COMPASS Therapeutic Notes on the Management of Bacterial Urinary Tract Infections in Primary Care

In this issue:

<table>
<thead>
<tr>
<th>Glossary of terms</th>
<th>Page</th>
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<tbody>
<tr>
<td>Bacteriuria</td>
<td>The presence of bacteria in the urine</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
</tr>
<tr>
<td>LE</td>
<td>Leucocyte Esterase</td>
</tr>
<tr>
<td>Lower Urinary Tract Infection</td>
<td>Evidence of a urinary tract infection with symptoms suggestive of cystitis (dysuria or frequency without fever, chills or back pain)</td>
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<tr>
<td>MSU</td>
<td>Mid-Stream Urine</td>
</tr>
<tr>
<td>NNT</td>
<td>Number Needed to Treat</td>
</tr>
<tr>
<td>Pyelitis</td>
<td>Inflammation of the lining of the renal pelvis of the kidney</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Inflammation of both the parenchyma of the kidney and the lining of its renal pelvis especially due to bacterial infection</td>
</tr>
<tr>
<td>Pyuria</td>
<td>The presence of white blood cells in the urine</td>
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<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
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<tr>
<td>Upper Urinary Tract Infection</td>
<td>Evidence of urinary tract infection with symptoms suggestive of pyelonephritis (loin pain, flank tenderness, fever, rigors or other manifestations of systemic inflammatory response)</td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary Tract Infection, the occurrence of pathogenic organisms in the urinary tract</td>
</tr>
<tr>
<td>VUR</td>
<td>Vesico-ureteric reflux, the abnormal flow of urine from the bladder to the ureter</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td>Lack of bladder control due to a brain, spinal cord, or nerve condition</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>Inflammation or infection of the prostate gland. Acute bacterial prostatitis is a potentially serious bacterial infection of the prostate. It is accompanied by infection of the urinary tract. Occasionally, there may also be associated epididymitis or urethritis. Acute prostatitis is not considered a sexually transmitted infection, so partners are not at risk.</td>
</tr>
<tr>
<td>Flank pain</td>
<td>Pain in one side of the body, between the upper abdomen and back</td>
</tr>
<tr>
<td>SPIN and SNOUT</td>
<td>SPIN and SNOUT are commonly used mnemonics: a highly &quot;S'pecific' test, when Positive, rules IN disease (SP-P-IN), and a highly 'S'ensitive' test, when Negative rules OUT disease (SN-N-OUT).</td>
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</table>

Introduction, Background & Diagnostic Tests

What has changed since 2007?
This is an update of the 2007 Management of Bacterial Urinary Tract Infections in Primary Care. The 2012 version contains an extra section on management of urinary tract infection (UTI) in children. Updated guidance is also included for each section. New and updated information is highlighted in the text:

Antimicrobial resistance is a huge problem and limiting the use of broad spectrum antibiotics is crucial in managing the problem. This has impacted on the management of UTI in primary care. The emergence of resistant bacteria in urinary tract infections further complicates treatment options. This will be discussed later in the text.

Background
UTI implies the presence of significant bacteriuria along with characteristic signs and symptoms. This is important to bear in mind when managing the patient. UTIs are one of most common bacterial infections managed in general practice; they are the reason for between 1% and 3% of all GP consultations. New and updated information is highlighted in the text:

How are UTIs classified?
UTI can be classified as either LOWER or UPPER. LOWER UTI occurs when infection is localised to the bladder and urethra (cystitis and urethritis). LOWER UTIs are caused mostly by the ascent of organisms from the gut flora into the bladder via the urethra. Cystitis is used as a synonym for lower UTI although technically it means inflammation of the bladder and there can be non-infectious causes (e.g. radiation, chemicals). UPPER UTI includes pyelitis (infection of proximal part of the ureters) and
pyelonephritis (infection of the kidneys and proximal part of the ureters).²

**When is a UTI termed “complicated” or “uncomplicated”?**

An **uncomplicated** UTI is an infection of the urinary tract by a usual pathogen (see “What organisms cause UTIs?”) in a person with a normal urinary tract and with normal kidney function.²

**Complicated** UTI occurs when anatomic, functional, or pharmacological factors predispose the person to persistent infection, recurrent infection, or treatment failure. For example:²

- Abnormal urinary tract (e.g. calculus, vesicoureteric reflux (VUR), reflux nephropathy, neurogenic bladder, indwelling catheter, urinary obstruction, recent instrumentation)
- Virulent organism (e.g. *Staph. aureus*)
- Impaired host defences (diabetes mellitus, immune-suppressive treatment)
- Impaired renal function, or post renal transplant.

**Is it an UPPER UTI or a LOWER UTI?**

Clinically, differentiating between UPPER and LOWER UTI may be difficult. LOWER UTI is characterised by:⁵

- Frequency
- Dysuria
- Urgency
- Polyuria
- Strangury (a condition marked by slow, painful urination, caused by muscular spasms of the urethra and bladder)
- Haematuria
- Suprapubic pain or tenderness
- A change in the smell of the urine.

In UPPER UTI, onset of symptoms is typically rapid and include:⁶

- Fever
- Rigors
- Vomiting
- Loin/flank pain or tenderness
- Other manifestations of systemic inflammatory response.

**What organisms cause UTIs?**

UTI is defined by the presence of organisms in the urinary tract, which is usually sterile. Most community-acquired UTIs are caused by bacteria, although viruses, fungi and parasites can also cause infection. *Escherichia coli* (E. coli) is the most common uropathogen, accounting for about 80% of UTIs acquired in the community.⁷ *Staphylococcus saprophyticus* is also common, particularly among young women. Other pathogens include *Proteus mirabilis*, *Pseudomonas species*, *Klesbiella* species or enterococci.²⁴⁵⁴¹ *Candida albicans* rarely causes UTI in the community, but can occur in hospital patients with risk factors such as indwelling catheters, immunosuppression, diabetes mellitus, and antimicrobial treatment.²

**What are ESBLs?**

Extended-Spectrum Beta-Lactamases (ESBLs) are enzymes produced by bacteria that make them resistant to a range of antibiotics. ESBLs were first described in the 1980s when they were mainly confined to the hospital setting. However, a new class of ESBL has now emerged that is widely detected in E. coli. These ESBLs are found most commonly in UTIs (although not simple cystitis).

**Resistance – a growing problem**

Most ESBL-producing E. coli are resistant to cephalosporins, penicillins, fluoroquinolones, trimethoprim, tetracycline and some other antibiotics, leaving very limited options for oral treatment in the community, usually only nitrofurantoin. The Health Protection Agency (HPA) hopes to extend its surveillance of E. coli to include ESBL-producing E. coli as a cause of UTIs in the community.¹⁰²

**How significant is asymptomatic bacteriuria?**

Bacteriuria alone is rarely an indication for antimicrobial treatment. The diagnosis of a UTI is primarily based on symptoms and signs.¹ In people less than 65 years of age bacteriuria is abnormal in the sense that most people do not acquire this. Bacteriuria is common in some populations of institutionalised women and people with long term indwelling urinary catheters.¹ Although treatment of asymptomatic bacteriuria in pregnant women is recommended, studies show no benefit from doing so in institutionalised elderly people.⁷

