Management of recurrent Urinary Tract Infections in women

Recurrent lower urinary tract infections (UTI) are a common problem affecting many women of various ages. Recurrent UTI is defined as ‘three or more episodes of UTI in the last 12 months or two or more in six months’(1). These recurrent infections may be due to re-infection (a prolonged interval between infections) or bacterial persistence (frequent recurrent infections within a short interval by the same organism).

It does not include episodes of bacteriuria without UTI symptoms (asymptomatic bacteriuria) which appear to play a protective role in preventing symptomatic recurrence so should not be treated (**except** in pregnant women).

# How to manage the initial presentation of recurrent UTI

There are several options for reducing the impact of recurrent UTIs - the aim is to minimise symptoms while also trying to minimise antibiotic exposure.

## First line

* Provide the PHE ‘[Treating your infection – UTI patient leaflet’](http://www.rcgp.org.uk/~/link.aspx?_id=9FCF9DA4B4A045519593320478DFD9E7&_z=z)

It is recommended that the following simple measures are tried before starting antibiotic prophylaxis:

* Encourage better hydration to ensure more frequent urination (1.6L/day);
* Encourage urge-initiated voiding and post-coital voiding;
* Ensure constipation is treated and prevented appropriately;
* Advise sexually active women that diaphragm and spermicide use are risk factors for cystitis;
* There is conflicting evidence for the use of cranberry products, however, patients may choose to purchase and try cranberry products e.g. high strength cranberry extract capsules may be more effective/acceptable than juice (2-4)*.* Avoid in patients taking warfarin (5) or if history of kidney stones (6); and
* For post-menopausal women with risk factors such as atrophic vaginitis consider prescribing intravaginal or oral oestrogens (7-10).These should be trialled for three to six months. Estriol 0.1% cream (Ovestin) and estradiol 10mcg vaginal tablets (Vagifem) are [formulary](https://www.eclipsesolutions.org/cornwall/info.aspx?paraid=233) choices.

If these simple measures fail to improve symptoms then:

1. Check series of MSU (and history of MSU samples sent to laboratory) to confirm diagnosis and establish sensitivities during acute UTI episode.
2. If continued problems consider renal tract ultrasound (to detect stones, cysts, tumours and other abnormalities) and post void bladder residual volume scan (to detect voiding dysfunction)

* If new presentation in post-menopausal women consider referral for cystoscopy to determine if symptoms are due to an intravesical lesion e.g. stone or tumour.
* Red flags that increase the importance of cystoscopy are persistent dysuria despite antibiotic therapy, persistent non-visual haematuria despite treatment and significant smoking history.

1. If investigations are normal and problems continue consider second or third line options.
2. If investigations are abnormal, then consider referring the patient to Urology.

## Second line

* A self-start /standby three day course(4,11-13) may be considered based on recent sensitivities:

Nitrofurantoin MR 100mg twice daily or Trimethoprim 200mg twice daily.

* Post coital antibiotic prophylaxis (12-15): Trimethoprim 100mg or Nitrofurantoin 100mg to be taken within two hours of intercourse (off-label use). Use of condoms (without spermicidal), post coital voiding and good hydration are all important non-pharmacological prophylactic measures to help prevent recurrent UTIs. Avoiding use of spermicidal products may also help to prevent recurrent UTIs.

## Third line

* Continuous antibiotic prophylaxis(11-14): Nitrofurantoin (immediate release) 50mg - 100mg or Trimethoprim 100mg at bedtime

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| **The patient should be counselled at an early stage that antibiotic**  **prophylaxis is not usually a life-long treatment.**  **Antibiotics are given in this way to allow a period of bladder healing**  **which makes UTI less likely.** |

There is no evidence that antibiotics have any additional benefit beyond six to twelve months treatment, therefore the treatment should be discontinued ideally after six months (14, 16).On prescribing a review date of six months should be documented in the medical notes and on the prescription. The patient should be reviewed with a view to stopping the treatment.

**If prophylaxis fails during the initial six month period**

1. A urine sample should be sent for culture and sensitivity testing.
2. Uncomplicated UTI should be treated with a three day course of a suitable antibiotic based on the urine culture results and the prophylactic antibiotic resumed following completion of the course with a different antibiotic if appropriate.
3. A longer course of antibiotics may be necessary in patients with impaired renal function, immunosuppressed or with abnormal urinary tract. These patients should be reviewed and assessed by a specialist.

**Other interventions to consider (1)**

* **Methenamine 1g every 12 hours:** ‘non-antibiotic’ option widely used in Europe that can be considered if there is no hepatic impairment, should be reviewed after three to six months.
* **Probiotics:** Limited evidence, but probiotic interventions have been found effective in treatment and prevention of urogenital infections as alternatives or co-treatments.
* **D-Mannose:** A simple sugar that seems able to hinder bacteria adhesion to the urothelium.
* **Vitamin D:** High dose supplementation has been shown to increase CAMP production in the human bladder epithelium in response to E coli (CAMP – surface cell receptor; a messenger for many biological processes).

