South Australian Perinatal Practice Guideline

Urinary Tract Infection in Pregnancy

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Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
 - Advising consumers of their choice and ensuring informed consent is obtained,
 - Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
 - Documenting all care in accordance with mandatory and local requirements

Note: The words woman/women/mother/she/her have been used throughout this guideline as most pregnant and birthing people identify with their birth sex. However, for the purpose of this guideline, these terms include people who do not identify as women or mothers, including those with a non-binary identity. All clinicians should ask the pregnant person what their preferred term is and ensure this is communicated to the healthcare team.

Explanation of the aboriginal artwork:

The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

The purpose of this guideline is to provide clinicians with information and treatment guidelines for recognition and management of urinary tract infections in pregnancy.



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Summary of Practice Recommendations

- Women should be given information about hygiene measures to avoid UTI
- Antenatal screening for asymptomatic bacteriuria should be undertaken at the first antenatal visit but no later than16 weeks' gestation
- Treatment of asymptomatic bacteriuria should be guided by sensitivities
- Commence empirical treatment of acute cystitis and pyelonephritis and adjust when sensitivities available
- Women with pyelonephritis need admission for intravenous antibiotics (minimum 48 hours) followed by oral antibiotics (total treatment 10-14 days)
- Women should have a repeat MSSU to ensure the infection has cleared 1-2 weeks following completion of treatment
- Women with recurrent acute cystitis/pyelonephritis or asymptomatic bacteriuria with risk factors for pyelonephritis require close surveillance with MSSU at each antenatal visit and consideration of daily antibiotic prophylaxis
- Nitrofurantoin should be avoided close to birth
- Amoxicillin + clavulanate should only be used if sensitivities show resistance to other antibiotic options
- Trimethoprim should be avoided in the first trimester

Abbreviations

ADHD	Attention deficit hyperactivity disorder
et al	and others
E. coli	Escherichia coli
GBS	group B streptococcus
IUGR	Intrauterine growth restriction
mg	milligram/s
mL	millilitre/s
MSSU	Mid-stream specimen of urine
UTI	Urinary tract infection

Definitions^{1,2,3}

Asymptomatic bacteriuria	The presence of \ge 100 000 colony-forming units/mL of urine in 2 consecutive urine samples in an asymptomatic patient
Acute cystitis	Significant bacteriuria (≥ 100 000 colony-forming units/mL of urine) or more than 100 colony-forming units/mL of urine with accompanying pyuria (> 7 white blood cells/mL) with associated bladder mucosal invasion and inflammation. It involves only the lower urinary tract with symptoms such as dysuria, urgency, frequency, nocturia, haematuria and suprapubic discomfort in afebrile women with no evidence of systemic illness
Pyelonephritis	The presence of \geq 100 000 colony-forming units/mL of urine with associated inflammation of the renal parenchyma, calices and pelvis in the presence of systemic illness. Symptoms include flank or renal angle pain, pyrexia, rigor, chills, nausea and vomiting, frequency, urgency and dysuria
Recurrent UTI	Two or more UTIs in pregnancy



Background^{1,2,3,4}

Urinary tract infection (UTI) is the most common bacterial infection in pregnancy with 5-10% of women experiencing a symptomatic UTI during pregnancy.

UTI may present as asymptomatic bacteriuria, acute cystitis (bladder infection) or pyelonephritis (kidney infection).

Rates of bacteriuria are similar between pregnant and non-pregnant women, however pregnant women are more likely to get recurrent infections and more severe infections due to physiological changes in pregnancy that predispose women to urinary retention and stasis:

- Smooth muscle relaxation leads to decreased bladder and ureteral tone, dilatation of the renal pelves and ureters, increased bladder volume, residual volume and vesicoureteric reflux
- Differences in urine pH and osmolality and pregnancy-induced glycosuria and aminoaciduria may facilitate bacterial growth
- Gravid uterus exerts pressure on the bladder and ureters leading to obstruction of urine flow
- Immunosuppression of pregnancy may contribute to lowered antibody response

Asymptomatic bacteriuria occurs in 2% to 10% of all pregnancies. If untreated, up to 40% of women will develop acute cystitis and up to 30% acute pyelonephritis. Overall rate of acute cystitis in pregnancy is 1-2% and pyelonephritis is 0.5-2% (although there are small variations in rates between sources).