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**Resistance**¹²²⁹²

- Unnecessary antibiotic treatment of asymptomatic bacteriuria is associated with *Clostridium difficile* (CDI) infection, meticillin-resistant *Staphylococcus aureus* (MRSA) infection, and the development of antibiotic-resistant UTIs.¹³⁰
- Resistance is increasing to all antibiotics used to treat UTI and there is no clear alternative to trimethoprim or nitrofurantoin. A prudent evidence-based antibiotic policy is therefore required.⁹⁶
- Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) increase risk of CDI, MRSA and resistant UTI - avoid for uncomplicated UTI.¹⁶⁹⁰
- Amoxicillin resistance is common in UTIs – use only if culture and sensitivity testing indicates.¹⁶³⁰
- Take urine culture to guide change of antibiotic for patients who do not respond to trimethoprim or nitrofurantoin.
- Fosfomycin is an unlicensed drug that may be used under the supervision of a Microbiologist in multi-resistant UTI.
- Laboratories should monitor resistance patterns of urinary pathogens and make this information routinely available to prescribers.
- Strategy for Tackling Antimicrobial Resistance (STAR) 2012-2017 has recently been published by the Department of Health (DOH). This document outlines key areas of work in addressing antimicrobial resistance. This can be accessed on the DOH website: [www.dhsspsni.gov.uk](http://www.dhsspsni.gov.uk)

In suspected UTI, which urine dipstick tests can be used?

Urine dipstick tests are the most widely used near-patient tests for UTI. Dipstick testing the urine of a patient with a suspected UTI involves detecting nitrite and *leucocyte esterase* (LE). See Table ONE. See later sections on individual patient groups for the appropriateness or otherwise of using dipstick tests in the diagnosis of UTI.¹
In the community, but can occur in hospital patients and include:

In **UPPER UTI**, onset of symptoms is typically rapid

- A change in the smell of the urine.
- Vomiting
- Rigors
- Urgency
- Frequency
- Other manifestations of systemic inflammatory reaction

**COMPASS Therapeutic Notes on the Management of Bacterial Urinary Tract Infections in Primary Care**

In a person with appropriate signs or symptoms, how should the results of a urine dipstick test be interpreted? See **Table TWO**

<table>
<thead>
<tr>
<th>Nitrite</th>
<th>Leucocyte Esterase (LE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive or negative</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
</tr>
</tbody>
</table>

*Note: when reading test WAIT for the time recommended by manufacturer.

**SECTION ONE: Management of UTI in Non-pregnant Women**

Half of all women will suffer from at least one UTI in their lifetime. Among (non-pregnant) women under 50 years of age, with acute symptoms such as dysuria, urgency, frequency or loin pain, over 70% will have bacteriuria.

How should UTI be diagnosed in non-pregnant women?

No single sign or symptom accurately predicts UTI. If dysuria and frequency are both present then the probability of a UTI is increased to greater than 90% and empirical antibiotic treatment is indicated. Symptoms suggesting vaginitis or cervicitis (such as vaginal irritation or discharge), reduce the likelihood of a diagnosis of LOWER UTI to about 20%.

**When is it appropriate to dipstick test the urine?**

In an otherwise healthy, non-pregnant woman, UTI can be diagnosed without a dipstick test of the urine and without urine culture when there are multiple typical symptoms and signs of UTI. Dipstick tests are now only recommended in women who have few symptoms and signs typical of UTI; the purpose of testing is to help decide who should be treated immediately and who should have urine cultured. See Tables ONE and TWO.

How should acute LOWER UTI in otherwise healthy women be treated?

Otherwise healthy, non-pregnant women with symptomatic LOWER UTI should receive empirical antimicrobial treatment with.
Antimicrobial courses – what is the recommended duration of therapy?

A three-day course of trimethoprim or nitrofurantoin is recommended for the treatment of simple UTI in non-pregnant women. Three days of antimicrobial therapy is similar to 5 to 10 days in achieving symptomatic cure for uncomplicated UTI in non-pregnant women, while causing fewer adverse events. Compliance is also better. Compared with prolonged treatment, a 3-day course does leave a higher risk of recurrent or persistent bacteriuria. Asymptomatic bacteriuria is associated with an increased risk of symptomatic UTI in the following week, thus 7 days treatment could be recommended for a minority of women in whom bacteriological eradication is more important (e.g. women suffering from recurrent episodes, planning a pregnancy). This decision should be taken with the patient, balancing the higher bacteriological cure rate versus the increased risk for adverse events.

Are there any other advantages to three-day courses of antimicrobials?

Most otherwise healthy women with a UTI will not have a systemic illness and frequency and dysuria usually resolve two to three days after starting treatment. This reduces the patient’s motivation to complete longer courses of treatment. Failure to complete a course can lead to an accumulation of unused medicines at home, which constitutes a hazard to children and raises the possibility of subsequent self-treatment with deteriorating or inappropriate drugs. Longer courses of antibiotics are also more expensive and associated with increased risk of adverse effects.

Are three day courses of trimethoprim being prescribed in Northern Ireland?

See Table THREE

What adverse effects are associated with trimethoprim?

Gastrointestinal disturbances and skin rashes are occasionally experienced by people taking trimethoprim. These are usually mild and are quickly reversible when trimethoprim is stopped.

Blood dyscrasias are infrequently seen, usually in people with a predisposition to folate deficiency (pregnant women, alcoholics). Regular blood counts should be undertaken with long-term trimethoprim use. On long-term treatment, patients / carers should be told how to recognise signs of blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.
Prescribing points – Trimethoprim
- Trimethoprim is a folate antagonist and therefore folate supplementation should be considered for patients on long-term trimethoprim who are taking other folate antagonists (e.g. phenytoin).
- Consider using an alternative antimicrobial for empirical treatment if trimethoprim has been taken in the past 3 months.

How should UPPER UTI in otherwise healthy women be treated?
See SECTION FIVE – Acute Pyelonephritis.

Are UTIs likely to recur?
More than 25% of women who have had a UTI will experience a recurrence.24 A patient who has three or more episodes per year of acute UTI 2,4 or two microbiologically confirmed UTIs in 6 months is said to have “recurrent” UTIs.
Women with recurrent UTIs can accurately self-diagnose a LOWER UTI.14 When a woman who has previously had LOWER UTI has symptoms suggesting a recurrence, there is an 84-92% chance that an infection is present.23,24

What are the risk factors for recurrent UTI?
In otherwise healthy, young/premenopausal women:
- Sexual intercourse
- Contraceptive use – particularly spermicides and diaphragms 13,25-27
- Antimicrobial use – can cause changes in the normal genital flora

In postmenopausal women:
- Oestrogen deficiency
- Urogenital surgery
- Incontinence
- High post-void residual

What strategies can be employed in an attempt to prevent recurrent UTIs?
Recurrent UTIs are a common and debilitating problem. Consider the following management options if there are three or more episodes per year:
- Imaging investigations – plain abdominal X-ray and ultrasound of kidneys, ureters and bladder
- Patient-initiated antimicrobials for new episodes (“stand-by antimicrobials”) OR
- Professional-initiated antimicrobials for new episodes (i.e. usual treatment when required) OR
- Antimicrobial prophylaxis, (see later)
- A trial of cranberry extract (see later).

How should antimicrobial prophylaxis be used?
Long-term antimicrobial prophylaxis against recurrent UTI can be given at bedtime, using nitrofurantoin 50mg at night or trimethoprim 50-100mg at night.16 Long-term prophylaxis usually entails administration for 6-12 months. Prophylaxis for recurrent urinary tract infection should not be undertaken until a negative culture 1 to 2 weeks after treatment has confirmed eradication of the urinary tract infection.103 Future infections will require a different choice of antibiotic for treatment.

