The Princess Alexandra Hospital NHS NHS Trust

NHS West Essex Clinical Commissioning Group

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 months. [1,11]

Healthcare professionals should not prescribe antibiotics to treat asymptomatic bacteriuria in adults with catheters and non-pregnant women[2]. 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) [3].

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

Consider whether the patient requires specialist referral for the following factors[4]:

Red Flags for Referral to Urology:

- All men
- 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
- Haematuria (in line with NICE guidance on suspected cancer)

In pregnancy:

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

Refer or **seek specialist advice** on further investigation and management for[11]:

- People with recurrent upper UTI[11]
- People with recurrent lower UTI when the underlying cause is unknown[11]
- For post-menopausal women with no obvious risk factors, consider referral to urology for further investigations, particularly if recurrent UTI is a recent problem[8].

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

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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 therapy. Patients should be counselled on how to provide a specimen to minimize the chance of contamination[5] (see page 10).

Urine cultures sent in the absence of symptoms are unlikely to be helpful, may detect asymptomatic bacteriuria and lead to inappropriate antibiotic use.

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

2. Management of Initial Presentation of Recurrent UTI in <u>non-pregnant females</u>

<u>First Line</u>: Conservative Measures:

- Share TARGET leaflet with patients
- Encourage better hydration and more frequent voiding.
- Advise Paracetamol or Ibuprofen for symptom relief [1 (Target)]
- 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.

Self-care

- Some women with recurrent UTI may wish to try D-mannose if they are not pregnant[11]. (D mannose is a sugar that is available to buy as powder or tablets; it is not a medicine).
- Some women with recurrent UTI may wish to try cranberry products if they are not pregnant (evidence of benefit is uncertain and there is no evidence of benefit for older women) [11]. Cranberry products work for some women[1,6]. Cranberry juice potentially increases the anticoagulant effect of warfarin, therefore avoid[7].
- Advise people taking cranberry products or D-mannose about the sugar content of these products, which should be considered as part of the person's daily sugar intake.

Intra-vaginal oestrogens:

- For post-menopausal women with risk factors such as atrophic vaginitis consider prescribing intra-vaginal or oral oestrogens[8].

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 following with the woman to ensure shared decision-making[11]:

- 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.

Vaginal oestrogen products are not licensed for preventing recurrent UTI, so use for this indication would be off-label. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Second Line: Antibiotic Prescribing Strategies

For 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 not effective or not appropriate.[11]
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.

Single dose/Post Coital Antibiotics
- For women with recurrent UTI who are not pregnant, ensure that any current UTI has been adequately treated then consider single-dose antibiotic prophylaxis for use when exposed to an identifiable trigger[11]
- For rUTIs that are triggered by sexual intercourse, this strategy is as effective as continuous antibiotic prophylaxis[9], and limits antibiotic exposure and risk of resistance emerging.
- 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.[11]
- When single-dose antibiotic prophylaxis is given, give advice about:
    - how to use the antibiotic
    - possible adverse effects of antibiotics, particularly diarrhoea and nausea
    - returning for review within 6 months
    - seeking medical help if there are symptoms of an acute UTI.[11]

Standby Antibiotics
- If the patient is able to wait, infection should first be confirmed by MSU prior to commencing standby antibiotics.
- A 'self-start' course of antibiotics, prescribing an agent according to previous known sensitivities and choosing the narrowest spectrum agent available. (Refer to West Essex Antibiotic Guidance available at https://westessexccg.nhs.uk).

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- Safety-net with advice to seek medical attention if they develop fever, loin pain, or symptoms are not improving by 48 hours. (See patient advise sheet on Page 10)
- This option limits antibiotic exposure and risk of resistance emerging, and may be the more suitable option for patients with <1 UTI per month.

Third Line: Continuous Antibiotic Prophylaxis

- 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
- Longer term antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance.
- Patients should be counselled at an early stage that antibiotic prophylaxis is not usually a lifelong treatment. [8]
- 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.

3. Treatment of Men and Pregnant Women

For men and pregnant women with recurrent UTI, ensure that any current UTI has been adequately treated then consider a trial of daily antibiotic prophylaxis if behavioural and personal hygiene measures alone are not effective or not appropriate, **with specialist advice.**

Trial of daily antibiotic prophylaxis[11]:

- 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 person's preferences for antibiotic use.
- When a trial of daily antibiotic prophylaxis is given, give advice about:
  - the risk of resistance with long-term antibiotics, which means they may be less effective in the future
  - possible adverse effects of long-term antibiotics
  - returning for review within 6 months
  - seeking medical help if there are symptoms of an acute UTI.

