NHS
Cheshire and Merseyside

Recurrent Urinary Tract Infection in Adults

GUIDELINE

Definition

Recurrent urinary tract infection in adults is defined as repeated upper or lower urinary tract infection (UTI) with a frequency of:

- three or more UTIs in the last 12 months or
- two or more UTIs in the last six months [1]

Prevalence

Recurrent UTIs may be due to reinfection with a different strain or species of the organism or relapse with the same organism. Recurrent infections are more common in women. 25-30% of women who experience an initial infection experience a second UTI, with 2.7% of women experiencing a third.

Diagnosis

Diagnosis of recurrent UTI in adults should be based on:

- Clinical diagnosis based on typical symptoms (refer to NICE and PHE guidelines)
- Urine should be sent for culture in all patients with recurrent UTI. Please state on the request form "recurrent UTI" and any recent or current antimicrobials prescribed so that appropriate additional sensitivity testing can be carried out

Patients with complex recurrent infections requiring investigation should be referred to Urology:

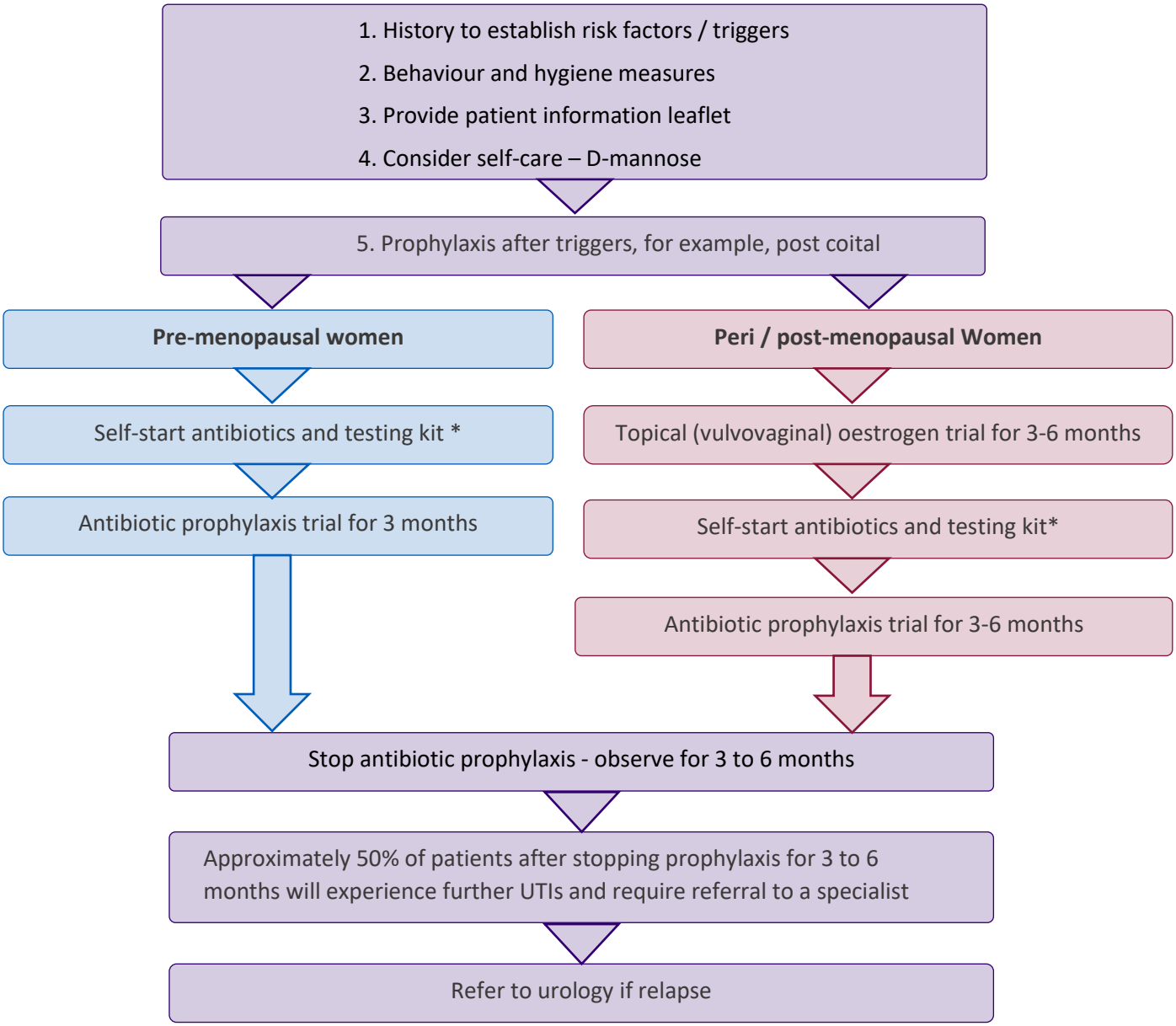
- Men
- Pregnant women
- Recurrent or severe pyelonephritis
- People with suspected cancer in line with the NICE guideline on suspected cancer: recognition and referral – Refer Urgently Urological cancers – recognition and referral | Health topics A to Z | CKS | NICE
  - Patients aged 45 and over with either: unexplained visible haematuria without urinary tract infection or visible haematuria that persists or recurs after successful treatment of urinary tract infection.
  - Patients aged 60 and over who have unexplained microscopic haematuria and either dysuria or a raised white cell count on a blood test (NB there is no recommendation to perform full blood counts on patients with recurrent UTI. This criterion represents to cross over of symptoms between recurrent UTI and those that may be displaying signs of urological cancer)
- Consider **non-urgent** referral for bladder cancer in people aged 60 years and over with recurrent or persistent unexplained urinary tract infection.
- People with suspected structural or functional abnormalities of the urinary tract, for example, renal stones
- People with neurological diseases, for example, spinal cord injuries
- Pneumaturia (bubbles in the urine) or faecaluria that may suggest fistula
- Recurrent UTI in women with previous radiation treatment or pelvic cancer (as they are at risk of fistula formation)
- People with a history of complex pelvic surgery or urogynae procedures with mesh

