Urinary tract infection (UTI) defines a condition in which the urinary tract is infected with a pathogen causing inflammation. Infection of the urinary tract is a common, distressing, and occasionally life-threatening condition. The clinical features, diagnosis, treatment, complications, and long term significance vary depending on the site of infection and the presence or absence of structural and functional abnormality within the system.

UTI is one of the most common diseases, occurring from the neonate up to the geriatric age group. Forty to fifty per cent of adult women have a history of at least one episode of UTI.

Definitions

Bacteriuria

It may be defined as the condition in which bacteria are established and multiplying within the urinary tract. Demonstration of bacteria is required for the diagnosis, but in some conditions like pyogenic abscess of kidney and perinephric tissues, obstructed pyonephrosis, or bacterial prostatitis, urine may be sterile. “Significant bacteriuria” is defined as the presence of $10^5$ or more of the same organism per ml of urine. If two urine samples have $10^5$ or more bacteria per ml, a diagnosis of bladder bacteriuria is 95% likely. In symptomatic women, it has a specificity of 99% and accuracy is enhanced by presence of pyuria, defined as more than 10 WBC per mm$^3$ of unspun urine.

Low count bacteriuria

Only one - half of symptomatic women will have $\geq 10^5$ CFU/ml. Low count ($10^2 - 10^4$ CFU/ml) bacteriuria might be an early or transitional phase. It is also explained by high fluid intake and infection by slowly growing organisms like $S. saprophyticus$. The clinical significance of low-count bacteriuria should never be under-estimated particularly in men, in whom contamination is uncommon.

Asymptomatic bacteriuria

It is frequently detected during routine investigations. Bacterial counts of $\geq 10^6$ CFU/ml in two consecutive clean-catch urine samples, permit to differentiate between asymptomatic UTI and contamination ($< 10^6$ CFU/ml). A lower cut-off level of $\geq 10^4$ CFU/ml is accepted in case of infection with $S. saprophyticus$ and Candida. It is extremely rare in children, increases with age in women and common in elderly males. One-third of patients on haemodialysis will have asymptomatic bacteriuria and leukocyturia. Additional clinical information is needed before deciding the treatment. Asymptomatic bacteriuria should not be treated except in pregnancy. Haemodialysis patients evaluated for renal transplantation should be given prophylaxis when they undergo invasive urological diagnostic procedures. Diabetic and immunocompromised patients should be frequently monitored before treatment.

Contamination

Contamination is likely when small numbers of bacteria or several bacterial species grow in urinary cultures. ‘True infection’ can be confirmed by urethral catheterisation or suprapubic aspiration. True polymicrobial infection is rare, except in patients with ileal conduit, neurogenic bladder, or vesico-colic fistula, and in patients with UTI complicated by stones, chronic renal abscesses, or long term indwelling urinary catheters. Polymicrobial infection should be interpreted cautiously.

Lower Vs upper UTI

Differentiation between lower and upper UTI is essential as they differ in their management and
prognosis. Patients with lower UTI are afebrile and
do not have elevation in acute phase reactants
whereas those with upper UTI are febrile and
develop leucocytosis and increased C-reactive
protein. Both invasive and non-invasive methods
to diagnose UTI may help to differentiate but in
clinical practice monitoring of bacteriuria may help
retrospectively. If bacteriuria disappears after one
day or short-term (3 days) treatment, the diagnosis
of lower UTI is likely.

Symptomatic abacteriuria
Bacterial infection with low counts of uropathogens
may present as the so called ‘urethral syndrome’.
Aetiology includes - renal abscess formation
without drainage into urinary tract, complete
ureteral obstruction, urinary tract tuberculosis,
chistosomiasis, antimiicrobial or antiseptic use,
infections with Chlamydia, Mycoplasma,
Trichomonas, Gonococci, or Candida and some-
times urological bladder problems like tumours.

Complicated Vs uncomplicated UTI
Complicated UTI implies infections of urinary
tracts, which are anatomically and functionally
altered, whereas uncomplicated UTI occurs in
otherwise healthy women with structurally normal
urinary tract and intact voiding mechanisms.
Factors complicating UTI are given in Table 1.
These complicating factors put individuals of both
genders at a higher risk of developing progressive
renal damage, bacteraemia, and urosepsis.

