# Urinary Tract Infections(UTIs)

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## Definition

- Urinary tract infections are acute or chronic inflammatory reactions caused by proliferation of pathogenic microorganisms existing in the urinary tract.

## Definition(cont.)

- Infections of the urinary tract can be subdivided into two general anatomic categories:
  - Lower tract infection (urethritis and cystitis)
  - Upper tract infection (pyelonephritis, intrarenal and perinephric abscesses)

## Classification of UTIs

| | |
|---|---|
| Type of UTI | Cystitis<br>Pyelonephritis<br>Asymptomatic bacteriuria |
| Symptoms | Symptomatic<br>Asymptomatic |
| Recurrences | Sporadic (≤1 UTI/6 mo and ≤2 UTIs/yr)<br>Recurrent (≥2 UTIs/6 mo or ≥3 UTIs/yr)<br>Relapse<br>Reinfection |
| Complicating factors | Uncomplicated<br>Complicated (see text) |

UTI = urinary tract infection.

## Epidemiology

- Worldwide, at least 150 million cases of symptomatic UTIs occur each year.
- The number of patients who have UTIs is lower than the number of cases.
- 90% of patients have cystitis and 10% have pyelonephritis.
- Sporadic in about 70% of patients and recurrent in 25%.
- About 2% have complicated infections related to factors that increase the risk of establishment and management of bacteriuria.
- If factors that can increase the severity are included, the frequency of complicated infections is about 8%.

## Epidemiology (cont.)

- In very young child, UTIs more common in boy.
- Later in childhood and adult, symptomatic UTIs are more common in females, who are also more likely to have asymptomatic bacteriuria.
  (short urethra, also be the result of sexual abuse)
- In young man under 50, UTIs are rare and are often the result of underlying infections of the prostate.
- In elderly people, both symptomatic and asymptomatic UTIs are common.
  - Women: often the result of atrophic vaginal mucosa
  - Men: often the consequence of prostate hyperplasia or cancer.

## Epidemiology (cont.)

- UTIs is also the most common type of hospital-acquired infection because of the frequent use of bladder-catheters. (catheter- associated infection)

## Microbial Etiology of UTIs

| ORGANISMS | CLINICAL CHARACTERISTICS |
|---|---|
| **GRAM-NEGATIVE BACTERIA** | |
| *Escherichia coli* | Typical |
| *Klebsiella pneumoniae* | Often reinfection |
| *Enterobacter* spp | Often reinfection and/or health care–associated infection* |
| *Proteus* spp | May indicate tumor or calculi |
| *Providencia stuartii* | Often reinfection and/or health care–associated infection* |
| *Morganella morganii* | Often reinfection and/or health care–associated infection* |
| *Serratia marcescens* | Often health care–associated infection* |
| *Acinetobacter baumannii* | Often health care–associated infection* |
| *Burkholderia* spp | Often health care–associated infection* |
| *Pseudomonas aeruginosa* | Often health care–associated infection* |
| *Stenotrophomonas maltophilia* | Often health care–associated infection* |
| **GRAM-POSITIVE BACTERIA** | |
| *Staphylococcus saprophyticus* | Most common during summer |
| *Staphylococcus aureus* | May indicate focus outside the genitourinary tract |
| *Enterococcus* spp | Often reinfection |
| Other gram-positive bacteria | In most cases contaminants |
| **FUNGI** | |
| *Candida* spp | May indicate focus outside the genitourinary tract |

*Includes hospital and nursing home care.

## Urethral syndrome

- About 1/3 of women with dysuria and frequency have either an insignificant number of bacteria in midstream urine cultures or completely sterile cultures ---previously defined as having urethral syndrome.
- ¼ no pyuria (and little objective evidence of infection)
- ¾ pyuria
  - Low counts($10^2$ to $10^4$/ml) of typical bacterial uropathogens
  - These bacteria are probably the causative agents and associated with pyuria
  - Can be isolated from a suprapubic aspirate
  - Respond to appropriate antimicrobial therapy

## Pathogenesis

- In the vast majority of UTIs, bacteria gain access to the bladder via the urethra.
- Ascent of bacteria from the bladder may follow and is probably the pathway for most pyelonephritis.
- In rare cases, bacteriuria and funguria may result from the hematogenous dissemination of bacteria to the kidneys.
- Hematogenous pyelonephritis occurs most often in debilitated patients who are either chronically ill or receiving immuno-suppresive therapy.
- Primary focus of the infection is usually an infection at a site outside the renal tract, such as endocarditis.