How should post-coital prophylaxis be used?
If UTI episodes occur frequently after sexual intercourse, antimicrobial prophylaxis can be prescribed. Post-coital prophylaxis is as effective as prophylaxis taken nightly.16 The following prophylactic doses can be taken every night or as a stat post-coital dose:
- Nitrofurantoin 50mg, or
- Trimethoprim 100mg.
This treatment can be continued for several years if necessary.28 It may be a more acceptable method of prophylaxis for some women.98

Chart ONE: Management of suspected LOWER UTI in non-pregnant women

<table>
<thead>
<tr>
<th>Woman with signs and/or symptoms of UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal itch or discharge? YES</td>
</tr>
<tr>
<td>Probability of UTI is low. Explore alternative diagnoses. Consider pelvic examination</td>
</tr>
<tr>
<td>Multiple symptoms of UTI? NO</td>
</tr>
<tr>
<td>≤ 2 symptoms or mild symptoms</td>
</tr>
<tr>
<td>Obtain a urine sample and dipstick test for nitrite and/LE</td>
</tr>
<tr>
<td>Nitrile positive? (LE positive or negative)</td>
</tr>
<tr>
<td>Probable LOWER UTI. Start empirical antimiicrobial</td>
</tr>
<tr>
<td>Nitrile negative AND LE negative?</td>
</tr>
<tr>
<td>UTI unlikely, reassure and give advice on managing symptoms. However if symptoms are severe a urine culture may be appropriate</td>
</tr>
<tr>
<td>Nitrate negative and LE positive?</td>
</tr>
<tr>
<td>UTI possible. Send urine sample for culture. Start empirical antimicrobial</td>
</tr>
</tbody>
</table>

(Ref – COMPASS Therapeutic Notes UTI 2007)
Is there a role for topical oestrogen creams in preventing recurrent UTI?
Topical application of an oestrogen cream to prevent recurrent UTI in post-menopausal women is not recommended in the UK. However some gynaecological specialists follow North American guidelines and continue to prescribe topical oestrogens and oestrogen containing prosthetic rings for this indication. None of the available vaginal oestrogen creams are licensed for this indication.

What has been shown to have NO association with recurrent UTI?
There is no association between recurrent UTI and:
- Pre- or post-coital voiding patterns
- Frequency of urination
- Delayed voiding habits

Is asymptomatic bacteriuria significant in pregnancy?
Asymptomatic bacteriuria (persistent bacterial colonisation of the urinary tract in the absence of specific symptoms) occurs in 5-10% of all pregnancies and has been associated with premature labour and delivery, clinical or subclinical chorioamnionitis (inflammation of the foetal membranes), postpartum fever in the mother and neonatal infection. UTI in pregnancy may lead to maternal complications such as septic shock, respiratory insufficiency, fluid balance disorders, and chronic renal insufficiency. Foetal complications include developmental delays, cerebral palsy and death.

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SECTION TWO: Management of UTI in Pregnant women
UTIs are among the most common health problems during pregnancy. They occur in 17% to 20% of pregnancies and have been associated with prematurity and delivery, clinical or subclinical chorioamnionitis (inflammation of the foetal membranes), postpartum fever in the mother and neonatal infection. UTI in pregnancy may lead to maternal complications such as septic shock, respiratory insufficiency, fluid balance disorders, and chronic renal insufficiency. Foetal complications include developmental delays, cerebral palsy and death.

Is asymptomatic bacteriuria significant in pregnancy?
Asymptomatic bacteriuria (persistent bacterial colonisation of the urinary tract in the absence of specific symptoms) occurs in 5-10% of all pregnancies. E. coli is the most common pathogen associated with asymptomatic bacteriuria. Other organisms include other gram negative bacteria and group B streptococci. While asymptomatic bacteriuria in non-pregnant women is generally benign, obstruction to the flow of urine in pregnancy leads to stasis and increases the likelihood that pyelonephritis will complicate asymptomatic bacteriuria. 10-30% of women with bacteriuria in the first trimester develop UPPPER UTI in the second or third trimester.

In contrast to other patient groups, treatment of asymptomatic bacteriuria in pregnancy does more good than harm.

Who should be screened for asymptomatic bacteriuria in pregnancy?
All pregnant women should be screened for bacteriuria at their first antenatal visit.

How should asymptomatic bacteriuria in pregnancy be screened for?
The performance of dipstick testing (leucocyte esterase or nitrite) is not sufficiently sensitive to be used as a screening test for bacteriuria in pregnancy. Quantitative urine culture remains the gold standard for diagnosis of bacteriuria in pregnancy.

Which dipstick tests are appropriate in pregnancy?
Dipstick testing for UTI (LE or nitrate) is not sufficiently sensitive to be used as a screening test. Urine culture should be the investigation of choice.

Is nitrofurantoin safe in pregnancy?
Nitrofurantoin is not an effective treatment for UPPPER UTI because it does not achieve effective concentrations in the blood and upper urinary tract. Amoxicillin is not suitable as empirical treatment; only use where sensitivity has been confirmed.

Which women should be referred for assessment by a specialist?
Consider referring women with recurrent UTI for specialist assessment after prophylaxis with an antimicrobial or cranberry product (see later) have failed.

How should asymptomatic bacteriuria in pregnancy be treated?
If bacteriuria is found, confirm its presence with a second urine culture. Treat confirmed asymptomatic bacteriuria for 7 days with an antimicrobial to which the organism is sensitive (first-line choices when sensitivities are known are shown in Table FIVE). Repeat urine cultures 7 days after completion of treatment, and then at every antenatal visit for the rest of the pregnancy. Women who do not have bacteriuria in their first trimester do not need repeated urine cultures.

How should symptomatic bacteriuria in pregnancy be treated?
At any stage of pregnancy, women with symptomatic UTI should be treated with an antimicrobial. A single urine sample should be taken before empiric antimicrobial treatment is started.

Table FIVE: Antimicrobial choices for the management of UTI in pregnancy (asymptomatic and symptomatic bacteriuria) when sensitivities are known.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefalexin</td>
<td>500mg three times daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Nitrofurantoin*</td>
<td>50 to 100mg four times daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>200mg twice daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500mg three times daily</td>
<td>7 days</td>
</tr>
</tbody>
</table>

* Nitrofurantoin is not an effective treatment for UPPPER UTI because it does not achieve effective concentrations in the blood and upper urinary tract.

Antimicrobial use should be interrupted in early pregnancy where possible (5-16 weeks) to avoid the theoretical risk of congenital malformations. Retrospective reviews and studies of well-defined groups of men with specified anatomical abnormalities (e.g. indwelling catheter, neurogenic bladder, vesicoureteric reflux, anatomical abnormalities) have bacteriuria in their first trimester do not need changed to one to which the organism is sensitive (first-line choices when sensitivities are known are shown in Table FIVE). Repeat urine cultures 7 days after completion of treatment, and then at every antenatal visit for the rest of the pregnancy. Women who do not have bacteriuria in their first trimester do not need repeated urine cultures.

How should symptomatic bacteriuria in pregnancy be treated?

At any stage of pregnancy, women with symptomatic UTI should be treated with an antimicrobial. A single urine sample should be taken before empiric antimicrobial treatment is started. The performance of dipstick testing (leucocyte esterase or nitrite) is not sufficiently sensitive to be used as a screening test for bacteriuria in pregnancy. Quantitative urine culture remains the gold standard for diagnosis of bacteriuria in pregnancy.