Acute and chronic pyelonephritis
It presents as low pain, fever with chills and rigors,
flank tenderness, and associated symptoms like
anorexia, nausea, vomiting, and generalised
myalgias; and involves one or both the kidneys.
Many patients give a history of cystitis within the
previous six months. Chronic pyelonephritis is a
radiological diagnosis based on the demonstration
of clubbed calyces associated with focal or diffuse
renal scarring. It develops as a result of infection
and VUR usually by the age of 4 years and many
adults are asymptomatic and abacteriuric and
present with hypertension or renal failure.

### Table I : Factors complicating UTI.

<table>
<thead>
<tr>
<th>Disorders of urine transport :</th>
</tr>
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<tbody>
<tr>
<td>Anatomical</td>
</tr>
<tr>
<td>Neurogenic</td>
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</table>

| Associated diseases :           |
| Polycystic kidney diseases      |
| Analgesic abuse                 |
| Sickle-cell anaemia             |
| Immunosuppression               |

| Miscellaneous :                |
| Diabetes mellitus              |
| Pregnancy                      |
| Prostatitis                    |
| Indwelling urinary catheter     |

Recurrent infection
It is of two types – re-infection and relapse.
Occurrence of bacteriuria with the same organism
within three weeks of completing treatment, which,
during treatment, rendered the urine sterile, is
termed as ‘relapse’. It can be diagnosed by urine
culture done before, during and between 10 and
21 days after treatment or on recurrence of
symptoms. Relapse indicates failure to eradicate,
which, most often occurs in association with renal
scars, stones, cystic diseases, or prostatitis, in
patients with chronic interstitial nephritis or in those
who are immunocompromised.

Re-infection is defined as eradication of bacteriuria
by appropriate treatment, followed by infection
with a different organism after 7 to 10 days. Re-
infection with the same organism is unlikely if the
patient has remained abacteriuric for 21 days.
‘Treatment failure’ may be used to describe failure
to eradicate bacteriuria during treatment, failure
to prevent relapse or re-infection.

Pathogenesis
Uropathogens are part of the normal faecal flora.
They colonise the peri-anal area and then around,
in females, the introitus which is a reservoir of
several pathogens. Colonisation spreads to the
peri-urethral area, urethra, and bladder–facilitated
by short urethra in females, turbulence while
voiding and sexual intercourse, increased vaginal pH (> 5) and oestrogen deficiency in postmenopausal females.

*E. coli* are the most common (90%) organisms infecting the urinary tract followed by *S. saprophyticus*. Proteus species affects males particularly the young boys due to colonisation of the preputial sac. Sporadic hospital acquired UTIs are caused by Gram-negative organisms like *Citrobacter*, *Serratia*, *Providentia*, *Gardenerella vaginalis*, *Haemophilus spp*, *Acenatobacter*, *Branhamella*, and Gram-positive uropathogens like *Enterococcus fecalis* and *Staphylococcus epidermidis*, and a variety of yeasts like *Candida albicans* and fungi. Cross infection in catheterised patients can occur due to *Pseudomonas*, *Klebsiella*, and *Serratia*. Stone formation is particularly associated with infection with urease producing organism like *Proteus* species and others like *Pseudomonas*, *Klebsiella*, and *Staph. saprophyticus* and rarely *Ureaplasma urealyticum*.

Various factors serve to make the urinary tract susceptible to infection. These susceptibility factors are given in table II. But in many cases more than one of these can be identified.

**Table II : Host susceptibility factors.**

<table>
<thead>
<tr>
<th>Secretor status</th>
<th>Residual urine</th>
<th>Outflow obstruction</th>
<th>Vesico-ureteric reflux</th>
<th>Calculi</th>
<th>Structural abnormalities</th>
<th>Pregnancy</th>
<th>Diabetes mellitus</th>
<th>Instrumentation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Congenital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Acquired</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

A variety of defense mechanisms (table III) in the urinary tract protect against microbial invasion. Besides these host responses, including hypersensitivity reactions, autoimmune mechanisms may also contribute to renal damage.

