

Guidelines for Recurrent Urinary Tract Infections in Adults: Antibiotic Prophylaxis

Definition

The symptoms of a lower urinary tract infection include: frequency, dysuria, urgency and suprapubic pain. Recurrent lower urinary tract infection (rUTI) is defined as:

**2 or more episodes of lower urinary tract infection in the last 6 months, or
3 or more episodes of lower urinary tract infection in the last 12 months¹.**

It does not include bacteriuria in the absence of symptoms or in catheterised patients i.e. asymptomatic bacteriuria. Asymptomatic bacteriuria should not be screened for or treated, unless prior to urological surgery or in pregnancy (positive cultures in pregnancy should be confirmed with a second culture confirming the same organism prior to treating)².

1. Consider whether referral is required for patient with recurrent UTIs:

Consider whether the patient requires specialist referral for the following factors^{1,3}:

Red Flags for Referral to Urology:

- All men
- Frank haematuria, even in the context of confirmed UTI
(refer to current '2 week wait' guidelines for further information)
- Neurological disease e.g. spinal cord injury, spina bifida
- Pneumaturia or faecaluria
- Proteus on repeat urine cultures
- Suspected stone
- Obstructive symptoms, or structural/functional abnormality, causing >200ml residual urine on bladder scan

In pregnancy:

- All recurrent UTIs in pregnancy should be discussed with the Obstetrics team.

Consider risk factors:

A sexual history and investigations for sexually transmitted infections should be performed if appropriate. In peri- and post-menopausal women, atrophic vaginitis may cause urinary symptoms and may increase the risk of bacteriuria.

Microbiological Confirmation:

Patients with rUTIs should have a mid-stream urine (MSU) sample sent for culture **prior** to antibiotics being initiated, in order to confirm infection and guide antibiotic therapy³. Patients should be counselled on how to provide a specimen to minimise the chance of contamination.

<http://patient.info/health/midstream-specimen-of-urine-msu>

Urine cultures sent in the absence of symptoms are unlikely to be helpful, may detect asymptomatic bacteriuria and lead to inappropriate antibiotic use. Antibiotic treatment of asymptomatic bacteriuria is more likely to be harmful than beneficial.⁴

‘Clearance’ cultures are not recommended if symptoms have resolved, with the exception of pregnant women.

2. Management of Initial Presentation of Recurrent UTI in non-pregnant females

The following conservative measures should be tried prior to antibiotic prophylaxis:

Conservative Measures:

- Encourage better hydration and more frequent voiding
- For sexually active women:
 - Advise post-coital voiding
 - Avoid use of contraceptive diaphragm and spermicide
- Avoid using cosmetic bath products or feminine hygiene douches.
- Perineal hygiene i.e. wiping front to back.
- Avoid using flannels. A clean non scented disposable wipe is preferable.

Intra-vaginal oestrogens:

- For post-menopausal women with recurrent UTIs, consider intravaginal oestrogens⁴.

Antibiotic Prescribing Strategies

The relative risks and benefits of the following antibiotic prescribing strategies should be discussed with the patient. These strategies should be in addition to conservative measures. Some patients may find cranberry juice or products helpful, however the evidence for their benefit is variable and compliance is low, so they are not routinely recommended⁶. It is also contraindicated in patients on Warfarin.

- **Standby Antibiotics**

- If the patient is able to wait, infection should first be confirmed by MSU prior to commencing standby antibiotics.
- A patient advice sheet and boric acid container for pre-antibiotic MSU should be provided to the patient, see pages 9-11.
- A 'self-start' course of antibiotics, prescribing an agent according to previous known sensitivities and choosing the narrowest spectrum agent available⁵. Refer to Nottinghamshire APC Antibiotic Guidelines for more information.
- Safety-net with advice to seek medical attention if they develop fever, loin pain, or symptoms are not improving by 48 hours.
- This option limits antibiotic exposure and risk of resistance emerging, and may be the more suitable option for patients with <1 UTI per month.

- **Post Coital Antibiotics**

- For rUTIs that are triggered by sexual intercourse, this strategy is as effective as continuous antibiotic prophylaxis⁷, and limits antibiotic exposure and risk of resistance emerging.