4. Choice of Agents[1]:

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. Nitrofurantoin and Trimethoprim 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[7] (For a complete list please refer to the SmPC)
First Line:		
Nitrofurantoin	**100 mg single dose when exposed to a trigger** (off-label) **or 50 to 100 mg at night**[11]	• 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, pulmonary disease, hepatic dysfuncion. • Monitor for pulmonary symptoms, 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. Discontinue if deterioration in lung function. • Advise the patient on the risk of peripheral and optic neuropathy, and the symptoms to report if they develop during treatment. • Avoid at term in pregnancy; may produce neonatal haemolysis (BNF, August 2018).
Trimethoprim	**200 mg single dose when exposed to a trigger** (off-label) **or 100 mg at night**	• 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. Care should be taken to avoid accumulation. • 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. • Teratogenic risk in first trimester of pregnancy (folate antagonist; BNF, August 2018). Manufacturers advise contraindicated in pregnancy (trimethoprim SmPC
Amoxicillin	**500 mg single dose when exposed to a trigger or 250 mg at night**	• Avoid if history of penicillin allergy
Cefalexin	**500 mg single dose when exposed to a trigger or 125 mg at night**	• Use with caution I previous history if penicillin allergy • Use with caution in renal impairment

See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breastfeeding.

Amoxicillin and Cefalexin not licensed for preventing UTIs, so use for this indication would be off-label. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed

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consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

If resistance to first and second line agents, other agents may be considered after discussion with Urology and/or Microbiology.

5. Reassessment

Review antibiotic prophylaxis for recurrent UTI **at least** every 6 months[11], with a view to stopping. The review should include:

- assessing the success of prophylaxis
- discussion of continuing, stopping or changing prophylaxis (taking into account the person's preferences for antibiotic use and the risk of antimicrobial resistance)
- a reminder about behavioural and personal hygiene measures and self-care treatments (see the recommendations on self-care).

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.

If antibiotic prophylaxis is stopped, ensure that people have rapid access to treatment if they have an acute UTI.

6. 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.

7. 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[8].

- The proportion of patients who will return to suffering recurrent UTIs after stopping continuous prophylaxis may be around 50%[9].
- 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.

8. Recurrence of UTI after stopping antibiotic prophylaxis

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- Consider referring patients who relapse after stopping continuous prophylaxis, if not already investigated.

- If appropriate investigations have already been done and shown no abnormality and there are no other concerning 'red flag' symptoms, then continuation of prophylaxis may be considered. The ongoing need for antibiotic prophylaxis should be reviewed again after three months[8].

9. Recurrent UTIs associated with urinary catheters:

- Cloudy or offensive urine alone does not merit treatment or investigation for UTIs in patients with urinary catheters.
- Do not use dipsticks to diagnose UTIs in patients with urinary catheters as symptomatic UTIs cannot be differentiated from asymptomatic bacteriuria on the basis of dipstick urinalysis.
- Look for associated localising or systemic features including flank pain, and exclude other potential sources of infection in catheterised patients who present with fever.
- **Do not** routinely offer antibiotic prophylaxis to prevent catheter-associated UTIs in people with a short-term or a long-term (indwelling or intermittent) catheter[12].
- Seek explicit guidance from a microbiologist before commencing antibiotic prophylaxis in patients with a urinary catheter.
- Obtain a urine sample from the sampling port of the catheter using an aseptic technique (in line with the NICE guideline on healthcare-associated infection[13]) and send for culture and susceptibility testing.
    - If the catheter has been changed, obtain the sample from the new catheter.
    - If the catheter has been removed obtain a midstream specimen of urine