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How should asymptomatic bacteriuria in pregnancy be screened for?
The performance of dipstick testing (leucocyte esterase or nitrite) is not sufficiently sensitive to be used as a screening test for bacteriuria in pregnancy. Quantitative urine culture remains the gold standard for diagnosis of bacteriuria in pregnancy.

Which dipstick tests are appropriate in pregnancy?
Dipstick testing for UTI (LE or nitrate) is not sufficiently sensitive to be used as a screening test. Urine culture should be the investigation of choice.
A Cochrane review was unable to determine if any particular antimicrobial was more effective for symptomatic UTI during pregnancy in terms of cure rates, recurrent infection, preterm delivery, premature rupture of membranes, admission to neonatal intensive care, need for change of antimicrobial and incidence of prolonged pyrexia.34

Given the risks of bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antimicrobial treatment as a test of cure, and then at every antenatal visit for the rest of the pregnancy.1,2

Is nitrofurantoin safe in pregnancy?
Data indicate that the use of nitrofurantoin during pregnancy has not been associated with an increased risk of congenital malformations. Retrospective reviews and a large number of case reports suggest that there is no significant increase in the risk of congenital malformations or other adverse pregnancy outcomes associated with use of nitrofurantoin during pregnancy.39 Nitrofurantoin can cause haemolysis in patients with G6PD deficiency leading to a theoretical risk of intratuterine haemolysis, particularly following third trimester exposure.35

Is trimethoprim safe in pregnancy?
The BNF and the manufacturers of trimethoprim warn against its use in pregnancy.32,43 This is based on the knowledge that as a folate antagonist, trimethoprim may limit the availability of folic acid to the foetus and impair normal development. The National Teratology Information Service, however, indicates that trimethoprim need only be avoided in women with low folate status (i.e. women with established folic acid deficiency or low dietary intake, or in those already taking known folate antagonists)44 and that in women with normal folate status, short-term use of trimethoprim is unlikely to induce folate deficiency. However, folate supplementation is recommended in all women treated with trimethoprim during the first trimester as a precautionary measure.44

Should any other measures be recommended in pregnancy?
- Paracetamol may be given for symptomatic relief.
- Urine alkalinizing products should not be used as there is insufficient evidence on their effectiveness.2

SECTION THREE: Management of UTI in Men

In men, issues such as pathogenesis, risk factors, investigations, follow-up, choice of antimicrobial and duration of treatment of UTI have received little attention in the medical literature. There is a lack of studies of well-defined groups of men with specified types of UTI.45-47

UTIs in men are usually viewed as complicated because they result from an anatomical or functional anomaly or instrumentation of the genitourinary tract.48 Additionally, between 52-90% of men with a UTI have prostatic involvement,42,43 which may lead to complications such as prostatic abscess or chronic bacterial prostatitis.

Conditions like prostatitis, chlamydial infection and epididymitis should be considered in the differential diagnosis of men with acute dysuria or frequency and appropriate diagnostic tests should be considered.

In this discussion, the term “LOWER UTI” implies infection of the bladder and possibly the urethra with no clinical evidence of prostatitis, epididymitis, or orchitis. “UPPER UTI” includes pyelitis and pyelonephritis. In patients with a history of fever or back pain the possibility of UPPPER UTI should be considered.

How common is UTI in men?
UTI is considerably less common in men than in women (except in the elderly and in men with long-term indwelling urinary catheters).46 In men, as in women, the incidence of UTI increases substantially with advancing age, co-existing illnesses, and institutional care.3 UTI is very uncommon in otherwise healthy young and middle-aged men.79

What are the risk factors for UTI in men?
Most UTIs in men are not associated with any risk factor. However, the following risk factors need to be excluded or managed, especially in recurrent UTI:
- Immunocompromised state.
- Previous urinary tract surgery.
- Incomplete bladder emptying (e.g. caused by obstruction with prostatic enlargement, blocked or misplaced indwelling catheter).
- Abnormalities of urinary tract function or structure (e.g. indwelling catheter, neurogenic bladder, vesicoureteric reflux, anatomical abnormalities).
- Incomplete bladder emptying (e.g. caused by obstruction with prostatic enlargement, blocked or misplaced indwelling catheter).
- Paracetamol may be given for symptomatic relief.
- Fever, cloudy or foul-smelling urine may be present.
- Changes in signs or symptoms.
- New or worsening urinary incontinence.
- Suprapubic discomfort and flank or loin tenderness.
- Signs of septicaemia and generalised illness.

Is it necessary to send a urine sample for culture and sensitivity testing if UTI is suspected in a man?
Yes, prior to starting an antimicrobial, culture the urine whenever UTI is suspected in a man. The results will usually help to confirm the diagnosis and guide
treatment. Note however that asymptomatic bacteriuria, particularly in very elderly men with prostatic enlargement, may also give positive results.

**How should LOWER UTI in a man be treated?**

Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones, cephalosporins) are no longer recommended first line due to antimicrobial resistance. The HPA now recommends a seven day course of trimethoprim or nitrofurantoin as first line treatments of lower UTI in men.

**What if there is prostatitis also present?**

Up to 90% of men with febrile UTI will have a concomitant infection of the prostate. Therefore the goal is not only to sterilise the urine but also to eradicate the prostatic infection. Quinolones (e.g. ciprofloxacin, norfloxacin, ofloxacin) reach free concentrations in prostatic tissue and prostatic fluid that exceed the minimum inhibitory concentrations of most of the causative bacteria.

**How to confirm prostatitis?**

Urine dipstick tests will suggest presence of white blood cells and bacteria in the urine. However, a urine culture will be required to confirm prostatitis. Prostatic secretions should not be collected.

**How to treat prostatitis?**

Bacterial UTI with symptoms suggestive of prostatitis should be treated empirically with a quinolone for four weeks. Trimethoprim also yields good concentrations in the prostate and is an alternative to quinolones provided the causative bacteria are fully sensitive to trimethoprim. In contrast, the use of β-lactam antimicrobials and nitrofurantoin should be discouraged because of the low concentrations attained by these agents in the prostate. Patients who do not respond to antimicrobial treatment should be referred for investigation for prostatitis.

**How should recurrent UTI in a man be managed?**

Each episode should be treated as an acute infection. If two or more episodes of UTI occur in 3 months, look for an underlying cause such as:

- Prostatitis
- Prostatic enlargement due to cancer or benign prostatic hypertrophy
- Calculi
- Bladder carcinoma
- Vesicoureteric reflux (VUR)

Also, in sexually active men, rule out chlamydial infection.

**Trimethoprim is not recommended if it has been used in the past 12 months – increased risk that infection is due to a resistant organism.**

**How should UTI in an elderly man be managed?**

UTI in an elderly man should be managed similarly to that in a younger man, but the following should be taken into account:

- In elderly men, UTI may present with non-specific features, including an acute confusional state
- UTI, especially recurrent UTI, in elderly men may be due to prostatic enlargement and/or prostatitis

**N.B. Asymptomatic bacteriuria in an elderly man should not be treated.**

**Which men need specialist referral?**

Referral for assessment by a specialist should be considered for men who have:

- Suspected UPPPER UTI
- Failed to respond to appropriate antimicrobial therapy
- Frequent episodes of UTI (e.g. two or more episodes within one or two years)
- Features of urinary obstruction
- A history of pyelonephritis, calculi, or previous genitourinary tract surgery.

