asymptomatic pregnant woman, bacteriuria is considered significant if two consecutive voided urine specimens grow > 105 cfu/mL of the same bacterial species on quantitative culture; or a single catheterised specimen grows > 105 cfu/mL of a uropathogen
- in a pregnant woman with symptoms compatible with UTI, bacteriuria is considered significant if a

voided or catheterised urine specimen grows > 103 cfu/mL of a uropathogen

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

UTIs in postmenopausal women

Risk factors

- In older institutionalised women, urine catheterisation and functional status deterioration appear to be the most important risk factors associated with UTI.
- Atrophic vaginitis.
- Incontinence, cystocele and post-voiding residual urine.
- UTI before menopause.
- Non-secretor status of blood group antigens.

Diagnosis

- Diagnosis of UTI in postmenopausal women should always consider the following:
- History, physical examination and urinalysis, including culture.
- Genitourinary symptoms are not necessarily related to UTI and an indication forantimicrobial treatment.

UTIs in postmenopausal women

- Treatment of acute cystitis in postmenopausal women is similar to that in premenopausal women, however, short-term therapy is not so well-established as in premenopausal women.
- Treatment of pyelonephritis in postmenopausal women is similar to that in premenopausal women.
- Asymptomatic bacteriuria in elderly women should not be treated with antibiotics.
- Optimal antimicrobials, doses and duration of treatment in elderly women appear to be similar to those recommended for younger postmenopausal women.
- Oestrogen (especially vaginal) can be administered for prevention of UTI, but results are contradictory.
- Alternative methods, such as cranberry and probiotic lactobacilli, can contribute but they are not sufficient to prevent recurrent UTI.
- If complicating factors, such as urinary obstruction and neurogenic bladder, are ruled out, antimicrobial prophylaxis should be carried out as recommended for premenopausal women.

Acute uncomplicated UTIs in young men

Men with acute uncomplicated UTI

Only a small number of 15-50-year-old men suffer from acute uncomplicated UTI.

Such men should receive, as minimum therapy, a 7-day antibiotic regimen.

Men with UTI and concomitant prostate infection

Most men with febrile UTI have a concomitant infection of the prostate, as measured by transient increases in serum PSA and prostate volume.

Urological evaluation should be carried out routinely in adolescents and men with febrile UTI, pyelonephritis, or recurrent infection, or whenever a complicating factor is suspected.

A minimum treatment duration of 2 weeks is recommended, preferably with a fluoroquinolone since prostatic involvement is frequent.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria in an individual without urinary tract symptoms is defined by a mid-stream sample of urine showing bacterial growth ≥ 105 cfu/mL in two consecutive samples in women and in one single sample in men.

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.

Recommendations	Strength rating
Do not screen or treat asymptomatic bacteriuria in the following conditions: • women without risk factors; • patients with well-regulated diabetes mellitus; • post-menopausal women; • elderly institutionalised patients; • patients with dysfunctional and/or reconstructed lower urinary tracts; • patients with renal transplants; • patients prior to arthoplasty surgeries; • patients with recurrent urinary tract infections.	Strong
Do not screen or treat asymptomatic bacteriuria in patients prior to cardiovascular surgeries.	Weak
Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa.	Strong
Screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment or single dose fosfomycin trometamol.	Weak

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

Complicated UTIs

A complicated UTI (cUTI) occurs in an individual in whom factors related to the host (e.g. underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g. obstruction, incomplete voiding due to detrusor muscle dysfunction) are believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.

Recommendations for the treatment of complicated UTIs	Strength rating
Use the combination of: • amoxicillin plus an aminoglycoside; • a second-generation cephalosporin plus an aminoglycoside; • a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.	Strong

Only use ciprofloxacin provided that the local resistance percentages are < 10% when; • the entire treatment is given orally; • patients do not require hospitalisation; • patient has an anaphylaxis for beta-lactam antimicrobials.	Strong
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last six months.	Strong
Manage any urological abnormality and/or underlying complicating factors.	Strong

COMPLICATED UTIs DUE TO UROLOGICAL DISORDERS

- Treatment strategy depends on the severity of the illness
- Hospitalisation is often necessary
- Patients with a complicated UTI, both community and hospital-acquired, tend to show a diversity of microorganisms with a higher prevalence of resistance against antimicrobials
- Enterobacteriaceae are the predominant pathogens, with *E. coli being the most common pathogen*, non-fermenters (e.g. *Pseudomonas aeruginosa) and Gram-positive cocci (e.g. staphylococci and* enterococci)
- Treatment encompasses three goals:

management of the urological abnormality, antimicrobial therapy, and supportive care

- The duration of therapy is usually 7-14 days but sometimes has to be prolonged for up to 21 days
- Referral to specialist always

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

Urosepsis

Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs.

