Urinary tract infection in women

W R Cattell, MD, FRCP, FRCPA, Consultant Physician and Nephrologist, Harley Street, London

Urinary tract infection (UTI) is a major health problem, a cause both of considerable morbidity among women and of expense to the National Health Service. Most often an isolated event, it becomes recurrent in 10–20% of women and, in a small but significant number, life-threatening. All aspects of UTI have been recently reviewed, this brief synopsis is confined to its management in women.

Key Points

**ISOLATED ATTACK OF CYSTITIS IN A WOMAN:**

- Can be confirmed by a bacterial count of >100 organisms/ml if pyuria is present
- Can be treated without bacterial confirmation if dipstick test for pyuria is positive
- Does not require follow-up or imaging if cured symptomatically

**RECURRENT CYSTITIS IN A WOMAN:**

- Renal imaging: IVU is still the definitive test
- If the urinary tract is normal, should be treated with three-day courses of antibacterials
- Should be treated with an antibacterial which eliminates introital colonisation

**CYSTITIS IN PREGNANCY:**

- Trimethoprim and co-trimoxazole should be avoided in the first trimester
- Fluoroquinolones such as ciprofloxacin are contraindicated
- Nitrofurantoin and cephalosporins are suitable

**IN ACUTE PYELONEPHRITIS:**

- Initial treatment should be in hospital if vomiting
- The same drugs are used as in cystitis but for 10–14 days
- In the presence of vomiting, gentamicin is a reasonable first choice
Diagnosis

UTI usually presents with acute urinary frequency and dysuria (cystitis). Until quite recently the criterion of diagnosis was 100,000 organisms/ml of urine or more in a clean-catch mid-stream sample, but up to 50% of symptomatic young women have a lower bacterial count. It is now accepted that in such women diagnosis can be based on at least 100 organisms/ml of urine plus pyuria (≥ 10 white blood cells/mm³ of unspun urine)². Current criteria for the diagnosis of UTI are given in Table 1.

Investigations

Definitive diagnosis of UTI requires demonstration of bacteriuria, but the indiscriminate despatch of urine samples to the laboratory is expensive. Treatment for acute cystitis is usually started at once, before laboratory results are available. It is now agreed that pre-treatment urine culture in isolated cystitis is unnecessary, especially if a leukocyte esterase dipstick test for pyuria is positive³. Post-treatment urine culture is also unnecessary if the patient becomes asymptomatic and dipstick tests for protein, blood and leukocyte esterase are negative. Urine cultures must be obtained:
- in pregnant women and diabetics
- if presentation is atypical
- if attacks are recurrent
- if there is no response to treatment.

Recognition of low-count bacteriuria can present problems for many laboratories where routine culture methods cannot identify counts less than 1,000 organisms/ml. When this problem is suspected it must either be discussed with the laboratory or urine be obtained by suprapubic aspiration (SPA).

Renal imaging is not required for patients with an isolated attack of UTI except when there is severe pyelonephritis. It is indicated in those with recurrent attacks to identify factors predisposing to infection or likely to complicate its management. Plain abdominal x-rays plus

Table 1. Criteria for diagnosis of bacteriuria.

| Syndrome                  | Modifying factors       | Empirical treatment                                      |
|---------------------------|-------------------------|----------------------------------------------------------|
| Symptomatic young women   |                         | 3 day course of:                                          |
|                           | (a) none                | - trimethoprim 200 mg bd                                 |
|                           |                         | - co-trimoxazole 160/800 mg bd                           |
|                           |                         | - amoxycillin 250 mg qds                                 |
|                           |                         | - nitrofurantoin 100 mg tds                              |
|                           |                         | - cephalexin 250 mg tds                                  |
|                           | (b) symptoms >7 days    | 7 day course of same drugs as for 1(a)                    |
|                           | (c) pregnancy           | 7 day course of:                                          |
|                           |                         | - amoxycillin 250 mg qds                                 |
|                           |                         | - nitrofurantoin 100 mg tds                              |
|                           |                         | - cephalexin 250 mg tds                                  |
|                           |                         | - trimethoprim 200 mg bd (after first trimester)         |
| Asymptomatic patients:    |                         |                                                          |
|                           | (a) mild-moderate       | 10–14 day course of:                                     |
|                           | pyelonephritis          | - trimethoprim in doses as for 1(a)                      |
|                           |                         | - co-trimoxazole in doses as for 1(a)                    |
|                           |                         | - amoxycillin in doses as for 1(a)                       |
|                           |                         | - ciprofloxacin 250 mg bd                                |
|                           | (b) severe with vomiting| Hospitalise. Parenteral treatment until afebrile with:   |
|                           |                         | - gentamicin 1 mg/kg 8 hourly +                         |
|                           |                         | - amoxycillin 500 mg 6 hourly                            |
|                           |                         | - trimethoprim 200 mg bd                                 |
|                           |                         | - cefuroxime 750 mg 12 hourly                            |
|                           |                         | - ciprofloxacin 200 mg 12 hourly                         |
|                           |                         | Continue as 2(a) for 14 days                             |
|                           | (c) pregnancy           | As for 2(b) but avoid:                                  |
|                           |                         | - gentamicin                                           |
|                           |                         | - ciprofloxacin                                        |
|                           |                         | - trimethoprim in first trimester                      |
| Complicated UTI           | (a) mild-moderate       | As for 2(a)                                             |
|                           | no vomiting             |                                                          |
|                           | (b) severe with vomiting| As for 2(b)                                             |
tomography, combined with ultrasonography, can identify most renal stones, upper urinary tract obstructions and renal scars, as well as assessing bladder emptying. More accurate identification of renal scars is achieved by DMSA scanning. None of these methods can define calyceal detail or ureteric anatomy, which is required to exclude papillary necrosis or medullary sponge kidney and which can affect the course and management of recurrent UTI. Intravenous urography remains the investigation of choice for clear definition of urinary tract anatomy.