**SECTION FOUR: Management of UTI in patients with long term indwelling catheters**

All patients with a long term indwelling catheter are bacteriuric, often with two or more organisms. The catheter provides a focus for bacterial biofilm formation. Antibiotics should not be given to patients with indwelling catheters with bacteriuria who are asymptomatic. Indeed there is evidence that repeated treatment of asymptomatic bacteriuria increases the risk of colonisation by drug-resistant bacteria.

**How should UTI be diagnosed in patients with indwelling catheters?**

Classical UTI signs and symptoms do not always apply. Symptoms that may suggest UTI in patients with catheters include fever, flank or suprapubic discomfort, nausea, vomiting, malaise or confusion. Fever is the most common symptom of UTI in patients with catheters. However it is non-specific and its absence does not exclude UTI.

**Should dipstick tests be used?**

Dipstick tests should not be used as they will not differentiate between symptomatic and asymptomatic bacteriuria in patients with catheters.

**Should a person with an indwelling catheter be screened routinely for asymptomatic bacteriuria?**

No, people with indwelling catheters should not be screened for asymptomatic bacteriuria. All persons with long-term indwelling catheters will have bacteriuria at some stage. SIGN guidelines recommend that:
● Urine be cultured only in those who become symptomatic
● Catheterised people with asymptomatic bacteriuria should not receive antimicrobial treatment.

**Renal impairment**

**Trimethoprim**
- Reduce dose in renal impairment:
  - GFR 15 to 30mL/min – use half the normal dose after 3 days
  - GFR < 15mL/min – use half the normal dose
  - (Monitor plasma trimethoprim concentration if GFR <10mL/min)
- Caution particularly in the elderly with chronic renal impairment – ensure a recent renal function test is performed when prescribing.

**Nitrofurantoin**
- People with renal impairment (GFR <60 mL/min) should not be treated with nitrofurantoin as.
- An effective concentration of antimicrobial in the urine is not achievable
- A toxic concentration of antimicrobial can occur in the plasma.

Should antimicrobial prophylaxis be prescribed to prevent catheter-related UTI?
In general, antimicrobial prophylaxis is not recommended for the prevention of symptomatic UTI in catheterised patients. Studies have shown that antibiotic prophylaxis reduces the number of cases of asymptomatic bacteriuria but not those of symptomatic bacteriuria. Antimicrobial prophylaxis may be considered in patients for whom the number of infections are of such frequency or severity that they chronically impinge on function and well-being.

**When to refer to hospital?**
If systematic symptoms such as fever, rigors, chills, vomiting or confusion appear.

**Intermittent catheterisation**
Patients sometimes intermittently self-catheterise in order to manage urinary retention or incontinence, often due to a neuropathic or hypotonic bladder. In intermittent catheterisation the catheter is inserted into the urethra several times a day. Current evidence suggests that these patients should be managed in the same way as patients with long term indwelling catheters.

**SECTION FIVE: Acute Pyelonephritis**

What is pyelonephritis?
Pyelonephritis is inflammation of the UPPER urinary tract, specifically of the parenchyma of the kidney and the lining of its renal pelvis. Pyelonephritis is mainly caused by bacterial infection and can be acute or chronic. The management of chronic pyelonephritis is outside the remit of this review.

Uncomplicated V complicated?
Pyelonephritis is considered to be uncomplicated if the infection is caused by a typical pathogen in an immunocompetent person who has normal renal anatomy and renal function. It is considered to be complicated if there are factors that increase susceptibility or reduce the person’s response to infection, such as:
- Anatomical abnormality
- Renal stone, urinary, ureteric, or nephrostomy catheter
- Immuno-compromise
- Instrumentation
- Obstruction
- Pregnancy

Routine use of antimicrobial prophylaxis during catheter change should be avoided.

How should symptomatic UTI in catheterised patients be managed?
Catheter care and function should be reviewed, including checking if the catheter is blocked. The catheter will need to be changed as it is likely to be the source of the infection. However, before doing so, send a urine sample for culture. If practical, withhold antimicrobials until the result of urine culture is available to guide the choice of antimicrobial. However, empiric antimicrobials could be started, taking into account the severity of the presentation and any co-morbidity.

If, following a diagnosis of UTI, the catheter is to be changed, this should be carried out under antibiotic cover.

If there is flank/loin pain or tenderness, treat as for UPPER UTI (see later, SECTION FIVE, Acute Pyelonephritis) otherwise, treat for 7-14 days with an antimicrobial appropriate for LOWER UTI (i.e. trimethoprim or nitrofurantoin). Take into account any previous treatments and culture results when choosing an antimicrobial for empirical treatment. Once urine cultures are available, if necessary change the antimicrobial to one to which the organism is sensitive.

What are the symptoms of acute pyelonephritis?
The following symptoms can develop rapidly over a few hours or a day and include:
- High fever
- Rigors
- Costovertebral angle (loin) pain – usually unilateral and may worsen on micturition
- Nausea
- Vomiting
- Diarrhoea

Symptoms of LOWER UTI (e.g. frequency, dysuria) and suprapubic pain may also be present. Because the symptoms of pyelonephritis can be minimal or even absent, silent (subclinical) pyelonephritis should be suspected in a person who presents with symptoms of LOWER UTI that has not responded to treatment. It has been suggested that silent pyelonephritis may be present in up to 30% of women with symptoms of LOWER UTI.

How should UPPER UTI be treated?
UPPER UTI can be accompanied by bacteraemia, making it a life-threatening infection. A mid-stream urine sample should be taken for culture and empirical antibiotics commenced. The HPA and the AMM
(Association of Medical Microbiologists) recommend that men and non-pregnant women (including those with a long-term, indwelling catheter) with suspected acute upper UTI should be started on ciprofloxacin (500mg twice daily) for 7 days or co-amoxiclav (500mg/125mg three times a day) for 14 days.¹ ¹, ¹⁸, ¹⁷ Hospitalisation should be considered in patients:
● unable to take fluids/medication
● showing signs of severe sepsis
● who do not respond to antibiotics within 24 hours (due to antibiotic resistance).³

Prescribing points – treating pyelonephritis with ciprofloxacin
► Ciprofloxacin is preferably avoided in pregnancy due to the theoretical risk of arthropathy. Ciprofloxacin should be reserved for serious life threatening conditions unresponsive to standard antibiotic therapy in pregnancy.
► Because quinolones can lower seizure threshold, avoid ciprofloxacin in people with epilepsy or conditions that predispose to seizures.³²
► Concurrent NSAID and quinolone use should also be avoided due to increased risk of convulsions.³³
► Ciprofloxacin can rarely cause tendon damage. Treatment should be stopped if pain or inflammation of a tendon occurs.³²
► Ensure that the patient has an adequate fluid intake during the ciprofloxacin course as there is a risk of crystalluria.
► Risk of C. difficile – recent strains of C. difficile are resistant to quinolones, which make them a major cause of C. difficile infection.³⁴

Remember to prescribe ciprofloxacin generically. (Ten Ciproxin® 500mg tablets cost £12.49 compared to £1.00 for ten non-branded ciprofloxacin 500mg tablets).³³

Prescribing points – upper UTI:
► Nitrofurantoin is an ineffective treatment for upper UTI because it does not achieve effective concentrations in the blood and upper renal tract.
► Resistance to trimethoprim is too common to recommend this drug for empirical treatment of suspected upper UTI. However, trimethoprim can be prescribed if culture results have been obtained and the uropathogens are susceptible.¹ ¹⁶

What else should be considered if a person is being managed at home?
In a person with pyelonephritis being managed at home (having obtained a urine sample for culture and sensitivity testing and started an empirical antimicrobial),³⁹
● Treat pain and fever with paracetamol (ibuprofen is best avoided as NSAIDs may impair renal function).
● Encourage intake of fluids and ensure adequate hydration.
● Advise the person to seek early medical advice if their condition is deteriorating or if there is no response to treatment in 24 hours.
● If there is no response to treatment in 24 hours, consider hospital admission.
● Review within 48 hours anyway, to assess response to treatment and to ensure the person is taking an appropriate antimicrobial.

