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# **Recurrent urinary tract infection**

## What is a recurrent urinary tract infection?

Recurrent urinary tract infection (UTI) is defined as two proven episodes within six months, or three within a year [1].

# **Epidemiology**

### **Aetiology**

Escherichia coli has been shown to be responsible for 70-95% of all UTIs [2] [3] . Staphylococcus saprophyticus, Proteus mirabilis and Klebsiella species are culprits less regularly.

#### Incidence

- Women have a lifetime risk of UTI of 1 in 2, and incidence increases with age [3].
- UTI is uncommon in otherwise healthy young and middle-aged men.
   UTI incidence is higher in older men [4].
- Most recurrences are thought to be re-infection with the same organism. Studies have shown between 30-44% of non-pregnant women with a first episode of cystitis will have a recurrence [5].
- In children presenting with UTI before the age of 1 year, around three quarters will have a recurrence and after age 1 year, 45% of girls and 39% of boys will have a recurrence [6].

#### **Risk factors**

There is evidence to suggest that genetic factors may play a part (usually through bacterial/vaginal mucosal adherence factors)  $^{[7]}$ . Diabetes is also a predisposing factor  $^{[8]}$ .

Recurrent UTI in women [3] [5]

- Sexual intercourse (honeymoon cystitis).
- Atrophic urethritis and vaginitis (postmenopausal).
- Abnormalities of urinary tracts (indwelling catheter, neuropathic bladder, vesico-ureteric reflux (VUR), outflow obstruction, anatomical anomalies).
- Incomplete bladder emptying (dysfunctional urination).
- Contraception diaphragm, spermicide-coated condoms.
- History of urinary tract surgery.
- Immunocompromise eg, HIV.
- First UTI under the age of 15.
- History of recurrent UTI in mother.

## Recurrent UTI in men [4]

- Abnormalities of urinary tracts as above.
- Incomplete bladder emptying (prostatic enlargement, chronic indwelling catheter).
- Previous urinary tract surgery.
- Immunocompromise.

## Recurrent UTI in children [9]

- Any condition that leads to urinary stasis (VUR, renal calculi, obstructive uropathy - or family history of VUR, voiding disorders) or poor urine flow - eg, phimosis.
- Constipation.
- Impaired immune function.
- Sexual abuse.
- Impaired renal function.

## **Presentation**

- Recurrent UTI symptoms include:
  - Dysuria
  - Frequency
  - Urgency
  - Nocturia
  - Haematuria
  - Suprapubic discomfort
- Signs may include:
  - Suprapubic tenderness.
  - Cloudy or foul-smelling urine.
  - In the elderly, incontinence, confusion, anorexia, fever, shock.

# **Investigations**

## **Primary care**

- MSU culture, urine microscopy:
  - MSU is recommended in cases of recurrent UTI, due to the increased likelihood of resistant organisms.
  - In children, a clean catch urine sample is the recommended method for urine collection. This is much easier in toilet-trained children.
- Consider ultrasound in children to visualise anatomical anomalies.
   See the separate Urinary Tract Infection in Children article for more details.
- Men with recurrent UTI should be referred to a urologist for further investigation. Those with haematuria should be referred urgently.

- Urgent referral is also recommended for women with recurrent UTIs
  associated with haematuria (visible or non-visible) for investigations
  to exclude urological cancer<sup>[3]</sup>.
- Women referred for investigations of recurrent UTI rarely have pathology <sup>[5]</sup>. There are no UK-based guidelines to guide the need for further investigations. European guidelines advise that an extensive routine workup including cystoscopy and imaging is not routinely recommended as the diagnostic yield is low <sup>[10]</sup>. However, they do recommend that further investigations should be performed without delay in atypical cases for example, if renal calculi, outflow obstruction, interstitial cystitis or urothelial cancer is suspected.

### Secondary care

Children should have [9]:

- Ultrasound during an acute infection
- Dimercaptosuccinic acid (DMSA) scanning 4-6 months after the acute infection
- Micturating cystogram.

CT scan is the imaging of choice for underlying pathology in women with recurrent UTI, although ultrasound may be used as an alternative with or without  $X-ray^{[1]}$ .