**Prevention**

Successful prevention of recurrent infection, without the long-term use of antibiotics, remains an elusive goal. Infection is by the ascending transurethral route and is preceded by heavy colonisation of the vaginal introitus and periurethral area with uropathogenic bacteria from the gut. Colonisation is facilitated by many factors beyond our control, including the female anatomy, adherence and virulence characteristics of the bacteria, and blood group secretor status. It is also facilitated by the use of the diaphragm (and possibly the cap) plus a spermicidal foam or gel and by vaginal changes due to oestrogen deficiency in post-menopausal women. These problems can be addressed in women with recurrent infection by change of contraceptive measures and the use of topical oestrogen cream, respectively.

Once colonisation is established, failure to eradicate it by the antibiotic used to treat the infection in the urine results in early reinfection. Eradication requires the use of antibiotics excreted in vaginal secretions. Trimethoprim and the fluoroquinolones are effective, but not amoxycillin, nitrofurantoin or the cephalosporins.

Other risk factors include sexual activity and delayed or incomplete bladder emptying, especially after intercourse. Celibacy is not a satisfactory treatment strategy, but bladder voiding after coitus is to be encouraged. Impaired bladder emptying requires urological assessment and, if possible, treatment.

**Treatment**

Regimens must be tailored to the particular presentation of UTI (Table 2). Complicated UTIs are defined as those in patients with anatomically or functionally abnormal urinary tracts or with associated conditions such as diabetes, analgesic nephropathy or immunosuppression. Table 2 gives a choice of drugs to be given empirically, but the drug chosen will depend on known resistance patterns in the community and may have to be changed when sensitivity results are available. Nitrofurantoin should always be prescribed in the macro-crystalline formulation (Macrodantin).

Single-dose therapy for acute uncomplicated cystitis of recent onset has been enthusiastically promoted, but has never received widespread support. Meta-analyses of large numbers of studies conclude that single-dose therapy is not as effective as three or more days' treatment with conventional oral antibiotics. It is clear, however, that a three-day treatment with commonly used drugs (nitrofurantoin, amoxycillin, co-trimoxazole (trimethoprim + sulphamethoxazole) and cephalaxin) is as effective as 7–10 days' treatment, and is associated with better compliance, fewer adverse effects and lower cost. Co-trimoxazole has been shown to be the most effective and cheapest, probably because of its ability to eliminate *Escherichia coli* colonisation of the rectum, vagina and urethra. It is probable, but not proven, that trimethoprim alone would be equally effective. Fluoroquinolones are as effective as co-trimoxazole, but should not be used as first-line drugs for cystitis since drug resistance emerges rapidly in the community.

**Recurrent urinary tract infection**

Reurrence of infection is usually due to reinfection. In 15% or fewer it is due to relapse – that is, failure to eradicate the initial organism which reappears, typically within two weeks. Reasons for this (eg stones, papillary necrosis, vesico-ureteric reflux) must

---

**Figure 1. Alternative treatment strategies for recurrent urinary reinfection. Prophylaxis drug doses: co-trimoxazole: 80 mg/400 mg; trimethoprim: 100 mg; nitrofurantoin: 50–100 mg; cephalaxin: 250 mg.**

- **Recurrent Urinary Reinfecion**
  - **≤ 2 per year**
    - 3 day self-treatment as for acute uncomplicated cystitis (Table 2)
    - Always follows coitus
    - Postcoital prophylaxis
    - Nightly or thrice weekly prophylaxis

  - **≥ 3 per year**
    - No relation to coitus

*Prophylaxis drug doses – co-trimoxazole 80/400mg; trimethoprim 100mg; nitrofurantoin 50–100mg; cephalaxin 250mg.*
be sought and, where possible, eliminated. If this is not possible, six weeks' treatment should be given. Reinfection requires elimination of possible predisposing factors, such as the use of the diaphragm, vaginal atrophy or delayed or incomplete bladder emptying. Three alternative treatment strategies are then available (Fig 1). The aim is to give the minimum amount of antibiotic consistent with prevention of recurrence of infection or prompt treatment of very occasional attacks. The duration of prophylactic treatment required is unclear, but a minimum of six months is usually prescribed. Successful and safe low-dose nightly or thrice weekly treatment over five years has been reported.