How should pyelonephritis in pregnancy be managed?
The incidence of pyelonephritis increases in pregnancy. Overall it occurs in 1-2% of all pregnancies.⁶² Because of the risks to mother and child, pregnant women with pyelonephritis should be admitted to hospital.⁵⁹

SECTION SIX: Management of UTI in Children
How common are UTIs in children?
UTI is a common bacterial infection causing illness in infants and children.⁷¹ Approximately 7 to 8% of girls and 2% of boys have a urinary tract infection during the first 8 years of life.⁶¹, ⁶²

Problems in diagnosing UTIs in children
It may be difficult to recognise UTI in children because:
● presenting symptoms and signs are non-specific, particularly in infants and children younger than 3 years.⁶⁸
● young children cannot clearly articulate symptoms
● when children wear nappies, parents are not aware of the classic dysuria and frequency symptoms as experienced by adults
● obtaining an adequate urine sample can be frustrating, time consuming, and costly.⁷¹ Diagnosis of UTI is therefore often delayed and may be missed in up to 50% of children presenting to primary care.⁷¹ Sometimes symptoms are incorrectly attributed to other causes, e.g. otitis media.⁷¹, ⁶¹

What are the risk factors for UTI in children?
The following can be present:
● Poor urine flow
● History suggesting previous UTI or confirmed previous UTI

How should pyelonephritis in pregnancy be managed?
The incidence of pyelonephritis increases in pregnancy. Overall it occurs in 1-2% of all pregnancies.⁶² Because of the risks to mother and child, pregnant women with pyelonephritis should be admitted to hospital.⁵⁹

Shoul
From this point this document will cover only management of UTIs in children over 3 months of age.

When to suspect a UTI in children over 3 months of age?
Suspect a UTI with any combination of the following signs and symptoms:
- Unexplained fever of 38°C or higher (most common presentation in preverbal children).
- Frequency, dysuria (most common presentation in verbal children).
- Poor response to treatment for a presumed alternative site of infection.
- Abdominal pain, loin tenderness, vomiting, poor feeding, malaise, lethargy, irritability, haematuria, offensive urine, cloudy urine, failure to thrive.
- Dysfunctional voiding, incontinence of urine or faeces, new onset of bedwetting.69

How to confirm a UTI in children?
- Preliminary diagnosis as per clinical symptoms PLUS
- Urine testing:
  - 3 months to 3 years: urgent microscopy (or dipstick if unavailable)
  - 3 years plus: urine dipstick for leukocyte esterase and nitrite (or microscopy if available),54,60
- A urine sample should be tested after 24 hours at the latest.68

TABLE SIX: NICE Clinical Guideline 54 –
Presenting symptoms and signs in infants and children over 3 months of age with UTI68

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>Most common</th>
<th>Least common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preverbal: Fever</td>
<td>Abdominal pain</td>
<td>Lethargy</td>
</tr>
<tr>
<td></td>
<td>Loin tenderness</td>
<td>Irritability</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>Haematuria</td>
</tr>
<tr>
<td></td>
<td>Poor feeding</td>
<td>Offensive urine</td>
</tr>
<tr>
<td></td>
<td>Failure to thrive</td>
<td></td>
</tr>
<tr>
<td>Verbal: Frequency</td>
<td>Dysuria</td>
<td>Fever</td>
</tr>
<tr>
<td></td>
<td>Dysfunctional voiding</td>
<td>Malaise</td>
</tr>
<tr>
<td></td>
<td>Changes to continence</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
<td>Haematuria</td>
</tr>
<tr>
<td></td>
<td>Loin tenderness</td>
<td>Offensive urine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cloudy urine</td>
</tr>
</tbody>
</table>

Table SEVEN: NICE Clinical Guideline 54 –
Interpretation of microscopy results in children68

<table>
<thead>
<tr>
<th>Microscopy Results</th>
<th>Pyuria positive</th>
<th>Pyuria negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriuria positive</td>
<td>The infant or child should be regarded as having UTI</td>
<td>The infant or child should be regarded as having UTI</td>
</tr>
<tr>
<td>Bacteriuria negative</td>
<td>Antibiotic treatment should be started if clinically UTI</td>
<td>The infant or child should be regarded as not having UTI</td>
</tr>
</tbody>
</table>

How to distinguish between LOWER and UPPER UTI in children?
Diagnose UPPER UTI (acute pyelonephritis) if:
- Fever of greater than 38°C (or history of fever) and bacteriuria
- Fever of less than 38°C (and no history of fever) with loin tenderness and bacteriuria.69

All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered to have LOWER UTI (cystitis).68
C-reactive protein alone should not be used to differentiate acute pyelonephritis/upper urinary tract infection from cystitis/lower urinary tract infection in infants and children.68

When to refer to a paediatric specialist?
Some children presenting with UTI symptoms will require referral to secondary care. It is important to distinguish between those children who require referral to a General Paediatric Clinic and those that require referral to a Paediatric Nephrologist:

General Paediatric Clinic68
- All children under 3 months of age will require an immediate referral.
- Children over 3 months of age if the UTI is recurrent OR who have abnormal imaging (if carried out at request of GP).
- Children with atypical features of UTI (see below for ‘what is ‘atypical’ UTI in children’) OR the child appears seriously unwell.
- Children presenting with dysfunctional voiding.

Paediatric Nephrologist
If child presents with any of the following refer to a nephrologist:
- Bilateral renal abnormalities
- Raised creatinine
- Raised blood pressure
- Proteinuria

What is ‘atypical’ UTI in children?
The following symptoms are suggestive of an atypical UTI:
- Seriously ill
- Poor urine flow
- Abdominal or bladder mass
- Raised creatinine
- Septicaemia
- Failure to respond to treatment with suitable antibiotics within 48 hours
- Infection with non-E. coli organisms.

Infants and children with atypical UTI should have ultrason of the urinary tract during the acute infection to identify structural abnormalities of the urinary tract such as obstruction. This is to ensure prompt management.68

How to manage LOWER UTI in children?
Accurate and timely diagnosis of UTI is important to allow appropriate treatment.51
Treatment is as follows:
- Oral antibiotic for 3 days.
- Choice of antibiotic will depend on locally developed multidisciplinary guidance. Avoid broad spectrum antibiotics.69 See ‘Choice of Antibiotic’ later.
- Treat empirically, then on basis of sensitivity.
- Treat fever and pain with paracetamol.50
- Encourage adequate fluid intake.69
- Emphasise importance of not delaying voiding.68

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Parents/carers should be advised to bring the child for reassessment if the child is still unwell after 24 to 48 hours. If an alternative diagnosis is not made, a urine sample should be sent for culture to identify the presence of bacteria and determine antibiotic sensitivity (if this has not already been carried out).68

Choice of antibiotic
The Northern Ireland Antimicrobial Guidelines for Primary Care recommends a three day course of either trimethoprim or nitrofurantoin for uncomplicated LOWER UTI in children.77

Trimethoprim
1 month – 12 years: 4mg/kg (max 200mg) twice daily for 3 days OR
3 – 6 months 6–8kg 30mg (3mL) twice daily
6 – 12 months 8–10kg 40mg (4mL) twice daily
1 – 5 years 12kg 50mg (5mL) twice daily
6 – 12 years 25kg 100mg (10mL) twice daily
Available as trimethoprim 50mg/5mL suspension.