- **Continuous Antibiotic Prophylaxis**

- Longer term antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance.
- A **6 month trial** of low-dose continuous antibiotic treatment may be beneficial if rUTIs are occurring ≥ 1 per month and are not triggered by sexual intercourse.
- Patients should be counselled at an early stage that antibiotic prophylaxis is not usually a lifelong treatment. Documenting and triggering a review date in the patient's record, and on the repeat prescription, is strongly advised to avoid prolonged courses of antibiotics without review.

Stopping continuous prophylaxis:

It is understandable for patients to be anxious about a return to frequent UTIs after stopping continuous prophylaxis. However, 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%.⁷
- This means a significant number of patients are able to stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of resistance emerging and side-effects.
- One option is to provide 'standby' antibiotics when stopping continuous prophylaxis which may give sufficient reassurance to patients for a trial off antibiotics.
- Consider referring patients who relapse after stopping continuous prophylaxis, if not already been investigated.
- Longer term prophylaxis may be helpful in those patients whose UTIs are suppressed when on prophylaxis and recur when prophylaxis is discontinued after 6 months.

Choice of Agents⁵:

Choice of antibiotic should be based on **confirmed culture and sensitivity results** (wherever possible), and consider the patient's co-morbidities, renal function and any contra-indicating factors. Trimethoprim and nitrofurantoin are licensed for the prophylaxis of rUTIs.

The risk of adverse effects (see box below), as well as common side-effects such as rashes, oral/vaginal thrush and gastro-intestinal upset, should be discussed with the patient.

Antibiotic	Dose	Cautions and Monitoring
Trimethoprim	100mg One dose post-coital (off label) or nightly	<ul style="list-style-type: none">• Hyperkalaemia: caution when prescribing with drugs such as spironolactone, ACE inhibitor or angiotensin inhibitors.• Renal Impairment: Avoid if eGFR <15ml/min. Discuss with renal physician if eGFR <30ml/min. May increase serum creatinine.• Patients should be counselled on the risk of blood disorders and advised to seek attention if fever, sore throat, purpura, mouth ulcers, bruising or bleeding occurs.

OR:		
Nitrofurantoin	50mg immediate release One dose post-coital (off label) or nightly	<ul style="list-style-type: none"> • Avoid if renal function eGFR <45ml/min. Consider checking renal function prior to commencing continuous prophylaxis, especially in the elderly. • Avoid if G6PD deficiency. • Use with caution in anaemia, diabetes, vitamin B or folate deficiencies. • Monitor full blood count, renal function and liver function tests every 3-6 months • Advise the patient on the risk of pulmonary and hepatic fibrosis, and the symptoms to report if they develop during treatment. Reactions can develop acutely or insidiously. • Advise the patient on the risk of peripheral and optic neuropathy, and the symptoms to report if they develop during treatment.

If resistance to both first line agents, other agents may be considered after discussion with Urology and/or Microbiology. Broader spectrum agents such as cefalexin, ciprofloxacin and co-amoxiclav have a higher risk of *C.difficile* diarrhoea and should not be routinely used for prophylaxis.

Methenamine

A Cochrane review in 2007 assessed the benefits of a urinary antiseptic agent, methenamine hippurate⁸. This is converted to formaldehyde in the acidic urine environment, which is directly toxic to bacteria. It concluded that in a sub-group of women without urinary tract abnormalities or neuropathic bladder, it may be of benefit in preventing rUTIs in the short-term but long-term benefit was not demonstrated. The studies were of poor quality and there was insufficient evidence to recommend its routine use. Methenamine may be advised by:

- Urologists or Infectious Diseases physicians (Amber 2 classification),

if there are no suitable alternative therapies, due to:

- Multi-resistant organisms
- Allergies, contraindications, or side-effects with prophylactic antibiotics.
- High-risk patients for whom prophylactic antibiotics are not appropriate e.g. *C.difficile* carriage

Treatment should stop after 6 months and patient should be referred back to the advising Specialist if relapses or side-effects occur.

Please refer to BNF for dosing advice.

3. Managing 'breakthrough' UTIs in patients on antibiotic prophylaxis:

- The first breakthrough infection should be treated according to culture and sensitivity results, with the original prophylaxis being re-started once the infection has resolved if the culture confirms it is still sensitive to the prophylactic agent.
- If the culture shows resistance to the prophylactic agent, or multiple breakthrough UTIs occur (≥ 2 UTIs in 6 months), prophylaxis has therefore proved ineffective and should be stopped.
- Consider referral to Urology at this point if not already been investigated.