Specialist investigation of recurrent UTI in men will include prostate assessment as well as investigation for other underlying abnormalities.

# Recurrent UTI treatment[1]

## Women [3]

In the case of a relapse, send an MSU and – unless systemic symptoms warrant immediate referral – advise simple analgesia and increased fluid intake. Consider the need for antibiotics, depending on severity of symptoms, risk of complications, and previous urine culture results and antibiotic use.

Treat the episode as per NICE guidance  $^{\left[12\right]}$  .

Refer/seek specialist advice on further investigation and management of:

- Women who have recurrent lower UTI where the underlying cause is unknown.
- Women with suspected underlying malignancy arrange an urgent two-week wait referral.

Consider offering a standby prescription for future infections.

Advise all women about behavioural and personal hygiene methods (eg, wiping from front to back after defecation. Advise about adequate fluid intake.

Postmenopausal women may wish to consider vaginal oestrogen:

- Consider the lowest effective dose of vaginal oestrogen (for example, estriol cream). for postmenopausal women with recurrent UTI if behavioural and personal hygiene measures alone are not effective or not appropriate. Discuss:
  - The severity and frequency of previous symptoms.
  - The risk of developing complications from recurrent UTIs.
  - The possible benefits of treatment, including for other related symptoms, such as vaginal dryness.
  - The possible adverse effects such as breast tenderness and vaginal bleeding (which should be reported because it may require investigation).
  - The uncertainty of endometrial safety with long-term or repeated use.
  - Preferences of the woman for treatment with vaginal oestrogen.
- Review treatment within 12 months, or earlier if agreed with the woman.

### Women with recurrent UTI who are not pregnant

- Consider a trial of antibiotic prophylaxis only if behavioural and personal hygiene measures, and vaginal oestrogen (in postmenopausal women), are ineffective or inappropriate.
- Ensure that any current UTI has been adequately treated; then consider single-dose antibiotic prophylaxis for use when exposed to an identifiable trigger (eg, coitus).

#### Take account of:

- The severity and frequency of previous symptoms.
- The risk of developing complications.
- Previous urine culture and susceptibility results.
- Previous antibiotic use, which may have led to resistant bacteria.
- The woman's preferences for antibiotic use.

When single-dose antibiotic prophylaxis is given, give advice about:

- How to use the antibiotic.
- Possible side-effects eg, diarrhoea and nausea.
- Returning for review within six months.
- Seeking medical help if there are symptoms of an acute UTI.

For women with recurrent UTI who are not pregnant and have had no improvement after single-dose antibiotic prophylaxis or have no identifiable triggers, ensure that any current UTI has been adequately treated; then consider a trial of daily antibiotic prophylaxis.

#### Take account of:

- Any further investigations (for example, ultrasound) that may be needed to identify an underlying cause.
- The severity and frequency of previous symptoms.
- The risks of long-term antibiotic use.
- The risk of developing complications.

- Previous urine culture and susceptibility results.
- Previous antibiotic use, which may have led to resistant bacteria.
- The woman's preferences for antibiotic use.

### Antibiotic options in non-pregnant women

#### First choice:

- Trimethoprim 200 mg single dose when exposed to a trigger or 100 mg at night.
- Nitrofurantoin (if eGFR>45 ml/minute) 100 mg single dose when exposed to a trigger or 50 mg or 100 mg at night.

#### Second choice:

- Amoxicillin 500 mg single dose when exposed to a trigger (offlabel indication) or 250 mg at night.
- Cefalexin 500 mg single dose when exposed to a trigger or 125 mg at night.

If there is no improvement after single-dose antibiotic prophylaxis or no identifiable triggers, ensure that any current UTI has been adequately treated; then consider a trial of daily antibiotic prophylaxis

### **Pregnant women**

Before prescribing, take into account the same factors as for women who are not pregnant.

- First choice nitrofurantoin (if eGFR ≥45ml/ minute) 50 to 100mg at night (trimethoprim should be avoided in pregnancy due to a risk of teratogenesis). Nitrofurantoin should be avoided at term (risk of neonatal haemolysis),
- Second choice as for non-pregnant women.