Nitrofurantoin
3 months –12 years: 750micrograms/kg four times a day for 3 days43,69,75
Available as nitrofurantoin 25mg/5mL suspension.

Should asymptomatic bacteriuria in children be treated?
No, asymptomatic bacteriuria in infants and children should not be treated with antibiotics.

How to manage UPPER UTI in children?
Acute pyelonephritis is the most common serious bacterial infection in childhood. Most cases are readily treated, provided diagnosis is prompt, though in some children fever may take several days to abate. Oral antibiotics OR short courses of IV therapy (2 to 4 days) followed by oral therapy may be used.72 Parenteral antibiotic therapy and hospitalisation should be considered for children who appear to be severely ill or dehydrated, who are unable to retain oral intake. As in LOWER UTI, infants under 3 months of age will require hospitalisation.73

Therefore, if treating in primary care, management is as follows:
● Oral antibiotic for 7 to 10 days68,69
● Obtain urine specimen before starting antibiotics.
● Consider co-amoxiclav or a cephalosporin (depending on local sensitivity patterns)68,73
● Treat fever and pain with paracetamol.68
● Encourage adequate fluid intake.68

Co-amoxiclav
3mths – 1 year: 0.25mL/kg of 125mg/31mg suspension TDS.
1 – 6 years: 5mL OR 0.25mL/kg of 125mg/31mg suspension TDS.
6 – 12 years: 5mL or 0.15mL/kg of 250mg/62mg suspension TDS.
NB – double dose in severe infection76
Available as co-amoxiclav 125mg/31mg and 250mg/62mg suspensions.

What follow-up will be required?
The incidence of recurrent UTI within 12 months of an initial UTI is approximately 12 to 30%.83,84 Parents/carers should be counselled on the possibility of a UTI recurring, the need for vigilance, and to seek prompt treatment from a healthcare professional for any suspected re-infection.85

Repeated UTIs in children can result in renal scarring, which can cause long term morbidity including hypertension, chronic renal failure (early adulthood) and eclampsia (in pregnancy).70

Long-term antibiotic prophylaxis and surgery are not routinely recommended but may be considered in some patients with recurrent UTIs (see later).68,73

When are imaging tests indicated?
● Recurrent episodes of infection are an indication for imaging tests.75 This is to detect any renal or urinary tract abnormalities that may predispose to repeated UTIs. The most common abnormality detected in children is vesicoureteric reflux.70
● Dysfunctional elimination syndromes and constipation should be addressed in infants and children who have had a UTI.68
● Children presenting with ‘atypical’ symptoms.

What is considered recurrent UTI in children?68
● Two or more episodes of UTI with acute pyelonephritis/upper urinary tract infection, or
● One episode of UTI with acute pyelonephritis/upper urinary tract infection plus one or more episode of UTI with cystitis/lower urinary tract infection, or
● Three or more episodes of UTI with cystitis/lower urinary tract infection.

When to use antibiotic prophylaxis in children?
Early diagnosis and treatment are the most effective prophylactic treatment against renal scarring in every case of pyelonephritis in children.77 Evidence is lacking that prophylactic antibiotics reduce the incidence of recurrent childhood UTI.76 prophylaxis has been shown to be effective in reducing the number of positive urine cultures, however a significant reduction in the number of symptomatic infections or new renal scarring have not been demonstrated.73,74,75 Therefore:
● Antibiotic prophylaxis should not be routinely recommended in infants and children following first-time UTI, but may be considered in infants and children with recurrent UTI.88,68
● If an infant or child is receiving prophylactic medication and develops an infection, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.
● Choice of antibiotic for prophylaxis include: nitrofurantoin and trimethoprim.75

Nitrofurantoin
3mths – 12 years: 1mg/kg at night.43

Trimethoprim
2mg/kg (max 100mg) at night OR
6 weeks – 6 months: 12.5mg at night
6 months – 6 years: 25mg at night
6 – 12 years: 50mg at night.75

What risks are associated with prophylaxis?
● Inconvenient for the patient and parent/carer.
● Poor adherence.
● Adverse effects, e.g. vomiting or gastrointestinal intolerance.
● Colonisation with resistant organisms in patient.
● Important to continually ensure that the dose is appropriate as the weight of the child increases over
time. This will be particularly important in very young children.
  ● Bacterial resistance in wider population.73,74,76,96

Any evidence for circumcision to reduce incidence of UTIs in children?
Circumcision has been shown to be associated with a reduced risk of urinary tract infection: circumcised male infants have a three to ten-fold reduced risk of UTI than non-circumcised boys.85,86,97 However, clinical benefit relates only to boys at high risk for urinary tract infection or boys with high-grade vesicoureteric reflux.73,86 Furthermore, routine circumcision is not a recommendation in Western European countries.97

Any evidence on the effectiveness of cranberry products reducing UTIs in children?
See SECTION SEVEN.

<table>
<thead>
<tr>
<th>Summary table – managing LOWER UTI in primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Group</strong></td>
</tr>
<tr>
<td>Non-pregnant women</td>
</tr>
<tr>
<td><em>Pregnant women</em></td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Patients with long-term indwelling catheters</td>
</tr>
<tr>
<td><em>Children (3mth+)</em></td>
</tr>
</tbody>
</table>

**SECTION SEVEN: Cranberry Products**

Cranberry products are a popular choice of complementary therapy for UTI. Cranberry has been used anecdotally for centuries, undergoing a revival in recent years for UTI management. Evidence is growing to support its use in the management of UTI, however, further research is still required to determine optimum benefit of cranberry.1,63,97

In which patient groups have cranberry products been shown to be effective?
Cranberry products have been shown to be more effective in preventing UTI in adult women with recurrent UTI than in any other patient group.65 The evidence is currently inconclusive in elderly men and women, patients requiring catheterisation, and in children.1,63,97
and concentrations may vary between batches of the concentration of active ingredients is not always stated, pharmacies, herbalists and supermarkets. Cranberry products are not available on prescription, with caution in people with diabetes.

What types of cranberry products are available?
Cranberry can be taken as tablets or capsules, juice drinks, or the fresh berries themselves. Cranberry tablets or capsules are convenient and are available as “high strength” formulations. Most of the cranberry tablets or capsules are convenient and are available as “high strength” formulations. Most of the "high-strength" capsules and tablets are stated to contain between 200mg and 400mg of cranberry extract, equivalent to between 5 to 10 grams of fresh cranberries (5 fresh cranberries weigh approximately 5 grams). Cranberry juice drinks probably contain a lot less active ingredients than tablets or capsules. In addition, juice drinks often contain a high concentration of sugar (to mask the bitter taste) and as such should be used with caution in people with diabetes. Cranberry products are not available on prescription, but are readily available from most health food shops, pharmacies, herbalists and supermarkets. Cranberry products are not regulated and as such, the concentration of active ingredients is not always stated, and concentrations may vary between batches of the same product.

What evidence exists?
A Cochrane Review concluded that cranberries were better than placebo in preventing recurrence of UTI in menopausal women without causing severe adverse effects. A RCT suggested beneficial results in terms of preventing symptomatic recurrences of UTI in children. No evidence to support use of cranberry products for reducing UTI in men has been located.