4. Managing a patient who has had a prolonged course of prophylactic antibiotics:

Identifying patients for review:

- Patients should be reviewed after 6 months of prophylactic antibiotics with a view to stopping (refer to 'Stopping Continuous Prophylaxis' page 4).
- 12 months is a suggested trigger for audit purposes for patients on long-term prophylaxis.
- Patients who have urine cultures confirming resistance to the prophylactic agent they are on, should have their prophylaxis stopped (exposure to antibiotic without benefit) and a clinical review to discuss ongoing management and/ or need for referral.

References

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2. Nicolle, L. E., Bradley, S., Colgan, R., Rice, J. C., Schaeffer, A., & Hooton, T. M. (2005). Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clinical Infectious Diseases*, 643-654.
3. NICE Clinical Knowledge Summaries: <https://cks.nice.org.uk/urinary-tract-infection-lower-women#!scenario:2> accessed 23/11/16
4. Scottish Intercollegiate Guideline Network Clinical Guideline 88. Management of Suspected Bacterial urinary Tract Infection. Updated 2012.
5. Public Health England. Diagnosis of UTI. Quick Reference Guide for Primary Care. Updated 2011.
6. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD001321. DOI: 10.1002/14651858.CD001321.pub5
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8. Lee BSB, Bhuta T, Simpson JM, Craig JC. Methenamine hippurate for preventing urinary tract infections. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD003265. DOI: 10.1002/14651858.CD003265.pub3

Summary of Management of Recurrent Lower UTIs (in non-pregnant adults):

≥ 3 symptomatic lower UTIs / 12 months or
≥ 2 symptomatic lower UTIs / 6 months

Consider red flag indications for Urology referral (see page 1)

Advice on Conservative Measures (see page 2)

Consider risks and benefits with the patient of:

1. Stand-by antibiotics
2. Post-coital antibiotics (if associated with intercourse)
3. Trial of continuous antibiotics

For Stand-by or Post-coital antibiotics:

- Review repeat prescriptions at 6 months to assess benefit and if any resistant urine cultures

Patients on continuous antibiotic prophylaxis:

- Trial of 6 months of nightly antibiotics (see page 3)

Breakthrough UTI whilst on
continuous prophylaxis

No breakthrough UTIs

After 6 months, stop antibiotics.

- Around half will not return to recurrent symptoms.
- Consider offering stand-by antibiotics if patient concerned.

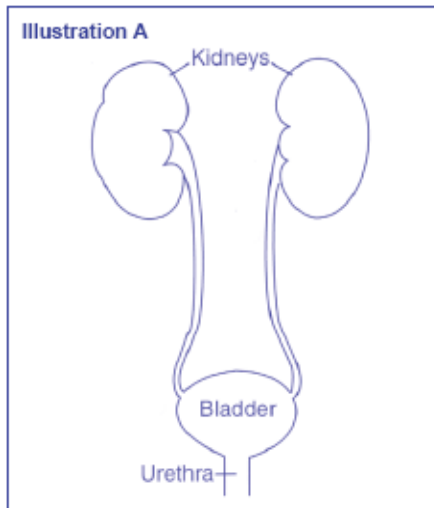
If recurrent UTIs
return after stopping,
consider referral.

If more than one breakthrough UTI,
or the urine cultures are resistant
to the prophylactic agent:
Antibiotic Prophylaxis has failed
and should be stopped.
Consider referral if not already investigated.

Patient Advice sheet:

Recurrent Urinary Tract Infections in Women

Urinary tract infections (UTIs) are a common problem for women. Bacteria often travel from the urethra to the bladder, causing a bladder infection (see Illustration A). Occasionally, the infection may also affect the kidneys.



Urinary tract infections may cause some, or all, of the following symptoms

- Lower abdominal pain or pressure
- Frequent and urgent urination
- Burning or stinging during urination
- Blood in the urine
- If the kidneys are involved, back pain and/or fever

Urinary tract infections may get better on their own within a few days, and drinking plenty of fluids can help. Sometimes, a short course of antibiotics is required. It is helpful to provide a urine specimen that can be sent for testing when the symptoms start, and this must always be done prior to starting antibiotics. Information on the correct technique is included at the end.