## Pathogenesis(cont.)

- The vaginal introitus and distal urethra are normally colonized by diphtheroids, streptococcal and staphylococcal species, lactobacilli, but not by the enteric G(-) bacilli.
- The factors that predispose to periurethral colonization with G(-) bacilli remain poorly understood.
- Alteration of the normal vaginal flora by antibiotics, other genital infections, or contraceptives (esp. spermicide) appear to play an important role.
- Loss of the normally dominant $H_2O_2$-producing lactobacilli in the vaginal flora appears to facilitate colonization by E.coli.

## Pathogenesis(cont.)

- In the normal male urethra, the distance between the end of the urethra and the bladder is too long to allow ascending transport of bacteria to the bladder.
- Transport is possible when there is a turbulent urine flow (such as with a stricture or obstruction of the urethra, as a result of prostate hyperplasia, and when the patient has a bladder catheter )

## Pathogenesis(cont.)

- The female urethra is short and allows transport of bacteria to the bladder in healthy individuals.
- With many uropathogens, such transport is facilitated by adherence of the bacteria to urethral epithelial cells.
- Sexual intercourse results in increased numbers of bacteria in the periurethral area of the vagina and the distal part of the urethra, increasing the risk of bacteriuria.

## Pathogenesis(cont.)

- When bacteria have reached the bladder, the establishment of bacteriuria is facilitated by incomplete bladder emptying
- Pyelonephritis results from ascending bacteriuria from the bladder through the ureter to the renal pelvis and the renal parenchyma.
- This transport may be facilitated by:
  - host factors such as anatomic defects of the ureters or the kidneys, vesicoureteral reflux
  - adhesion to the ureter mucosa

## Pathogenesis(cont.)

- Whether bladder infection occurs depends on interacting effects of the pathogenicity of the strain, the inoculum size, and the local and systemic host defense mechanism.

## Bacterial Virulence Factors

- Uropathogenic E. Coli:
  - belongs to a small no. of specific O, K and H serogroups.
  - Easy to adherence to uroepithelial cells (fimbriae)
  - After attachment, initiates some important events in epithelial cells(secretion IL6, IL8, induction of apoptosis and epithelial cell desquamation)
  - Secretion hemolysin and aerobactin and are resistant to the bactericidal action of human serum
- These properties are not needed for infection of the compromised urinary tract

## Host factors complicating bacteriuria

| OUTCOME | FACTORS |
|---|---|
| Facilitated establishment and maintenance of bacteriuria | Residual bladder urine after voiding<br>Physiologic<br>Neurogenic bladder<br>Prostate hyperplasia/tumor<br>Turbulent urethral urine flow<br>Strictures<br>Foreign bodies<br>Catheters<br>Calculi<br>Tumors<br>Atrophic vaginal mucosa after menopause<br>Vesicoureteral reflux<br>Anatomic defects<br>Pregnancy |
| Worse prognosis of urinary tract infections involving the kidneys | Childhood pyelonephritis<br>Diabetic nephropathy<br>Malignant hypertension<br>Chronic pyelonephritis |

## Bladder catheterization and UTIs

- Bladder catheterization leads to bacteriuria or funguria in almost all patients who have had their catheters for more than 1 week.
- Formation of a biofilm on the catheter surfaces facilitates the growth of microorganisms.
- Urosepsis, resulting from disssemination of bacteria from the urine to the blood may happen during the removing or changing the catheter.
- The urethral mucosa may also be damaged by crystals that form on the catheter surface.

## Pregnancy and UTIs

- UTIs are detected in 2-8% of pregnant women.
- Asymptomatic bacteriuria frequently harbor organisms that less virulent than those causing symptomatic infections.
- Fully 20-30% of pregnant women with asymptomatic bacteriuria subsequntly develop pyelonephritis.

