



Laboratory Investigation of **UTI**



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better medicine

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All information is intended for use by competent health care professionals and should be utilised in conjunction with pertinent clinical data.

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Key messages

- Women with symptoms of uncomplicated UTI do not require a urine culture
- Screening for asymptomatic bacteriuria is not recommended except in pregnant women
- *Chlamydia trachomatis* urethritis can cause similar symptoms to a UTI

Introduction

This resource focuses on the diagnosis of infection in the urinary tract. In particular uncomplicated and complicated urinary tract infection (UTI), urethral infection with *Chlamydia trachomatis* and issues around the investigation of asymptomatic bacteriuria.

Urinary tract infections are common. Studies in the US have shown that approximately 50% of all women will have a urinary tract infection in their lifetime, of these 25% will have recurrent infections (Mehnert-Kay, 2005). Each year approximately 5% of women present to their GP with frequency and dysuria (Prodigy).

In 2005, almost 800 000 urine cultures were performed in New Zealand, at a cost of over \$12.5 million (Laboratory claims data). Many women with UTI will have 'uncomplicated' infections that do not require urine culture. Streamlining the diagnostic process by only requesting urine culture when appropriate could improve patient satisfaction and decrease costs without compromising care.

Epidemiological data on *Chlamydia trachomatis* infection in New Zealand suggests we are well behind other OECD countries in the control of this infection (Perkins, 2004). When patients have symptoms of UTI, and sexual history indicating they may be at risk, *Chlamydia trachomatis* urethritis should be considered.

The occurrence of asymptomatic bacteriuria increases with age with up to 50% of elderly people having asymptomatic bacteriuria (Nicolle, 2005). There is no evidence to suggest this group of patients benefit from antibiotic treatment; while on the other hand, there is evidence of increased adverse effects, emergence of resistant organisms and cost associated with the use of antibiotics.

Uncomplicated versus complicated UTI

- People with symptoms of uncomplicated UTI do not require a urine culture. They can be treated empirically and no follow-up is required unless symptoms do not improve.
- People with complicated UTI require urine testing for culture and susceptibility testing.

Uncomplicated UTI...

- Classic presentation: dysuria, frequency, urgency, suprapubic pain.
- Occurs in women with a normal, unobstructed genitourinary tract, no history of recent instrumentation, and symptoms confined to the lower urinary tract.
- Occurs most frequently in young sexually active women.
- No complicating factors.
- Urine culture is unnecessary in women with uncomplicated UTI. Women can be treated empirically.

Complicated UTIs are those occurring in...

- Men
- Children
- Pregnancy
- People with suspected pyelonephritis
- People with recurrent UTI
- Failed antibiotic treatment or persistent symptoms
- Catheterised patients
- Hospital-acquired infections
- Recent urinary tract instrumentation
- Impaired host defences
- People with abnormalities of genitourinary tract
- People with renal impairment

Urine culture is not helpful for women with uncomplicated lower urinary tract infections as it does not improve outcomes.

Classical presentation of uncomplicated UTI includes:

- Painful urination (dysuria)
- Frequency
- Urgency
- Pressure in the lower pelvis

Most uncomplicated urinary tract infections occur in women who are sexually active. *Escherichia coli* is the most common cause of uncomplicated UTI and accounts for approximately 80 to 85 percent of infections. *Staphylococcus saprophyticus* accounts for about 5 to 25 percent of infections (Hooton, 2004). Other Enterobacteriaceae, such as *Klebsiella*, *Proteus* and *Enterococcus*, occasionally cause UTI.

For women with classical presentation of uncomplicated UTI appropriate management is empirical treatment with a three day course of trimethoprim (seven days for elderly women). Single-dose therapy results in lower cure rates and more recurrences than longer courses (Prodigy). Nitrofurantoin is an alternative if there is allergy to trimethoprim. There is no need for follow up unless symptoms persist or recur since the goal of treatment is resolution of symptoms.

In women with classical presentation of uncomplicated UTI and with no vaginal discharge or irritation, the pretest probability of UTI is 90% (Bent, 2002). This means the decision to treat can be made on the strength of clinical presentation. Further tests such as dipstick urinalysis or urine culture do not influence management. In a recent New Zealand study, 3 out of 4 women who presented with dysuria and frequency, but had a negative urine dipstick for nitrites and leukocytes benefited from antibiotic treatment (Richards, 2005).

One downside to empirical treatment of UTI is that cumulative susceptibility data from local laboratories can not be used to monitor the susceptibility of uropathogens causing uncomplicated UTIs. Periodic surveys may be needed for this purpose.