- People with persistent infection caused by resistant organisms
- Alternative diagnosis likely (culture negative UTIs or antibiotics ineffective)
- People who do not respond to prophylactic antibiotics, including two or more episodes of UTIs returning after stopping prophylactic antibiotics
- Proteus on repeat urine cultures – a potential cause of kidney stones
- Catheterised patients
- People with chronic kidney disease – risk of deterioration in renal function

Referral to other specialities

- All recurrent UTIs in pregnancy – refer to antenatal care, or obstetrics and gynaecology.
- Immunocompromised patients – refer to medical speciality.

Management of women with recurrent UTI in primary care



* Testing kit to include a boric acid containing sample pot. For women under 65 years a universal sample pot plus testing strips may be appropriate to guide therapy.

Patient history

- Distinguish between a persistent or relapsing UTI (same organism with small gaps, typically < 2 weeks, between treatment) or a recurrent UTI (different organisms or resolution of symptoms and significant gaps between episodes)
- Establish any triggers or risk factors
  - Post coital infection
  - Low oestrogen levels / atrophic vaginitis
  - Uncontrolled diabetes
  - Constipation
  - Menstruation
- Exclude sexually transmitted diseases

Behavioural and personal hygiene measures

In all patients with recurrent UTI the following lifestyle modifications should be explored:

- Encourage better hydration (aim for 1.5 litres fluid/day) and more frequent voiding to achieve pale-coloured urine
- Avoid delaying urination
- For sexually active women, advise post-coital voiding and avoid the use of contraceptive diaphragm and spermicide
- Wash only with water and avoid using cosmetic bath products or feminine hygiene douches
- Advise perineal hygiene, i.e., wiping from front to back
- Provide patients with one of the following information leaflets:
  - Urinary tract infection resource suite: Patient-facing materials (rcgp.org.uk)
  - Urinary infection (adult) | The British Association of Urological Surgeons Limited (baus.org.uk)

Self-Care Options

Some patients may wish to try self-care treatments. Offer advice on the limitations of the evidence and the safety concerns with delayed treatment.

- D-mannose (2 g once daily in the evening) is a carbohydrate-based food supplement which appears to impair urothelial adhesion by bacteria. Limited evidence suggests that d-mannose taken regularly is superior to no treatment in preventing recurrent UTIs. D-mannose is not a medicine and is available to buy without a prescription, for example, from health food shops (approx. cost £10 -20 per month). Patients should be advised about the sugar content. Avoid in pregnancy.
- There is limited evidence of benefit for other self-care options including cranberry and probiotics.

Post-coital prophylaxis or prophylaxis after other specific triggers

Consider this **before** long-term antibiotic prophylaxis.

- Only applicable if UTI is strongly associated with intercourse or other well-defined triggers
- Treatment should be based on previous sensitivities
- Post-coital antibiotic prophylaxis should be taken within two hours of coitus.
- Appropriate choices (all single dose, off-label use) include:
  - Nitrofurantoin immediate release (I/R) 100 mg (if eGFR >= 45 ml/minute)
  - Trimethoprim 200 mg
  - With culture results and susceptible bacteria: amoxicillin 500 mg (higher resistance rate)
- In the absence of culture results nitrofurantoin is the preferred agent (if eGFR >= 45 ml/minute)

Topical (vulvovaginal) oestrogens

- Vulvovaginal atrophy can have significant impact leading to recurrent UTI symptoms
- Topical (vulvovaginal) oestrogen is recommended for recurrent UTI in peri or post-menopausal women where lifestyle modifications are not effective