Any comparison to other prophylactic therapies?
It has been reported that cranberry products are not as effective as nightly antibiotic treatment given for six months, or post-coital antibiotic prophylaxis for six months, in preventing UTI. One study showed that trimethoprim had only limited advantage over cranberry in preventing recurrent UTI in older women (and had more adverse effects).

How does cranberry work against UTI?
No definitive mechanism has been established. However it has been postulated that cranberry inhibits the uropathogen E. coli at the uroepithelium. That is to say, cranberry prevents bacteria sticking to the walls of the bladder and causing infection.

What type of cranberry products are available?
Cranberry can be taken as tablets or capsules, juice drinks, or the fresh berries themselves. Cranberry tablets or capsules are convenient and are available as “high strength” formulations. Most of the “high-strength” capsules and tablets are stated to contain between 200mg and 400mg of cranberry extract, equivalent to between 5 to 10 grams of fresh cranberries (5 fresh cranberries weigh approximately 5 grams). Cranberry juice drinks probably contain a lot less active ingredients than tablets or capsules. In addition, juice drinks often contain a high concentration of sugar (to mask the bitter taste) and as such should be used with caution in people with diabetes. Cranberry products are not available on prescription, but are readily available from most health food shops, pharmacies, herbalists and supermarkets. Cranberry products are not regulated and as such, the concentration of active ingredients is not always stated, and concentrations may vary between batches of the same product.

Are there any safety issues for people taking cranberry products?
In studies, no serious adverse effects of cranberry products were reported, but high drop-out rates suggest that they may not be well tolerated. An unpleasant taste was often given as a reason for drop out. Cranberry juice has been reported to interact with warfarin – see Prescribing Point.

References
Cranberry products are not available on prescription, with caution in people with diabetes. Extract, equivalent to between 5 to 10 grams of fresh "high juice.

How does cranberry work against UTI?

In older women (and had more adverse effects).67 Cranberry juice drinks probably contain a lot less active ingredients than tablets or capsules. 2 In addition, juice cranberry products to try to ensure consistency in daily amount consumed, healthy individuals taking warfarin may not have e.g. salicylate in commercial cranberry juice may cause

What evidence exists?

Recent studies have shown that cranberry does not see Prescribing Point.


BMA / RPSGB. BFNo3. 63. 2012.


BMA / RPSGB. CBNP 2011-2012.


Anon. Northern Ireland Antimicrobial Guidelines for Primary Care 2012. Public Health Agency/Health and Social Care

101. HPA Extended-Spectrum Beta-Lactamases (ESBLs) [www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ESBLs]


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This material was prepared on behalf of the Northern Ireland Health and Social Care Board by:

Michelle Bradley MPHarm MSc MPS
Medicines Management Information Pharmacist
COMPASS Unit
Pharmaceutical Department
NI Health and Social Care Board
2 Franklin Street, Belfast
BT2 8DQ

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Please note that every effort has been made to ensure that the content of the COMPASS Therapeutic Notes is accurate at the time of publication. Readers are reminded that it is their responsibility to keep up-to-date with any changes in practice.

With thanks to the following for kindly reviewing this document:

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The editorial panel for this edition of COMPASS Therapeutic Notes:

Dr Bryan Burke (General Practitioner)
Miss Veranne Lynch (Medicines Management Advisor, Belfast LGC)
Dr Ursula Mason (General Practitioner)
Dr Thérèse Rafferty (Medicines Management Information Analyst, HSCBSO)
Mrs Stephanie Sloan (Community Pharmacist)
Ms Kathryn Turner (Medicines Management Lead, Health and Social Care Board)
COMPASS THERAPEUTIC NOTES ASSESSMENT
Management of Bacterial Urinary Tract Infections in Primary Care

COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 250 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.

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- **Doctors** and **nurses** should submit their answers at: www.medicinesni.com
- **Pharmacists** should submit their answers at: www.nicpld.org

Are you a
Pharmacist?☐ Community ☐ Hospital ☐ Other (please specify) ____________
GP? ☐ Enter your cipher number: __________
Nurse? ☐ Enter your PIN number: __________

Title: Mr/Mrs/Miss/Ms/Dr
Surname: __________ First name: __________
Address: __________________________________________
________________________________________
Postcode: __________________________________________

**GPs and Nurses:**
Complete the form overleaf and return to:
COMPASS Unit
Pharmaceutical Department
HSC Business Services Organisation
2 Franklin Street
Belfast
BT2 8DQ

**Pharmacists:**
Complete the form overleaf and return to:
Northern Ireland Centre for Pharmacy Learning & Development
FREEPOST NICPLD
Belfast BT9 7BL
Successful completion of these assessment questions equates with 2 hours Continuing Professional Development time. Circle your answer TRUE (T) or FALSE (F) for each question. When completed please post this form to the relevant address shown overleaf. Alternatively, you can submit your answers online:

- Doctors and nurses should submit their answers at: www.medicinesni.com
- Pharmacists should submit their answers at: www.nicpld.org

1 In the management of urinary tract infections in NON-pregnant women:
   a. Dysuria and frequency are highly suggestive of UTI. 
   b. UTI in an otherwise healthy non-pregnant woman can be diagnosed without a dipstick test of the urine and without urine culture when there are multiple typical symptoms and signs of UTI. 
   c. A three-day course of trimethoprim or nitrofurantoin is recommended for the treatment of simple UTI in non-pregnant women. 
   d. A woman who has three or more episodes per year of acute UTI, or two microbiologically confirmed UTIs in 6 months, is said to have "recurrent" UTIs.

2 In pregnant women:
   a. All pregnant women should be screened for bacteriuria at their first antenatal visit. 
   b. Asymptomatic bacteria should be treated in all pregnant women. 
   c. A three day course is sufficient for uncomplicated UTI in pregnant women. 
   d. Given the risks of bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure, and then at every antenatal visit for the rest of the pregnancy.

3 In the management of urinary tract infections in men:
   a. It is not necessary to send a sample of urine for culture and sensitivity testing. 
   b. Co-amoxiclav should be considered as first line therapy for uncomplicated UTI in men. 
   c. In a man with an uncomplicated lower urinary tract infection, a three-day course of antibiotics is appropriate. 
   d. Failure to respond to appropriate antibiotic therapy is an indication for referral to a specialist.

4 In the management of patients with indwelling catheters:
   a. Classical signs and symptoms of UTI do not always apply; fever is the most common symptom. 
   b. Dipstick tests may be used to differentiate between asymptomatic and symptomatic bacteriuria. 
   c. Patients should receive antibiotic treatment for bacteriuria regardless if clinically symptomatic or not. 
   d. Nitrofurantoin is a suitable choice for patients with renal impairment.

5 In the management of urinary tract infection in children:
   a. Infants under three months of age may be managed in primary care. 
   b. A three day treatment with trimethoprim or nitrofurantoin should be used empirically in children over 3 months of age. 
   c. Antibiotic prophylaxis of UTI in children has been shown to be effective in reducing the incidence of recurrent UTI. 
   d. A higher dose of the prophylactic antibiotic should be prescribed if the child develops an infection.

6 Cranberry products:
   a. There is some evidence to support the effectiveness of cranberry products in the treatment of urinary tract infections. 
   b. Cranberry products are not regulated and as such, the concentration of active ingredients is not always stated, and concentrations may vary between batches of the same product. 
   c. Cranberry products have been shown to be effective for UTI prophylaxis in men. 
   d. Cranberry products should be used with caution in patients also taking warfarin.