In women with dysuria and a history of vaginal discharge or vaginal irritation the pretest probability of UTI is lower. Investigations for sexually transmitted infections and genital infections as well as urinary tract infection are appropriate.

Dipstick urinalysis in the practice may provide useful information when the diagnosis is in doubt. The presence of nitrites has a high predictive value for UTI, since nitrites are formed only as a metabolic product from bacteria. If the dipstick is positive to either nitrites or leukocytes this increases the probability of UTI to about 80% while a dipstick negative to both nitrites and leukocytes reduces the probability of UTI to about 20% (Bent, 2002).

For further information on the appropriate use of urine dipsticks see appendix 1. When treating women with recurrent UTIs, you may be asked about the role of cranberry. For an overview of this see appendix 2.

When is urine culture helpful?

1. Urine culture is recommended when women with UTI have complicating features

Urine culture is advisable for women with symptoms of UTI, if there are complicating features such as:

- Abnormal urinary tract e.g. stone, reflux, catheter,
- Impaired host defences e.g. pregnancy, diabetes, immunosuppression,
- Impaired renal function,
- Suspicion of pyelonephritis,
- More than three UTIs in one year, or
- UTI recurrence within two weeks.

2. Urine culture is recommended for pregnant women

Women identified with asymptomatic bacteriuria in early pregnancy have a 20-30 fold increased risk of developing pyelonephritis during pregnancy compared to women without bacteriuria (Smaill, 2001). These women are also more likely to experience premature delivery and have infants of low birth weight.

Screening all pregnant women for asymptomatic bacteriuria using urine culture at 12-16 weeks gestation is strongly recommended. If bacteriuria is detected by screening, the patient should be treated and a urine culture performed monthly throughout the pregnancy (Prodigy).

The duration of antimicrobial therapy should be 7 days (Prodigy). The results of susceptibility testing will guide the choice of antibiotic. Trimethoprim should be avoided during the first trimester. Nitrofurantoin is safe to use in early pregnancy, but must be avoided at fullterm as it may cause haemolysis in neonates (Smaill, 2001).

Urine culture should be performed for:

1. Women with UTI with complicating factors
2. All pregnant women
3. Men with suspected UTI
4. Suspected acute pyelonephritis
5. Prostatitis

A request for a urine culture should not delay the initiation of empirical antibiotic therapy when this is clinically appropriate. The results of the culture will help to confirm the choice of antibiotic.

3. Urine culture is indicated for lower UTI in Men

All UTIs in men are considered complicated, therefore a urine culture is always taken, even if the urine dipstick is negative. This is because lower urinary infections are uncommon in young men. The occurrence increases with age mainly because of prostatic enlargement and decreased defences against infection. It is appropriate to initiate a seven-day course of trimethoprim after taking a urine sample and review this choice when the results are back (Prodigy).

4. A urine culture is always taken when acute pyelonephritis is suspected

Pyelonephritis is a serious infection with risk of bacteraemia. A urine culture is always taken when this diagnosis is suspected and antibacterials are commenced while awaiting the results. Dipstick testing of the urine may be useful if clinical findings are equivocal.

The spectrum of acute pyelonephritis is wide, ranging from mild illness to sepsis (Ramakrishnan, 2005). To diagnose pyelonephritis GPs must rely on evidence of UTI along with signs and symptoms suggesting upper UTI (fever, chills, flank pain, nausea, vomiting, costovertebral angle tenderness). Lower UTI symptoms may or may not be present.

Clinical findings of pyelonephritis may be atypical in elderly people, pregnant women, people with diabetes, immunocompromised people, or people with a past history of pyelonephritis or UTI before the age of 12 years, or three or more UTIs in the previous year (Prodigy).

Hospital admission may be required for people with suspected acute pyelonephritis especially in the presence of severe illness, social barriers to effective care at home, pregnancy, diabetes, abnormality of the urinary tract, an immunocompromised state, or uncertainty about the diagnosis.

Following treatment, all patients should be reviewed after 48 hours, to assess response to treatment, and to ensure the person is taking the correct antibiotics based on culture and sensitivity results. Earlier review may be necessary.

Post-treatment urine cultures are recommended in all patients one to two weeks after completion of antibiotic therapy (Ramakrishnan, 2005). Further investigations are indicated for all men with acute pyelonephritis and for women who have had recurrent episodes.