**Table III : Defense mechanisms of the urinary tract.**

<table>
<thead>
<tr>
<th>Non-specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal flora of the vagina</td>
</tr>
<tr>
<td>Flushing effect of urine flow and voiding</td>
</tr>
<tr>
<td>Bladder glycocalyx</td>
</tr>
<tr>
<td>Tamm-Horsfall glycoprotein</td>
</tr>
<tr>
<td>Endotoxin induced shedding of bladder epithelial cells</td>
</tr>
<tr>
<td>Phagocytosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretary IgA</td>
</tr>
<tr>
<td>Circulating IgM, IgG</td>
</tr>
</tbody>
</table>

The balance between the defense system of urinary tract and the virulence of the pathogen determines the frequency and severity of UTI. Virulence factors for *E. coli* and *Proteus mirabilis* are well established. *P. fimbriae*—"pyelonephritis associated pili", attach to the epithelial receptors of urogenital tract and ascend from the bladder upto the kidney. Other factors include synthesis of aerobactin, enterobactin and haemolysin. K-antigen rich *E. coli* are relatively resistant to destruction by complement system. *Staphylococci* display strongest ability to attach and invade uroepithelium. IL-6 are found elevated in women with acute pyelonephritis and decreased in pregnant women predisposing them for UTI.

**Diagnostic workup**

**Urine microscopy**

The presence of 1-10 organisms per microscope field is an evidence of more than $10^5$ CFU/ml. A leucocyte excretion rate of $> 4 \times 10^5$ leucocytes/hr. correlates with symptomatic UTI which is equivalent to a leucocyte count of $> 10$ per mm$^3$. Hence “pyuria” is defined as more than 10 leucocytes/mm$^3$.

**Dipstick test**

It is an accepted screening test for UTI. Chemical test strips operate by detection of leucocyte esterase and a nitrate reductase activity. A negative dipstick test is usually sufficient to exclude UTI.
Enterobacteriaceae convert nitrate to nitrite in urine, which will be detected by 'nitrite test'. Several other uropathogens do not reduce nitrate to nitrite and this test is of no value. A urine pH of $\geq 7.5$ suggests UTI. Some foodstuffs containing nitrate/nitrite can give a false positive test.

Imaging

A diagnosis of lower or upper UTI based on clinical signs and symptoms may be inaccurate sometimes and significant proportion of those with bladder symptoms had upper UTI. Radiological imaging should be performed in all those with suspected upper UTI. Ultrasound is the method of choice especially in emergency conditions and when normal, does not necessarily rule out renal involvement.

Plain abdominal radiographs, and if required, intravenous urography can be performed. Uroflometry and cystometry should be performed in patients with outflow obstruction, stress incontinence, and urge incontinence. An accurate and cost-effective method for detecting renal scarring is renal scintigraphy with ($99 \text{ m Tc}$) dimercaptosuccinic acid (DMSA). It has 10-fold high sensitivity than ultrasonography in detecting cortical changes. SPECT scanning is superior in detecting renal lesions.

CT Scanning is the most precise method to detect
renal parenchymal infection but nephrotoxicity of contrast material is a problem. Non-contrast study is of limited value. It is more sensitive than sonography in detecting lesions of below 2 cm in diameter.

**MCU**

It is the method of choice for the diagnosis of vesico-ureteric-reflux (VUR). It is recommended in infants, children of less than 7 year of age and all children who have UTI with systemic signs of infection. It is rarely necessary in adults with UTI, though VUR appears more common in adults. Renal transplant recipients with recurrent or chronic UTI should undergo MCU as VUR adversely affects graft outcome.

**Cystoscopy**

In patients with recurrent UTI, cystoscopy should be performed to exclude bladder pathology and to detect urethral narrowing – especially in elderly males, to detect bladder cancer.

**Management**

All symptomatic patients with UTI should receive antimicrobial therapy, but the duration of treatment varies. The algorithm for the approach to the management of asymptomatic and symptomatic UTI is given in figures 1 and 2.

**Uncomplicated UTI**

In women with uncomplicated lower UTI, 3-day empirical therapy is effective and sufficient. In those with frequent attacks, 80% of patients can be cured by 7-10 days of therapy and almost all by three weeks. In case of treatment failure, fluoroquinolones are indicated and oral cephalosporins are an effective alternative.