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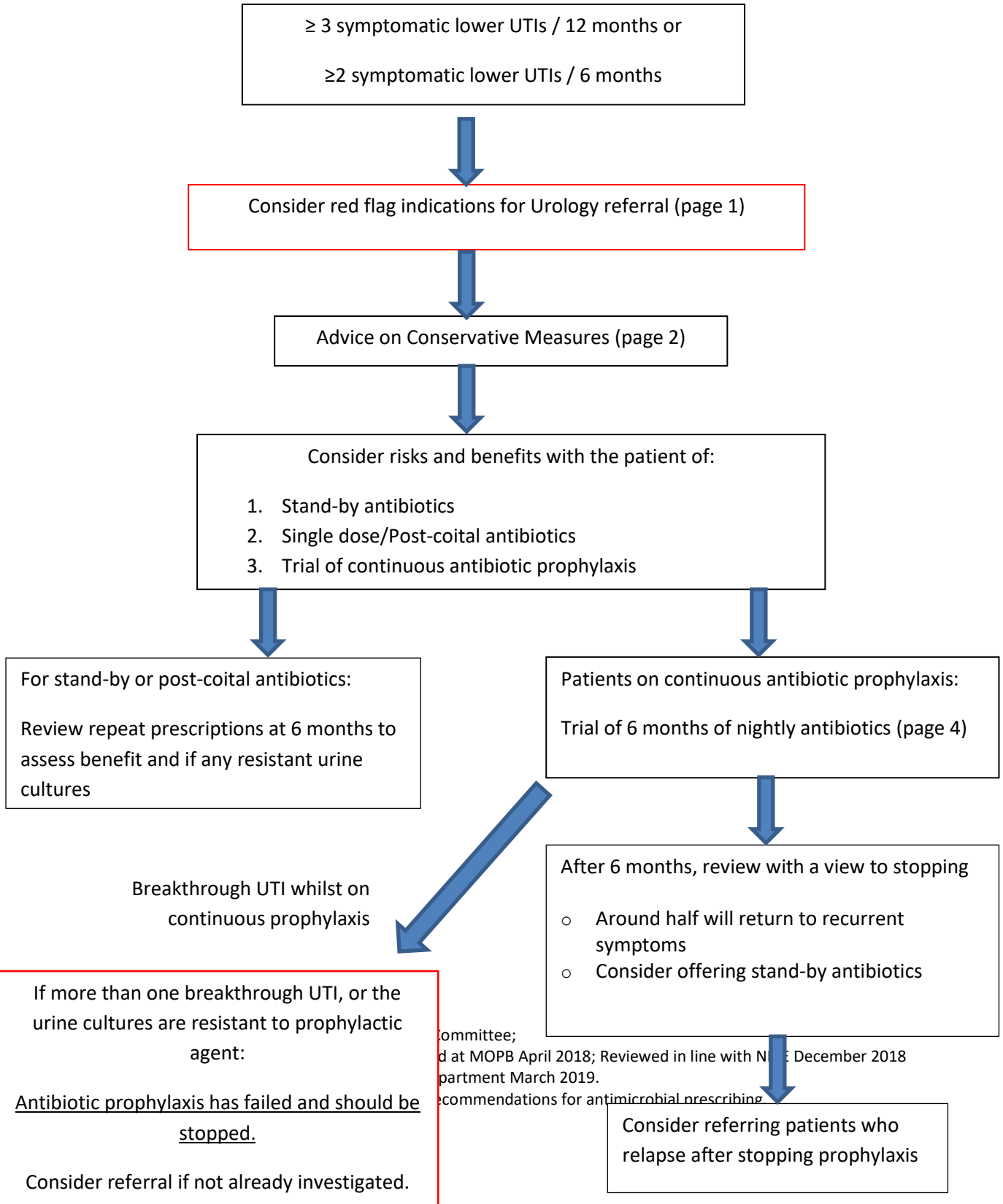
12. NICE NG113 Urinary tract infection (catheter-associated): antimicrobial prescribing (November 2018) https://www.nice.org.uk/guidance/ng113
13. NICE CG139 Healthcare-associated infections: prevention and control in primary and community care (March 2012; Last updated February 2017) https://www.nice.org.uk/guidance/cg139

Further resources:

- Treating Your Infection – Urinary Tract Infection Leaflets: UTI and UTI for older adults http://www.rcgp.org.uk/clinical-and-research/toolkits/target-antibiotics-toolkit.aspx
- Recurrent Cystitis in Women. Leaflet available online at https://patient.info/pdf/4437.

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



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Advice sheet for

URINARY TRACT INFECTION - Self-Management and Standby Antibiotics

You have been provided with a urine sample pot and a standby 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, and to obtain a new sample pot and standby pack of antibiotics. The GP will check whether the same antibiotics are still appropriate for your next standby 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				

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Patient

View this article online at: patient.info/health/midstream-specimen-of-urine-msu

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.

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