# How to manage a patient who has had a prolonged course of prophylactic antibiotics

**Identifying patients for review**

* Ideally patients should be reviewed after six months of prophylactic antibiotics (16) with a view to stopping them, which is why it is helpful to document a review date in the patient’s notes and also on the prescription.
* If prophylactic antibiotics were initiated by Urology then they should be contacted prior to stopping unless specifically discharged to the GP to carry out the review after six months.

**Discussing patient concerns**

* The risks of long term antibiotics in terms of vaginal thrush, Clostridium difficile and increased likelihood of infection with resistant organisms are important considerations for the doctor and patient and should be fully discussed.
* It is understandable for patients to feel anxious about returning to suffering recurrent UTIs. However, after a prolonged period of antibiotic treatment in most cases this has allowed the bladder wall to ‘heal’ making UTI’s less likely.
* Offering advice about a trial of cranberry products (2-3) and ‘stand by’ antibiotics (16) to be taken at the first symptoms of UTI can sometimes give sufficient reassurance to the reluctant patient. They should also be given appropriate advice regarding continuation of simple measures to prevent UTI (11) and given the PHE ‘[Treating your infection – UTI patient leaflet’](http://www.rcgp.org.uk/~/link.aspx?_id=9FCF9DA4B4A045519593320478DFD9E7&_z=z) if they’ve not seen it before.

**Recurrence of UTI after stopping prophylaxis**

* It is important to ensure the patient is complying as far as possible with the first line simple measures outlined on page one. If they have not already had a renal tract ultrasound and post void bladder residual volume scan now is a good time to consider doing this.
* In post-menopausal women consider the possibility of atrophic vaginitis as a risk factor for UTI and manage appropriately. If recurrent UTI is a relatively ‘new’ problem in a post-menopausal woman consideration should also be given to referral for cystoscopy. (7)
* However, if appropriate investigations have already been done and shown no abnormality and there are no other concerning ‘red flag’ symptoms and cranberry extract has already been tried (or is inappropriate, e.g. if the patient is on warfarin) then a further course of prophylaxis can be considered.
* The ongoing need for antibiotic prophylaxis should be reviewed after six months. For patients continuing on prophylaxis beyond 6 months the on-going need should be discussed on an annual basis as part of the standard repeat medication review.

# References

These guidelines have been adapted from the Adapted from ‘Antibiotic management of recurrent UTI in adults’ Cumbria CCG NECS & ‘Recurrent UTIs in women’ BNSSG CCG July 2017.

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# Appendix: Management of recurrent UTI in women flowchart

**Does the patient meet the definition for recurrent UTI?**

i.e. >3 microbiologically confirmed UTIs in 12 months **or** >2 microbiologically confirmed UTIs in six months



* **Continue simple measures** see under ‘First line’
* **Check series of MSU results to confirm diagnosis and establish sensitivities during acute UTI**
* **Previous UTI – was treatment complete?**
* **Consider other investigations** e.g. renal tract ultrasound (for stones, cysts or tumours), post void residual volume scan, or refer for cystoscopy (if new presentation post menopause)

**Prophylaxis not indicated.** Simple measures only:

* Provide the [PHE patient UTI leaflet](http://www.rcgp.org.uk/~/link.aspx?_id=9FCF9DA4B4A045519593320478DFD9E7&_z=z)
* Hydration – to ensure frequent urination (1.6L/day)
* Urge-initiated voiding and post-coital voiding
* Cranberry products (conflicting evidence – patients can buy OTC, avoid if taking warfarin or kidney stones)
* Intravaginal oestrogen (If post-menopausal for atrophic vaginitis, trial for three to six months).



**Third line option**

* **Continuous low dose prophylactic antibiotics:** Nitrofurantoin 50-100mg or Trimethoprim 100mg at night (long term nitrofurantoin may be associated with lung fibrosis and hepatitis; and is ineffective when used in patients with GFR < 30)
* **Give prophylaxis for six months:** Document review date in notes and on prescription
* **Advice to patient:** 
  + Treatment not usually life-long;
  + Given to allow a period of bladder healing, which makes UTI less likely;
  + No evidence of additional benefit beyond six to twelve months;
  + Risk of bacteria in the body developing resistance to antibiotic with long term use; and
  + Side effects of antibiotics (antibiotic dependent but may include thrush, C. difficile, antibiotic resistance).

**Second line options**

* **A self-start/standby three day course of antibiotics** (based on recent sensitivities): Nitrofurantoin MR 100mg twice daily or Trimethoprim 200mg twice daily
* **Post-coital antibiotic prophylaxis:** Trimethoprim 100mg or Nitrofurantoin 100mg to be taken within two hours of intercourse (off-label use)

**Do investigations show normal renal structure?**

Consider urology/uro-gynae advice as patient may have structural risk factors for recurrent UTI.

**Other interventions to consider**

* Methenamine – 1g every 12 hours
* Probiotics
* D-mannose
* Vitamin D

**Stop** antibiotic prophylaxis **after six months** and discuss patient concerns (consider stand-by antibiotics)

If **prophylaxis fails** during the six month period:

* Confirm with MSU and treat with three day course of suitable antibiotic
* Resume prophylactic antibiotic following completion of this course