## Pregnancy and UTIs(cont.)

- The predisposition to upper tract infection during pregnancy results from:
  - Decreased ureteral tone
  - Decreased ureteral peristalsis
  - Temporary incompetence of the vesicoureteral valve
  - Bladder catheterization during or after delivery
- Risk of UTIs during pregnancy
  - Increased incidences of low-birth-weight infants
  - Premature delivery
  - Newborn mortality

## Genetic Factors and UTIs

- Host genetic factors influence susceptibility to UTIs.
- A maternal history of UTI is more often found among women who have experienced recurrent UTIs than among controls.
- The number and type of receptors on uroepithelial cells to which bacteria may attach are at least in part genetically determined.
- Many of these structures are components of blood group antigens and are present on both erythrocytes and uroepithelial cells

## P blood group

- **P blood group system,** classification of human blood based on the presence of any of three substances known as the P, $P_1$, and $P^k$ antigens on the surfaces of red blood cells.
- There are five phenotypes in the P blood group system: $P_1$, $P_2$, $P_1^k$, $P_2^k$, P
  - $P_1$ phenotype --- displays all three P antigens
  - $P_2$ phenotype --- consists of the P and $P^k$ antigens
  - $P_1^k$ phenotype -- $P_1$ and $P^k$ antigens
  - $P_2^k$ phenotype --- $P^k$ antigen only
  - p phenotype --- no antigens

**Extremely uncommon**

## P blood group antigens assigned roles in the pathophysiology of UTIs

- The P blood group antigens are glycan structures , expressed not only on red cells, but also on other tissues, including the urothelium .
- A role for P blood group antigens in the pathogenesis of UTIs is implied by the observation that various uropathogenic strains of *Escherichia coli* express adhesins that bind to the Galα1–4Gal moiety of the $P^k$ and $P_1$ antigens.
- The $P_1$ determinant is expressed on the urothelium of $P_1$ individuals and may facilitate bacterial infection by mediating attachment of bacteria to the lining of the urinary tract

## P blood group antigens assigned roles in the pathophysiology of UTIs (cont.)

- This hypothesis is supported by the observation that $P_1$ phenotype has a higher risk, relative to $P_2$ phenotype, for UTIs and pyelonephritis.
- It is also supported by the observation that adhesion of a pyelonephritic strain of *E. coli* to renal tissue is mediated by a bacterial adhesin specific for the Galα1–4Gal structure and that deficiency of the adhesin severely attenuates the pyelonephritic phenotype of the organism.

## Clinical manifestations

- Cystitis
- Pyelonephritis
- Urosepsis

## Cystitis

- The onset of cystitis is rapid, and symptoms develop over less than 24 hours.
- Patients with cystitis usually report dysuria, frequency, urgency, and suprapubic pain.
- Urine is bloody in ～30% of cases.
- Clinically, it is often impossible to differentiate between cystitis and urethritis caused by chlamydia, ureaplasma, or gonococci.

## Cystitis (cont.)

- Fever is unusual among patients with cystitis.
- In sexually active women, cystitis commonly occurs 24 to 48 hours after intercourse, esp. without post-voiding .
- Cystitis patients normally have symptoms for 3 to 5 days. Antibiotic therapy does not markedly reduce the duration.

## Pyelonephritis

- Pyelonephritis also has a rapid onset, with or without preceding cystitis symptoms.
- The patients are often with the fever and flank pain.
- About 1/3 of patients develop bacteremia.
- The typical flank pain results from inflammation and edema of the renal parenchyma.

## Differential diagnosis of pyelonephritis

- An important differential diagnosis is renal calculi, which may result in a similar location of the pain but characteristically do not cause fever.
- Patients with appendicitis and cholecystitis can present with flank pain similar to that in a patient with right-sided pyelonephritis.
  (urinanalysis can make differential diagnosis)

## Urosepsis

- Urosepsis is a life-threatening condition caused by dissemination of bacteria from the urine in a patient with bacteriuria.
- The most common reason for urosepsis is withdrawal (and sometimes insertion) of a bladder catheter.
- Therefore, uroseptic patients do not always have a renal infection.

## Clinical symptoms of UTIs

| TYPE OF URINARY TRACT INFECTION | TYPICAL SYMPTOMS |
|---|---|
| Cystitis | Frequent voiding<br>Burning during and after voiding<br>Suprapubic pain<br>Hematuria and/or cloudy urine |
| Pyelonephritis | Fever<br>Chills<br>Flank pains<br>Cystitis symptoms (may be absent) |
| Urosepsis | Fever<br>Chills<br>Septic shock |

## Diagnosis

- Laboratory findings
- Imaging
- Differetial diagnosis

## Urinanalysis

- Pyuria should be demonstrated in patients with acute UTIs, and its absence calls the diagnosis into question.
- Tested in 3 ways:
  - Best done by staining uncentrifuged urine and counting leukocytes in a Bürker chamber.
  - The second best technique is to use a leukocytes esterase stick test, which is highly sensitive and allows a crude quantification of pyuria.
  - The technique of counting leukocytes in the sediment obtained after centrifugation was once used routinely, but it is impresice and is not recommended.