**Asymptomatic bacteriuria**

It is still controversial and there is no concensus on indications for treatment (Fig. 3). However, children and pregnant women should be treated. Bed-ridden elderly patients may be considered because of the risk of urosepsis.

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**Fig. 2 : Management of symptomatic UTI in adults.**

**Recurrent UTI**

In case of recurrent UTI, non-drug management (Table IV) should be advised to the patient. As the recurrent rates are greater after shorter periods of prophylaxis, administration of drugs (Table V) should be continued for 6-12 months in case of frequent, symptomatic recurrences.

**Table IV : Non-drug management.**

- Increased fluid intake
- Void at 2-3 hr. intervals
- Void at bed time and after coitus
- Avoid diaphragm or spermicide use
- Avoid diapers
- Intra-vaginal application of lactobacilli
- Intra-vaginal oestrogen application in postmenopausal women.
Table V: Prophylaxis for recurrent acute uncomplicated UTI.

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose (mg)</th>
<th>frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-trimoxazole</td>
<td>40/200</td>
<td>OD</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>40/200</td>
<td>Twice weekly</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>100</td>
<td>OD</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>250</td>
<td>OD</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>125/or 250</td>
<td>OD</td>
</tr>
<tr>
<td>*Norfloxacin</td>
<td>200 mg</td>
<td>OD</td>
</tr>
</tbody>
</table>

*Quinolones are better avoided in pregnancy.

Complicated UTI

The presence of complicated UTI should be suspected if bacteraemia does not resolve or if clinical signs and symptoms persist over 48 hours of antibiotic therapy (Table VI). Fluoroquinolones are especially useful in the outpatient management of complicated UTI. If admission is required, parenteral drugs are preferable which can be changed to oral therapy later on. The approach to management of UTI, both complicated and uncomplicated is given in Figure 4.

The renal transplant recipient

UTI is the most common form of bacterial infection in this group of patients. If unrecognised, it adversely affects the graft function. UTI may be completely painless in transplanted patients. UTI may provoke rejection episodes and can be complicated by papillary necrosis especially in the early post transplant period. Beyond this high-risk period, UTI is supposed to be more benign. These patients should be treated for 4-6 weeks by oral antibiotics within the first 3 months after transplantation and for 10-14 days later on. Recurrence or relapse should be thoroughly evaluated.

Pregnancy

In 25% of pregnant patients with asymptomatic bacteriuria, symptomatic upper UTI develops. Symptomatic UTI increases maternal and foetal mortality and morbidity. Treatment for at least 7 days is recommended with oral drugs that are safe in pregnancy. Symptomatic upper UTI should be treated with intravenous antibiotics.
Table VI: Drug regimens for the treatment of complicated UTI.

**Oral:**
- Ciprofloxacin 500 q12h
- Levofoxacin 200-500 q 24h
- Oflofoxacin 200-300 q 12h
- Co-trimoxazole 160/800 q 12h
- Cefpodoxime 200 q 12h
- Cefixime 400 q 12h
- Ampicillin 500 q 8h

**Parenteral:**
- Ceftriaxone 1000-2000 q 24h
- Cefepime 1000-2000 q 12h
- Ciprofloxacin 200-400 q 12h
- Levofoxacin 250-500 q 24h
- Gentamicin 3-5mg/kg q 24h
  (+ Ampicillin) or 1mg/kg q 8h
- Ampicillin + Gentamicin 1000 q 6h
- Ampicillin + Sulbactam 1500 q 6h
- Ticarcillin + Clavulanic acid 3200 q 8h
- Piperacillin + Tazobactam 3375 q 6-8h
- Imipenem + Ciclastatin 250-500 q 6-8h

(Dose of all the drugs in mgs.)

**Diabetes**

The prevalence of asymptomatic bacteriuria in diabetes mellitus is high, especially in diabetic women. Uncomplicated UTI should be treated for at least 10 days, and for 3 weeks in case of diabetic renal transplant recipients. A potentially life threatening complication of upper UTI is “Emphysematous pyelonephritis” and needs prompt diagnosis and early treatment.

**References**