5. Prostatitis

Acute Prostatitis

Entry of micro-organisms into the prostate gland almost always occurs via the urethra. The flora of acute prostatitis reflects the spectrum of agents causing genital infection or UTI. The typical signs and symptoms of acute prostatitis include fever, dysuria, pelvic or perineal pain, and cloudy urine. Urine culture is useful in acute prostatitis because it may prove a urinary pathogen and susceptibility results will guide antibacterial use. If urine culture is negative, STIs (*C. trachomatis*, *N. gonorrhoeae*) should be excluded. However antibacterials, e.g. cotrimoxazole 2 tabs bd should be started before the results of urine culture are available because acute prostatitis is a serious illness and may be complicated by bacteraemia and prostatic abscess. Specific therapy may need to be altered depending on the culture results. Prostatic massage is not recommended because it is painful and may cause bacteraemia.

Chronic prostatitis

Chronic prostatitis should be considered in men who have dysuria and frequency in the absence of signs of acute prostatitis and in those who have recurrent UTIs in the absence of bladder catheterisation. Gram-negative bacilli are the most common etiologic agent, but enterococci and Chlamydia have also been associated with chronic infection.

Organisms are typically recovered from the urine. Urethral swabs may be requested for gonococcal culture or urine nucleic acid amplification tests for *Chlamydia trachomatis* to exclude STIs if urine culture is negative. Prostatic massage to produce prostate secretions for culture is complicated but may differentiate between abacterial and bacterial chronic prostatitis.

Although PSA elevation may be caused by prostatitis measurement is not helpful. Men with chronic prostatitis usually require urological referral with antibacterial treatment while awaiting an appointment.

For more information on urine collection and urine characteristics see Appendix 3.

Asymptomatic bacteriuria should not be tested for except in pregnant women.

The prevalence of asymptomatic bacteriuria varies across selected population groups, for example asymptomatic bacteriuria has a prevalence of 1 – 5% in healthy premenopausal women, 1 – 27 % in people with diabetes, 15 – 50% in people in long term care facilities and up to 100% in people with long term catheter use (Nicolle,2005).

Asymptomatic bacteriuria is a microbiological diagnosis based on the isolation of a specified quantitative count of bacteria in a urine specimen obtained from a person without signs or symptoms of a UTI.

1. Non pregnant women

Routine culture of urine in non pregnant women, for example during health checks, is not useful.

2. Testing for asymptomatic bacteriuria not required in elderly people

Asymptomatic bacteriuria in the elderly occurs frequently and is not associated with increased morbidity. There is no benefit from treating asymptomatic bacteriuria.

The diagnosis of UTI in this age group should be made based on clinical signs and symptoms in conjunction with culture results rather than on the basis of dipstick or culture results alone.

Clinical indications for urine culture in elderly people:

- Dysuria, fever > 38°C or change in frequency
- Lesser degree of fever with new or worsening urgency, frequency, suprapubic pain, urinary incontinence, or gross haematuria.

Screening for asymptomatic bacteriuria is not recommended for:

1. Non pregnant women
2. Elderly people
3. People with indwelling urinary catheter.
4. People with spinal cord injuries.

When people living in long-term care institutions, such as rest homes, develop urinary tract infections this is often from urinary pathogens resident in each institution with local patterns of antibiotic resistance. For this reason it is worthwhile for institutions to keep registers of urinary pathogens and their antibiotic susceptibilities so initial empiric treatment for people with new urinary infections can be guided by the local data.

3. Regular urine culture or dipstick testing is not indicated for people with in-dwelling catheters

Screening for or treatment of asymptomatic bacteriuria is not indicated for people with in-dwelling catheters. All in-dwelling catheters inevitably become colonised with bacteria.

Urine specimens obtained for culture through an indwelling catheter will grow organisms reflecting the bacteriology of the catheter biofilm rather than the bladder urine. Growth of bacteria from a catheter urine sample does not imply antibiotics are needed if the person is asymptomatic.

Most catheterized patients remain free of discomfort and systemic symptoms even when urinary tract infection is present. In the absence of obstruction, urinary infection does not cause damage. However, if fever develops, blood cultures and a urine sample are recommended. Blood cultures are indicated since catheter urine samples often grow a mixture of bacteria, even if the patient has pyelonephritis due to a particular bacterium.

Intermittent catheterisation has a much lower risk of symptomatic UTI and is preferred to indwelling catheterisation whenever possible.

In catheterised patients urine and blood culture is recommended for:

- Fever or rigors without identified cause.
- New-onset delirium or costovertebral tenderness.