Asymptomatic bacteriuria

Treatment of asymptomatic bacteriuria is unnecessary except in pregnant women, diabetics and prior to urological surgery, and indeed may predispose to acute symptomatic attacks. Results of sensitivity testing should be available, so three-day treatment with an appropriate drug should suffice in pregnancy and before urological surgery, but a seven-day course is recommended for diabetics. Post-treatment culture should be obtained.

Acute pyelonephritis

This is a clinical diagnosis based on the presence of loin pain and tenderness, fever and bacteriuria. Bladder symptoms may or may not be present. Further investigations are rarely merited but in doubtful or atypical cases, diagnosis is best confirmed by CT scanning when band-like or wedge shaped areas or reduced enhancement of the parenchyma can be seen after the administration of contrast medium.

References

1. Cattell WR (ed). Infections of the kidney and urinary tract. Oxford: Oxford University Press, 1996.
2. Stamm WE, Counis GW, Running KR, Stephen WHCS, et al. Diagnosis of coliform infection in acutely dysuria women. N Engl J Med 1982;307:463–8.
3. Williams DN. Urinary tract infection: emerging insights into appropriate management. Postgrad Med J 1996;72:189–204.
4. Webb JAW. Imaging in urinary tract infection. In: Cattell WR (ed). Infections of the kidney and urinary tract. Oxford: Oxford University Press, 1996:64–114.
5. Hooton RM, Scholes D, Hughes JP, Winter ARNP, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med 1996;335:468–74.
6. Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med 1993;329:753–6.
7. Hooton TM, Winter C, Tiu F, Stamm WE. Randomized comparative trial and cost analysis of 3-day antimicrobial regimens for treatment of acute cystitis in women. JAMA 1995;273:41–5.
8. Bailey RR. Management of uncomplicated urinary tract infection. In: Cattell WR (ed). Infections of the kidney and urinary tract. Oxford: Oxford University Press, 1996:129–57.
9. Norbury SR. Short term treatment of uncomplicated urinary tract infection in women. Rev Infect Dis 1990;12:458–67.
10. Leibovici L, Wysenbeek AJ. Single-dose antibiotic treatment for symptomatic urinary tract infections in women: a meta-analysis of randomized trials. Q J Med 1991;78:43–57.
11. Nicolle LE, Harding GKM, Thomson M, Kennedy J, et al. Efficacy of five years of continuous low dose trimethoprim-sulfamethoxazole prophylaxis for urinary tract infection. J Infect Dis 1989;157:1239–42.
12. Lee KJT, McClennan NL, Melson GL and Stanley RJ. Acute focal bacterial nephritis: emphasis on grey scale sonography and computed tomography. Am J Roentgenology 1980;135:87–92.

Membranous nephropathy

Peter Mathieson PhD, MRCP, Professor of Renal Medicine, University of Bristol

Presentation

Membranous nephropathy (MN) is the type of glomerulonephritis found in 25% of adults with nephrotic syndrome, of whom one-third progress to renal failure. Proteinuria (with or without microscopic haematuria) may be clinically silent, being discovered only as an incidental finding on health screening or during investigation of another problem. Other presentations may be with hypertension or impaired renal excretory function. Patients with nephrotic syndrome have an increased tendency to venous thrombosis due to intravascular volume depletion, tense oedema, immobility and preferential loss of antithrombotic plasma proteins. Renal vein thrombosis, which may cause macroscopic haematuria, loin pain and deterioration in renal function, is particularly common with MN for reasons which are poorly understood.

Diagnosis

Diagnosis is by renal biopsy. The term 'membranous glomerulonephritis' refers to a morphological pattern of tissue injury in the kidney: there is uniform thickening of the glomerular basement membrane (GBM), usually without any associated cellular proliferation (Figs 1a and b). IgG and complement components are deposited in a granular pattern along the GBM; on electron microscopy these immune deposits are seen to be situated in the subepithelial position (ie on the urinary space side of the GBM) (Fig 1c). In about 80% of cases no underlying cause can be identified, and so the patient is referred to as suffering from 'primary' or 'idiopathic' membranous nephropathy (IMN).

Secondary membranous nephropathy

Identical glomerular morphology is seen in the 20% of cases where the renal lesion is 'secondary'. The most