## Urine culture

- The ways to get the urine sample:
  - The most reliable result is obtained if the sample is taken by suprapubic aspiration
    (frequentlu used in infants but rarely in older children and adults)
  - Sampling by bladder catheterization
    (carries about a 2% risk of introducing bacteria into the bladder and subsequently causing bacteriuria)
  - To collect a midstream urine sample
    (requires the patient to be well informed about the sampling procedure)

## Correct sampling procedure

- Men should withdraw the foreskin, and women should keep the labia apart.
- Washing of the genital tract before sampling is not recommended.
- During voiding, the first and last parts of the urine should not be sampled.
- After sampling, the urine should be chilled (but not frozen) to prevent growth during transportation to the lab.

## A nitrite test can be used for screening of bacteriuria

- It's a stick test that demonstrates the presence of nitrite in the urine.
- G(-) bacteria, with the exception of P. aeruginosa, metabolize nitrate to nitrite, which can be demonstrated by a color reaction on a paper stick.
- G(+) bacteria and fungi do not metabolize nitrate.
- The technique is rapid (<1 min) and inexpensive.
- It has a high degree of specificity but is rather insensitive
- It is not suitable for use in patients with recurrent infections (enterococal is common).

## The result of the culture

- Bacteria are usually present in the urine in large number ($10^5$/ml).
- Samples of urine from the ureters or renal pelvis may contain< $10^5$/ml bacteria and yet indicate infection.
- The presence of bacteriuria of any degree in suprapubic aspirates or of $10^2$/ml bacteria of urine obtained by catheterization usually indicates infection.
- In some circumstances (antibiotic treatment, high urea conc. High osmolarity, low PH), urine inhibits bacterial multiplication, resulting in relatively low bacterial colony counts despite infection.

## Pyuria in the absence of bacteriuria

- Sterile pyuria may indicate:
  - Infection with unusual bacterial agents, such as mycobacterium tuberculosis.
    (the urine sample should be obtained for direct microscopy and culture for mycobacterium tuberculosis)
  - May be demonstrated in noninfectious urologic conditions, such as interstitial nephritis, polysystic disease, SLE, nephrocalcinosis.

## Blood culture in diagnosis

- Blood cultures should be obtained in all patients with suspected pyelonephritis or urosepsis.
- It is recommended that at least two cultures be obtained.

## Image

- Radiography and ultrasound examination are not helpful in the acute pyelonephritis unless there is suspicion of a blockage of the urine flow.
- When the patient has recovered, such investigations are recommended in those with recurrent infections to exclude complicating factors.
- pyelography or ultrasound examination is enough.
- For the diagnosis of vesicoureteral reflux, special radiographic techniques are used.

## Differential diagnosis
(acute pyelonephritis and cystitis)

- Patients with acute pyelonephritis, have increased levels of C-reactive protein in blood.
- The erythrocyte sedimentation rate is less helpful, because it takes several days to increase in acute pyelonephritis.
- In patients with acute pyelonephritis, leukocyte casts can often be demonstrated in urine sediment.

## Differential diagnosis (cont.)
(acute pyelonephritis and cystitis)

- When a patient has become afebrile, the diagnosis of acute pyelonephritis can be supported by testing urine osmolality, which is markedly reduced for at least 1 month after the onset of symptoms.
- Demonstration of antibody-coated bacteria in the urine is neither sensitive nor specific and is no longer recommended.

## Treatment of UTIs

- All symptomatic UTIs should be treated.
- The purpose of early treatment of cystitis is to reduce the risk of progression to pyelonephritis.
- In patients with pyelonephritis, early treatment is important to:
  - reduce the duration of symptoms,
  - eliminate microorganisms from the renal parenchyma,
  - reduce the risk of dissemination to the blood

## The principles of UTIs treatment

- Drink more water to promote the elimination of bacteria and inflammatory secretions from the urine.
- Factors predisposing to infection should be identified and corrected
- Urine culture is important not only to the diagnosis, but also to the treatment (direct therapy ) as well.
- Relilef of clinical symptoms does not always indicate bacteriologic cure
- In general, uncomplicated infections confined to the lower urinary tract respond to short courses of therapy (3-5days), while upper tract infection required longer treatment (14 dalys).