4. Asymptomatic bacteriuria and people with spinal cord injuries

People with spinal cord injuries have a high prevalence of bacteriuria, as well as high incidence of symptomatic urinary tract infection. Urinary tract infection in people with paraplegia may cause non-specific symptoms, such as vomiting and increased spasticity. Urine culture is useful in these situations.

***Chlamydia trachomatis* urethritis**

Always consider *Chlamydia trachomatis* urethritis when UTI is suspected

Chlamydia trachomatis urethritis is commonly asymptomatic, but may present with dysuria. Chlamydia infection should be considered when a urinary tract infection is suspected in a patient at risk of STIs or when a urine sample shows sterile pyuria, i.e. white blood cells in the urine but no urinary pathogen isolated. A positive leucocyte esterase test on urinalysis may be due to urethritis rather than a UTI. Causes of urethritis include STIs such as *C. trachomatis*, *N. gonorrhoeae*, *Trichomonas vaginalis* and herpes simplex virus; Chlamydia being the commonest cause. Chlamydia does not produce nitrites but the presence of nitrites does not exclude a concomitant Chlamydia infection.

It has been estimated that 20%–40% of women with untreated Chlamydia will progress to pelvic inflammatory disease (PID), and be exposed to complications of infertility, chronic pelvic pain, and ectopic pregnancy.

Testing for Chlamydia

For women when a genital tract infection is suspected, endocervical swabs, a high vaginal swab and a urethral sample (either first-catch urine or urethral swab) will exclude most causes of genital tract infection.

For diagnosis of *Chlamydia trachomatis* urethritis in men, and screening in either men or women, a urine sample can be used. Testing can be performed on a first pass urine sample (the initial stream of urine that will wash organisms out of the urethra of men or women) of approximately 10 mL. Preferably the patient has not urinated for at least one hour before collecting the first-catch urine. Urethral swabbing in men or women has little advantage over urine testing and may be painful and poorly tolerated with potential for obtaining an inadequate quality specimen.

Most chlamydia testing (urine or swabs) is now performed by nucleic acid amplification. Although these tests are highly sensitive and specific, they are not 100%. The predictive value of a positive test depends on the prevalence of infection in the population tested. If confirmation of *Chlamydia* is required for medico-legal reasons culture should be performed. Culture is not as sensitive as nucleic acid amplification but is more specific.

Positive Chlamydia results

If *Chlamydia trachomatis* infection is detected on a urine sample, a complete STI evaluation is recommended to exclude co-infection with other sexually transmitted bacteria, protozoa and viruses. Uncomplicated chlamydial infection can be treated with a 1g dose of azithromycin. Other STIs may also be detected and require further treatment.

Appendices

Appendix 1 Point-of-care urine dipstick analysis

To obtain accurate results in your surgery it is important that correct technique is used when testing urine samples.

- Check the expiry date on the container
- Strips should be stored at room temperature away from direct light.
- The bottle contains a desiccant so the reagent strips must be kept in the bottle with the cap tightly closed to maintain reagent reactivity.
- The reagent pads should be completely immersed in the carefully mixed urine and the strip removed immediately.
- Wipe the edge of the strip as it is removed to avoid mixing with adjacent reagent areas.
- Read the results only after the specified reading time and in the correct order.

	Significance	Limitations
Glucose	Diabetes mellitus is the main cause of glucosuria.	The test is specific for glucose; no other substance excreted in urine is known to give a positive result.
Blood	This will test positive for intact red cells, free haemoglobin or myoglobin. Haematuria can be divided into two groups: <ul style="list-style-type: none"> • Benign or relatively benign transient haematuria – The most common causes of haematuria are UTI, menstrual contamination and vigorous exercise • Perisistent pathological haematurias – these are less common and may include urinary tract stones, tumours and trauma 	The test is less sensitive in urine with high specific gravity and ascorbic acid content. The sensitivity is greater to free haemoglobin and myoglobin than to intact erythrocytes. The appearance of green spots (speckled pattern) on the reagent pad indicates the presence of intact erythrocytes in the urine.
Protein	Minimal proteinuria (1+) can be due to infection. A protein of 2+ or higher increases the possibly of glomerular disease. If proteinuria persists a 24-hour protein test should be requested. The protein dipstick is not sensitive to microalbuminuria, therefore this test must be specifically requested.	The test is more sensitive to albumin than globulin, haemoglobin, Bence-Jones protein, or mucoprotein; therefore a negative result does not rule out the presence of other proteins.
Leukocytes	Leukocyte esterase is produced by neutrophils and is most often positive due to the presence of a UTI. Organisms such as Chlamydia should be considered in patients with pyuria and negative urine cultures.	The manufacturers specifications should be followed for the time required before assessment of colour change.
Nitrite	This test depends upon the conversion of nitrate, which comes from the diet, to nitrite by the action of many gram negative bacteria. Nitrite tests may be negative if the causative organism is not nitrate-reducing (eg enterococci, S. Saprophyticus, Acinetobacter)	The nitrite dipstick is sensitive to air exposure. After one week of exposure, one third of strips give false positive results, and after two weeks three quarters give false positive results.