### Refer if there is repeated failure of treatment.

The consensus on cranberry juice is that there is very little evidence to support its use for the prevention of UTIs in non-pregnant women, and no evidence to support its use in post-menopausal women.

## Men<sup>[4]</sup>

There is little high-quality evidence to inform this section, due to the relative rarity of UTI in men, compared with women.

- Exclude chlamydial infection in sexually active men . Consider urethritis as an alternative diagnosis.
- Prescribe an antibiotic to be taken for seven days. Trimethoprim or nitrofurantoin are usual first-line choices, as per non-pregnant women.
- Recurrent cystitis in a man is likely to be secondary to associated conditions - eg, prostatitis, prostatic hyperplasia, calculi in the genitourinary tract, or VUR.
- Refer men with recurrent UTI for investigation for underlying causes and for advice about prophylactic antibiotics where required.

## Children General principles

- Treat urinary tract infection as per NICE guidance [13].
- Children with a high risk of serious illness and/or younger than 3
  months should be referred immediately to secondary care. This
  should be assessed in accordance with NICE guidance on feverish
  illness in children (see Further Reading, below).
- Do not delay treatment if the sample cannot be obtained and the infant or child is at high risk of serious illness.
- Treat each episode of acute UTI the same as a first episod

NICE guidelines advise, in order to try to prevent recurrence in children who have had a UTI, that:

- Dysfunctional elimination syndromes and constipation should be addressed.
- Adequate fluid intake should be encouraged.
- Children should have ready access to clean toilets when required and should not be expected to delay voiding.

Antibiotics should not be used for prophylaxis after a single UTI. If the infection recurs, consider seeking specialist advice before initiating antibiotic prophylaxis. . Single-use prophylaxis should be tried first, but if this does not work, daily antibiotics should be offered, with a review every six months.

If antibiotics are to be prescribed, the following options should be considered:

### First choices for children aged 3 months and over

(If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the NICE guideline on acute pyelonephritis for antibiotic choices [14].)

- Trimethoprim:
  - 3 months to 5 months: 2 mg/kg at night (maximum 100 mg per dose) or 12.5 mg at night.
  - 6 months to 5 years: 2 mg/kg at night (maximum 100 mg per dose) or 25 mg at night.
  - 6 years to 11 years: 2 mg/kg at night (maximum 100 mg per dose) or 50 mg at night.
  - 12 years to 15 years: 100 mg at night.
- Nitrofurantoin (if estimated glomerular filtration rate (eGFR) is 45 ml/minute or more):
  - 3 months to 11 years: 750 micrograms/kg four times a day for three days.
  - 12 years to 15 years: 50 mg four times a day or 100 mg modifiedrelease twice a day for three days.

Second choices for children aged 3 months and over (if no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice is not suitable):

- Nitrofurantoin (if eGFR is 45 ml/minute or more and it was not used as first-choice):
  - 3 months to 11 years: 750 micrograms/kg four times a day for three days
  - 12 years to 15 years: 50 mg four times a day or 100 mg modifiedrelease twice a day for three days
- Amoxicillin (only if culture results available and susceptible):
  - 1 month to 11 months: 125 mg three times a day for three days.
  - 1 year to 4 years: 250 mg three times a day for three days.
  - 5 years to 15 years: 500 mg three times a day for three days.

#### Cefalexin:

- 3 months to 11 months: 12.5 mg/kg or 125 mg twice a day for three days.
- 1 year to 4 years: 12.5 mg/kg twice a day or 125 mg three times a day for three days.
- 5 years to 11 years: 12.5 mg/kg twice a day or 250 mg three times a day for three days.
- 12 years to 15 years: 500 mg twice a day for three days.

In infants and children, there is no need to treat asymptomatic bacteriuria with prophylactic antibiotics.

See also the separate Urinary Tract infection in Children article for more detail.

## **Complications**

Most people will recover fully with treatment. However, recurrent UTI is a risk factor for pyelonephritis, which can cause renal scarring. This in turn can lead to hypertension and impaired renal function.

## **Further reading**

• Fever in under 5s: assessment and initial management; NICE Guidance (last updated November 2021)

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