There are a number of things you can do to prevent urinary tract infections:

- Avoid long intervals between urination.
- Have at least eight to ten drinks (mug-size) daily. These could be water, cranberry juice, squash or other fluids. Caffeinated drinks are best avoided.
- Shower instead of taking a bath. Avoid using bubble bath or other cosmetic bath products.
- Avoid using any feminine hygiene sprays and scented douches.
- Avoid using a vaginal diaphragm for birth control.
- Empty your bladder after sexual intercourse, as intercourse can often trigger UTIs.
- After urination, wipe from front to back.
- After a bowel movement, clean the area around the anus gently, wiping from front to back and never repeating with the same tissue. Soft, white, non-scented tissue is recommended.

Self-Management and rescue pack advice sheet

Version one, ratified 20/1/17. Review date January 2020. Authors: Dr Amelia Joseph Microbiology Specialty Registrar NUH, Mr Richard Parkinson Consultant Urologist NUH, Dr Jane Coleman GP.

You have been provided with a red-top urine sample pot and a rescue pack of antibiotics.

What to do if you experience urinary tract infection symptoms:

1. Collect a mid-stream sample of your urine in the sample pot provided.
2. Place the pot of urine in a sealed plastic bag and hand in to the GP reception straight away. If there is a delay, store in the fridge and hand in on the next working day.
3. Take the first dose of the antibiotic supplied.
4. Follow the instructions for taking the full course of antibiotics.
5. Contact your GP practice to discuss the results of the urine culture (usually available 24-72 hours after handed into the practice), and to obtain a new sample pot and rescue pack of antibiotics. The GP will check whether the same antibiotics are still appropriate for your next rescue pack (if the antibiotic will still work against the bacteria in the urine).

What to do if the symptoms of urinary tract infection do not improve:

Your symptoms should start to improve once you start taking the antibiotics. If you have not improved within 48 hours, or the symptoms have got worse, or you feel feverish, develop new back pain or feel generally unwell, contact the GP practice, or call 111 if the GP practice is shut.

Urinary Infections Diary

	Date of start of symptoms	Date urine sample provided	Date of start of antibiotics (if given)	Date symptoms settled
1				
2				
3				
4				
5				
6				
7				
8				

Midstream Specimen of Urine (MSU)

A midstream specimen of urine (MSU) is tested to look for infection.

What is the purpose of a midstream specimen of urine (MSU) test?

- **To confirm the diagnosis of a urine infection.** The usual symptoms of a urine infection are pain when you pass urine and passing urine frequently. However, symptoms are not always typical, particularly in children and the elderly, so a urine test may be needed.
- **To decide the best antibiotic to use.** Some germs (bacteria) are resistant to some antibiotics. If the test shows that bacteria are in the urine then the bacteria are tested against various antibiotics. This finds which antibiotics will kill the bacteria in the urine.

How do I do a midstream specimen of urine (MSU)?

The aim is to obtain a sample (specimen) of urine from the middle of your bladder. Urine does not normally have any germs (bacteria) in it (urine should be sterile). If bacteria are found in the sample, it means that the urine is infected. A midstream sample is best, as the first bit of urine that you pass may be contaminated with bacteria from the skin.

Before doing an MSU, wash your hands and ideally your genitals as well.

Women - hold open the entrance to the vagina (your labia). Men - pull back your foreskin. Pass some urine into the toilet. Then, without stopping the flow of urine, catch some urine in a clean (sterile) bottle. (The bottle is usually provided by a doctor or nurse.) Once you have enough urine in the bottle, finish off passing the rest of your urine into the toilet.

Do not open the sterile bottle until you are ready to take the sample. Avoid touching any part of your genitals with the bottle, as this will increase the risk of contamination. Put the cap back on the container. You do not need to fill the bottle to the top; a small amount will do. Some specimen bottles contain a powder, which helps the sample last longer for testing (a preservative). If this is the case, a mark on the bottle will indicate the ideal amount of urine. However, if that is difficult, any amount is better than none.

The sooner the sample is given in to the doctor's surgery, or to the laboratory, the better. Within two hours is best. If that is not possible, put the sample in the fridge until you take it to the doctor or laboratory.

If it is difficult to aim your urine stream into the bottle, you may use another container such as a jam jar or a disposable plastic cup. You can then pour the urine into the sterile bottle. If you do this, make sure the container you pass water into is as clean as possible. Wash it well and rinse it with boiling water. You should still pass the first part of your urine stream into the toilet. In this way, you are collecting the urine from the bladder.

The result of an MSU takes 2-7 days.