## The principles of UTIs treatment(cont.)

- If common antibiotics are ineffective, the following microorganisms should be considered:
  - Resistant bacteria
  - Unusual microorganisms, including anaerobic bacteria, mycobacterium tuberculosis, L bacterium, mycoplasma

## Antibiotics used to treat cystitis

| ANTIMICROBIAL | DOSE* AND DURATION |
|---|---|
| Trimethoprim | 100-150 mg q12h for 3 days |
| Trimethoprim/sulfamethoxazole | 80/400 mg q12h for 3 days or 320/1600 mg single dose |
| Nitrofurantoin | 50 mg q8h for 5-7 days |
| Amoxicillin/clavulanic acid | 250 mg (amoxicillin dose) q8h for 5-7 days |
| Cefuroxime axetil | 250 mg q8h for 5-7 days |
| Cefpodoxime proxetil | 200 mg q8h for 5-7 days |
| Cefixime | 400 mg/day for 5-7 days |
| Ceftibuten | 400 mg/day for 5-7 days |
| Cefprozil | 250 mg/day for 5-7 days |
| Norfloxacin† | 200 mg q12h for 7 days |
| Ciprofloxacin† | 100 mg q12h for 7 days |
| Levofloxacin† | 250 mg/day for 7 days |
| Fosfomycin | 400 mg single dose |

*Doses given are for adults with normal renal function. The need to reduce dosages because of renal impairment related to infection in the kidneys, other renal diseases, or advanced age should always be considered.
†Should be reserved for recurrent and/or complicated cystitis.

## Antibiotics used to treat pyelonephrits

| ROUTE OF ADMINISTRATION AND ANTIMICROBIAL | DOSE* | COMMENTS |
|---|---|---|
| INJECTABLE | | |
| Cefepime | 2 g q12h | Health care–associated infections† |
| Cefotaxime | 1 g q12h | Community-acquired infections |
| Ceftazidime | 1 g q12h | Health care–associated infections† |
| Ceftriaxone | 2 g/day | Community-acquired infections |
| Cefuroxime | 750 mg q8h | Community-acquired infections |
| Amikacin | 15 mg/kg/day | Monitor renal function |
| Gentamicin | 4.5 mg/kg/day | Monitor renal function |
| Netilmicin | 4.5 mg/kg/day | Monitor renal function |
| Tobramycin | 4.5 mg/kg/day | Monitor renal function |
| Ciprofloxacin | 200 mg q12h | |
| Levofloxacin | 250 mg/day | |
| Trimethoprim/sulfamethoxazole | 160/800 mg q12h | Community-acquired infections |

## Antibiotics used to treat pyelonephrits

| ROUTE OF ADMINISTRATION AND ANTIMICROBIAL | DOSE* | COMMENTS |
|---|---|---|
| ORAL | | |
| Amoxicillin/clavulanic acid | 500 mg (amoxicillin dose) q8h | Only step-down therapy |
| Cefuroxime axetil | 250 mg q12h | Only step-down therapy |
| Cefpodoxime proxetil | 200 mg q8h | Only step-down therapy |
| Cefixime | 400 mg/day | Only step-down therapy |
| Ceftibuten | 400 mg/day | Only step-down therapy |
| Cefprozil | 250 mg/day | Only step-down therapy |
| Norfloxacin | 400 mg q12h | |
| Ciprofloxacin | 100 mg q12h | |
| Levofloxacin | 250 mg/day | |

## Treatment of bacteriuria

- Bacteriuria in patients with catheters should not be treated unless the patient is febrile or has other evidence of systemic infection.
- Administration of antibiotics to catheterizaed patients with asymptomatic bacteriuria inevitably results in multi-resistant and difficult-to-treat organisms

## Treatment of urosepsis

- In patients with suspected urosepsis, antibiotic treatment must start as early as possible.
- Antibiotis should be given intravenously.
- Previous antibiotic treatment should always be ascertained, because such treatment may have resulted in resistant organisms.