Recommendations for the diagnosis and treatment of urosepsis	Strength rating
Perform the quickSOFA score to identify patients with potential sepsis.	Strong
Take a urine culture and two sets of blood cultures before starting antimicrobial treatment.	Strong
Administer parenteral high dose broad spectrum antimicrobials within the first hour after clinical assumption of sepsis.	Strong
Adapt initial empiric antimicrobial therapy on the basis of culture results.	Strong
Initiate source control including removal of foreign bodies, decompression of obstruction and drainage of abscesses in the urinary tract.	Strong
Provide immediate adequate life-support measures.	Strong

Table 4: Suggested regimens for antimicrobial therapy for urosepsis

Antimicrobials	Daily dose	Duration of therapy
Cefotaxime	2 g t.i.d	7-10 days Longer courses are appropriate in patients who have a slow clinical response
Ceftazidime	1-2 g t.i.d	
Ceftriaxone	1-2 g q.d	
Cefepime	2 g b.i.d	
Piperacillin/tazobactam	4.5 g t.i.d	
Ceftolozane/tazobactam	1.5 g t.i.d	
Ceftazidime/avibactam	2.5 g t.i.d	
Gentamicin*	5 mg/kg q.d	
Amikacin*	15 mg/kg q.d	
Ertapenem	1 g q.d	
Imipenem/cilastatin	0.5 g t.i.d	
Meropenem	1 g t.i.d	

** Not studied as monotherapy in urosepsis*

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

CATHETER-ASSOCIATED UTIs

- Bacteriuria develops in up to 25% of patients who require a urinary catheter for > 7 days, with a daily risk of 5%.

Prevention

- An indwelling catheter should be introduced under antiseptic conditions.
- The catheter system should remain closed.
- The duration of catheterisation should be minimal
- Topical antiseptics or antibiotics applied to the catheter, urethra or meatus are not recommended.
- Benefits from prophylactic antibiotics and antiseptic substances have never been established, therefore, they are not recommended.
- Chronic antibiotic suppressive therapy is generally not recommended.

Catheter-associated UTIs

Catheter-associated UTI refers to UTIs occurring in a person whose urinary tract is currently catheterised or has been catheterised within the past 48 hours.

Recommendations for diagnostic evaluation of CA-UTI	Strength rating
Do not carry out routine urine culture in asymptomatic catheterised patients.	Strong
Do not use pyuria as sole indicator for catheter-associated UTI.	Strong
Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI.	Strong

Recommendations disease management and prevention of CA-UTI	Strength rating
Treat symptomatic catheter-associated-UTI according to the recommendations for complicated UTI.	Strong
Take a urine culture prior to initiating antimicrobial therapy in catheterised patients in whom the catheter has been removed.	Strong
Do not treat catheter-associated asymptomatic bacteriuria in general.	Strong
Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions (e.g. transurethral resection of the prostate).	Strong
Replace or remove the indwelling catheter before starting antimicrobial therapy.	Strong
Do not apply topical antiseptics or antimicrobials to the catheter, urethra or meatus.	Strong
Do not use prophylactic antimicrobials to prevent catheter-associated UTIs.	Strong
Do not routinely use antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal.	Weak
The duration of catheterisation should be minimal.	Strong
Use hydrophilic coated catheters to reduce catheter-associated UTIs.	Strong
Do not routinely use antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal or in patients performing intermittent self-catheterisation.	Weak

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 – What to Focus on in History and Examination
History:

- **History**:
- Symptoms related to the urinary system (previous occurrences),
- Presence of abnormalities,
- Family history,
- Chronic constipation,
- Pinworms,
- Previous episodes of fever.
- **Examination**:
- General condition assessment: pulse, temperature, blood pressure,
- Physical development evaluation: height, weight gain,
- Exclusion of respiratory tract infections,
- Abdominal examination: enlarged bladder, tenderness, Goldflam's sign,
- Evaluation of the lumbar area,
- Examination of external genitalia: signs of inflammation, in boys – examination of the foreskin and glans penis, in girls – labial adhesions, and foreskin retractability.

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

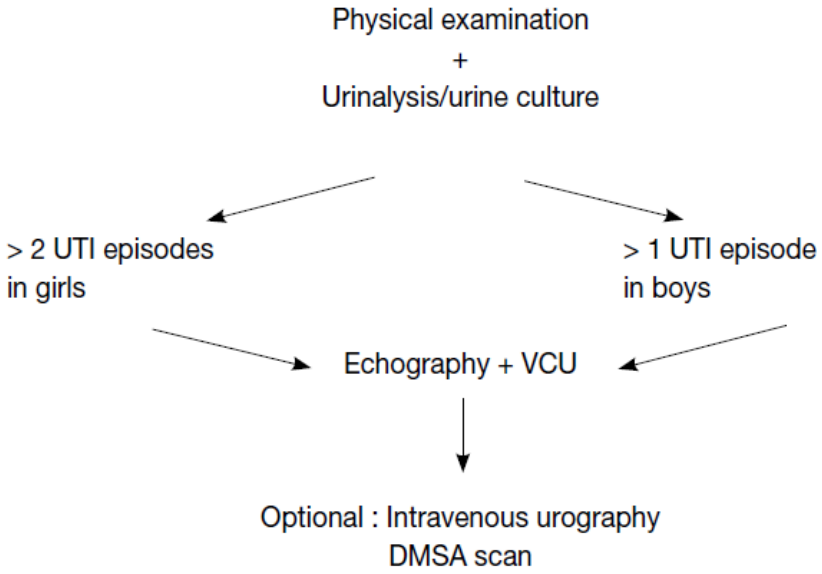
UTIs IN CHILDREN diagnosis

- ***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

- From a therapeutic and clinical point of view, gonorrhoeal urethritis has to be differentiated from non-specific urethritis.
- In Central Europe, non-specific urethritis is much more frequent than gonorrhoeal urethritis
- Pathogens include *N. gonorrhoeae, C. trachomatis, Mycoplasma genitalium and Trichomonas vaginalis*
- Mucopurulent or purulent discharge, alguria, dysuria and urethral pruritus are symptoms of urethritis
- Patients should be instructed to abstain from sexual intercourse until 7 days after therapy is initiated and sexual partners have been adequately treated.

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)