Recurrent urinary tract infection in adults

- Rationale: declining oestrogen levels are associated with changes in the bladder microbiome which lead to a significantly higher risk of UTI
- Topical (vulvovaginal) oestrogen may be used in combination with antibiotic prophylaxis if required
- Review impact after 3 months then annually. Advise patients that it may take 3-6 months before there is any reduction in UTI frequency
- Do not offer oral oestrogens (hormone replacement therapy) specifically to reduce the risk of recurrent UTI in postmenopausal women. Vaginal oestrogen for recurrent UTI may be used in combination systemic HRT.
- The use of vaginal oestrogens solely for the prevention of recurrent UTIs is an off-license indication. Therefore, prescribers should follow relevant professional guidance, taking full responsibility for the decision, and ensuring informed consent is taken.
- Note that symptoms of vaginal atrophy can mirror symptoms of UTI

Dosing recommendations

For management of vulvovaginal atrophy with recurrent UTI symptoms apply estriol cream, topically to the vulva in combination with either vaginal estradiol via pessary (10 micrograms) or vaginal estriol via pessary (30 micrograms) or estradiol ring (Estring to be replaced after 90 days).

For further guidance see Genitourinary Syndrome of the Menopause (GSM) (British Society of Sexual Medicine 2021)

Refer to the BNF for specific information for individual products

Self-start antibiotics

- Consider this **before** long-term antibiotic prophylaxis
- Requires a well-motivated and well-informed patient to ensure the antibiotics are taken appropriately. Not suitable for all patients
- This may be used as a long-term strategy for managing UTIs where patients find this acceptable
- If the patient can wait, an infection should be confirmed by MSU prior to commencing self-start antibiotics.
- The patient should collect a mid-stream urine sample in a boric acid universal container prior to self-initiating- any antibiotics and take the sample to the GP surgery
- If the samples are repeatedly negative, then a referral should be made to identify another cause of symptoms
- For empirical antibiotic choice refer to past culture and sensitivity results if available or follow local guidance on the treatment of acute UTIs
- Advise the patient to seek medical attention if they develop fever, loin pain, or symptoms not improving within 48 hours
- The patient must discuss the outcome of each episode with their GP

Long-term low-dose antibiotic prophylaxis

- Choice of antibiotic should be based on confirmed culture and sensitivity results and considering comorbidities, renal function, and contra-indications
- Advise patients that prophylaxis will be provided for a period of 3 to 6 months followed by a treatment free period to evaluate the response
- Appropriate antibiotics for long-term prophylaxis (see treatment recommendations):
  - Trimethoprim 100 mg at night
  - Nitrofurantoin I/R 100 mg at night (if eGFR >= 45 ml/minute)
  - Before prescribing long-term nitrofurantoin, baseline investigations should be completed:
    - liver function tests (LFTs),
    - renal function
    - Advise on signs of pulmonary, neurological, and hepatic toxicity - to stop taking nitrofurantoin immediately and contact GP Nitrofurantoin: reminder of the risks of pulmonary and hepatic adverse drug reactions - GOV.UK (www.gov.uk)

Second line

- With culture results and susceptible bacteria: amoxicillin 250 mg at night
- If culture results demonstrate resistance to these agents: contact Microbiology

- Long-term low-dose antibiotic prophylaxis should be tried for 3-6 months initially, and then reviewed with a view to stopping - see stopping continuous prophylaxis below
- Antibiotic cycling (i.e., the use of different agents in rotation) for prophylaxis is not evidence-based and locally is not advised
- Patients advised by specialists to continue on long-term nitrofurantoin should receive six-monthly liver function and renal function tests plus a discussion with the patient about pulmonary symptoms and signs of hepatitis as part of a routine six-monthly review
- For further monitoring information refer to BNF

Stopping continuous prophylaxis

- A prolonged period of antibiotic treatment may allow bladder epithelial healing, reducing the risk of future UTIs when antibiotics are then stopped.
- The proportion of patients who will return to suffering recurrent UTIs after stopping continuous prophylaxis may be around 50% [1].
- If infection-free after 3 months, antibiotic treatment should be withdrawn.
- Ensure that patient has access to treatment for acute UTI.
- Continue behaviour and hygiene measures.
- Refer patients who experience breakthrough infection or further infections (without triggers) after stopping prophylaxis. Re-initiation may be considered whilst waiting for specialist review.

Treatment of breakthrough infections whilst on antibiotic prophylaxis

- Stop prophylaxis
- Urine culture to check for resistant organisms
- Use a different agent to treat the acute episode
- Restart prophylaxis after treatment of single acute episode if resistance has not developed
- If more than one breakthrough infection whilst on prophylaxis - refer to a specialist
- Non-response to antibiotic treatment courses with culture negative urine samples is suggestive of alternative aetiology - these patients should be referred for further investigation.
- Patients experiencing persistent infection (initial response to antibiotics but symptoms recurring within a few days) - discuss treatment with specialist

Methenamine hippurate

Methenamine as a non-antibiotic option for prophylaxis of recurrent urinary tract infection is currently under review. Current use of this drug is being considered with a plan to address its non-formulary status. The plan to review the status of methenamine will be prioritised as part of the formulary harmonisation process for the Cheshire and Merseyside formulary.

References

1. National Institute for Health and Care Excellence (2018) Urinary tract infection (recurrent): antimicrobial prescribing [online] [Accessed 30 March 2022]