## Treatment of funguria

- Funguria can be treated with fluconazole 400 mg once daily for 1 day, followed by 200 mg once daily for 7 to 14 days.
- Funguria in catheterized patients should be treated only when there is a symptomatic UTI.

## Follow-up

- Patients with sporadic, uncomplicated cystitis do not require follow-up.
- Patients with symptomatic recurrences, pyelonephritis, or complicated UTI should be observed.
- Follow-up cultures are important because bacteriuria may persist and cause renal damage in afebrile pyelonephritis patients.

## Follow-up procedures in patients with UTIs other than sporadic cystitis

| PROCEDURE | RECOMMENDATION |
|---|---|
| Urine culture | All patients with pyelonephritis, complicated infections, or frequent recurrences; 4-5 days and 3-4 wk after treatment |
| Pyuria test | Always perform together with urine culture |
| C-reactive protein | 4-5 days and 3-4 wk after treatment of pyelonephritis |
| Radiography or ultrasonography | After pyelonephritis to exclude scars from childhood infections in patients with recurrent infections and to exclude complications |
| Serum creatinine | Before treatment in elderly; 3-4 wk after treatment in patients with pyelonephritis |
| Urine osmolality | Verification of suspected pyelonephritis |

## Decision process for upper(pyelonephritis) and lower(cystitis) urinary tract infections

| | CYSTITIS | PYELONEPHRITIS |
|---|---|---|
| SIGNS AND SYMPTOMS | | |
| Fever | No | Yes |
| Dysuria | Yes | May be present |
| Frequency | Yes | May be present |
| Flank pain | No | Yes |
| DIAGNOSIS | | |
| Pyuria | Yes | Yes |
| Nitrite test | Normally positive | Normally positive |
| Bacteriuria | Yes | Yes |
| C-reactive protein | Normal | Increased |
| Blood cultures | Negative | Positive in ≈30% |

## Decision process for upper(pyelonephritis) and lower(cystitis) urinary tract infections

| | CYSTITIS | PYELONEPHRITIS |
|---|---|---|
| TREATMENT | | |
| First line | Trimethoprim or trimethoprim-sulfamethoxazole for 3 days | Fluoroquinolone or trimethoprim-sulfamethoxazole for 2 wk orally |
| Second line | Fluoroquinolone for 3 days or cephalosporin for 5-7 days | Injectable cephalosporin until afebrile, followed by oral step-down for total of 2 wk |
| Pregnant women | Nitrofurantoin or cephalosporin for 5-7 days | Injectable cephalosporin until afebrile, followed by oral cephalosporin for 2 wk |

## Prevention

- The most important is for sexually active women to urinate shortly after sexual intercourse.
- Another usefule suggestion is for patients with recurrent UTIs to practice double or triple voiding.
- Increased fluid intake was previously advocated, probably because of the risk of crystalluria with old-sulfonamides; there are no obvious benefits of excessive diuresis.

## Prevention (cont.)

- Cranberry products have been proposed for the prevention of recurrent UTIs. Analyses of studies suggest that these products might have a low preventive effect in young and middle-aged women, but the use of cranberries is not recommended.
- In postmenopausal women with atrophic vaginal mucosa and recurrent symptomatic UTIs, replacement therapy with oral or vaginal estriol should be considered.

## Antimicrobial prophylaxis

- Prophylaxis is sometimes used in patients with frequently recurring UTIs, esp. when there are no defined, treatable complications.
- In such patients, one daily dose of nitrofurantoin 50-100mg, taken at bedtime, is recommended.
- Antimicrobial prophylaxis should not be used in catheterized patients because it results in the selection of micrbes resistant to the antimicrobial used.

## Prognosis

- The prognosis of uncomplicated cystitis and pyelonephritis is generally good unless urosepsis occurs. Secondary morbidity is rare.
- Patients with urosepsis have a poor prognosis, with fatality rates of about 30% or higher. Factors increasing the risk of death are advanced age and underlying diseases, as well as inadequate antibiotic treatment.

## Prognosis(cont.)

- In patients with complications such as renal scars from childhood pyelonephritis, chronic pyelonephritis or glomerulonephritis, or other chronic renal diseases, acute pyelonephritis may lead to a further reduction of renal function.
- Infections with Proteus species or other ammonia-producing organisms may lead to the formation of calculi or the worsening of existing ones.


Thanks for your attention!