Appendix 2 The role of Cranberry in UTI

A patient presenting with UTI or a history of UTI may ask about the role of cranberry in preventing UTI. Cranberry was used traditionally by Native Americans for the treatment of bladder and kidney 'ailments' and there is documentation from the 17th century of the therapeutic uses of cranberry. Despite this long history there is no reliable evidence supporting the use of cranberry for treatment of UTI, although it may have a role in the prophylaxis of UTI.

The conclusion from a 2004 Cochrane review of the role of cranberries for preventing urinary tract infections (Jepson, 2004) was there is some evidence from two good quality RCTs that cranberry may decrease the number of symptomatic UTIs over a 12 month period in women. It is not clear if it is effective for other groups such as children and the elderly. The large number of dropouts/withdrawals from some of the trials indicates that cranberry may not be acceptable over long periods of time. In addition it is not clear what is the optimum dosage or method of administration (e.g. juice or tablets). The review group recommended that further properly designed trials with relevant outcomes are needed.

In a recent edition of Bandolier there was an update on the use of cranberry (Bandolier, 2006). They acknowledged the sporadic and somewhat complicated nature of research, but they felt they could say with reasonable certainty that cranberry does not affect UTI rates in people with neurogenic bladder. The one area in which cranberry appears to show consistent benefit is in preventing UTI in susceptible women. Overall the numbers of UTIs in susceptible women were reduced by about half. In practical terms this means for every 10 women at increased risk of UTI who take cranberry juice daily for 6 or 12 months, one fewer will have a UTI.

Bandolier expressed this as:

- 7 out of 10 women wouldn't have a UTI anyway
- 2 out of 10 women will have a UTI anyway
- 1 out of 10 women will not have a urinary tract infection because they used cranberry juice.

Although cranberry is not reported to cause drug interactions, it may cause GI upset and as a result may not be well tolerated. Many studies use different dosages and formulations of cranberry, for example concentrated cranberry extract twice daily, or 250 mL pure unsweetened cranberry juice three times daily (Lynch, 2004). This volume of juice may be unacceptable for some people.

Women who are considering cranberry should be informed of the proven alternatives of post coital trimethoprim or a home supply of trimethoprim to commence at the onset of symptoms. Urinary symptoms in older women may be caused by atrophic vaginitis and benefit from topical oestrogen cream.

Appendix 3 Urine collection

Although bladder stab is the gold standard for urine collection, midstream urine is routinely the best method of urine collection. There are no benefits to prior cleansing and a recent study (Lifshitz, 2000) found contamination rates to be similar in specimens obtained with and without prior cleansing (32 versus 29 percent).

If a midstream specimen can not be obtained from a woman, in-and-out catheterisation may be used to obtain a urine sample (Nicolle, 1993). For men, it may be necessary to apply a uridome collection device.

Patients with long-term indwelling urethral catheters should have urine obtained by aspiration of the catheter port and not from the drainage bag. Unless obstruction is suspected, it is not necessary to change the catheter to better assess bladder (or kidney) microbiology (Warren, 1982).

Urine characteristics

If a patient complains of unusual coloration or odour of their urine, it may be worthwhile considering a number of other causes of abnormal urine appearance. Some causes may be more sinister, but others may be the result of some food or drug.

Foods, medications, metabolic products, and infection can cause abnormal urine colours. Cloudy urine may be the result of precipitated phosphate crystals in alkaline urine. Purple discolouration can result from indirubin in plastic urinary catheter bags mixing with indigo in urine. Some bacteria degrade indoxyl sulphate, derived from metabolising tryptophan, into indirubin and indigo.

The normal odour of urine is described as urinoid; this odour can be strong in concentrated specimens but this does not mean infection. Diabetic ketoacidosis can cause urine to have a fruity or sweet odour, and alkaline fermentation can cause an ammoniacal odour after prolonged bladder retention. While people with UTIs often have urine with a pungent odour, other causes include gastrointestinal-bladder fistulas (associated with a faecal smell), cysteine decomposition (associated with a sulfuric smell), and medications and diet (e.g. asparagus).

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