Pregnancy Outcome

Asymptomatic bacteriuria has been associated with an increased risk of low birthweight, preterm birth and preeclampsia. 1,2

Acute cystitis does not have the same increased risk of low birthweight, preterm birth and pyelonephritis, possibly because women with symptoms usually receive treatment for the $\rm UTI.^2$

Pyelonephritis is associated with a number of adverse outcomes including:^{1,2,3}

Maternal

- Hypertension and preeclampsia
- Anaemia, haemolysis and thrombocytopenia
- Acute kidney injury
- Sepsis
- Acute respiratory distress

Fetal / Infant

- Preterm birth
- Low birthweight and IUGR
- Hypoxic events leading to hypoperfusion of the placenta
- Potential effects on fetal brain development that may lead to increased risk of cerebral palsy⁵, epilepsy, ADHD and intellectual impairment.³

Microbiology and Antibiotic Use

Escherichia coli is the most common pathogen associated with asymptomatic bacteriuria (70-80 % of isolates). Other organisms include *Klebsiella pneumonia* (3-5%), *Proteus mirabiliis* (5%), *Staphylococcus saprophyticus* (3%), *Enterobacter* species (3%), *group B streptococcus* (*GBS*) (2-5%), and other *Proteus* species (2%).^{1,2}

Antibiotic treatment of asymptomatic bacteriuria reduces the risk of developing pyelonephritis in pregnancy. Some suggest that this effect may be up to 90%⁴, whilst other meta-analyses suggest that determination of the effect estimate is limited given the strength of current evidence.⁶ There is also some limited evidence that there may be a group of women with asymptomatic bacteriuria who are unlikely to benefit from antibiotic treatment,⁶ and this is likely to vary by organism: For example, *GBS* is a coloniser organism and whilst identification warrants intrapartum antibiotic prophylaxis, it is unclear whether antibiotics during pregnancy in the asymptomatic woman is helpful.

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Note: No randomised controlled trials in the Cochrane review⁶ assessed the adverse outcomes of antibiotic treatment for the woman or fetus/infant.

A Cochrane review concluded that a standard short course of antibiotics (4-7 days) was the most effective treatment of asymptomatic bacteriuria.⁷

A Cochrane review of treatment for symptomatic UTI in pregnancy found no single treatment (antibiotic choice or duration) better than another, with a range of options being effective.⁸ Similarly, the Cochrane review of interventions for preventing recurrent symptomatic UTI in pregnancy⁹ was unable to draw a conclusion re the optimal intervention with daily antibiotic prophylaxis no better than surveillance (routine clinic visits with MSSU and treatment if positive) alone, although it did reduce asymptomatic bacteriuria. Others have suggested that post-coital prophylaxis rather than continuous may be as effective as continuous prophylaxis where sexual activity is linked to UTI.²

A number of authors describe both increasing antimicrobial resistance and potential adverse consequences of antibiotic use.^{2,10,11} Ghouri et al in their systematic review of UTI prevention found that hygiene methods (wiping 'front to back', voiding after intercourse, washing hands before going to the toilet, washing genitalia 'front to back', using liquid soap rather than bar soap, adequate fluid intake and not 'holding on') were effective in reducing UTI. Other methods such as cranberry juice, ascorbic acid or specific herbal supplementation and immunisation were assessed as safe and effective, but the studies were of insufficient quality to recommend the intervention.¹¹

In addition, resident urinary bacteria (urinary microbiome), that are not detectable on standard MSSU have been discovered. Development and maintenance of a healthy urinary microbiome may play an important role in the prevention of UTI but more research in this area is required.³

Risk factors^{1,4}

- History of previous urinary tract infections
- Neurogenic bladder retention
- Structural abnormality of urinary tract
- Presence of renal stones
- Diabetes mellitus
- Sickle cell trait
- Immunosuppression
- Tobacco use
- Low socio-economic status
- Late presentation for antenatal care
- Sexual intercourse 3 or more times/week

Antenatal education

Explain that urinary tract infections are common in pregnancy; the risk beginning in week 6 and peaking during weeks 22 to 24.

Routine hygiene measures (wiping 'front to back', voiding after intercourse, washing hands before going to the toilet, washing genitalia 'front to back', using liquid soap rather than bar soap, adequate fluid intake and not 'holding on') reduce the risk of developing a UTI.

Advise women if they experience symptoms (sense of urgency, painful and frequent urination of small volumes, straining or with a residual feeling of incomplete emptying), to contact their maternity care provider or GP.

Antenatal screening

Routine midstream specimen of urine (MSSU) for all women at their first antenatal visit or not later than 16 weeks gestation. May be undertaken at GP prior to hospital 'booking' visit.



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Indications for repeat screening

- Contaminated specimen
- History of recurrent infections outside of pregnancy
- Structural abnormality of the urinary tract
- Symptomatic of UTI

Diagnosis

Quantitative MSSU culture is the only gold standard for diagnosis of ALL suspected UTI.

Asymptomatic bacteriuria

More than 100,000 colony-forming units/mL without symptoms of UTI, generally indicates asymptomatic bacteriuria.

A bacteria count of more than 100,000 colony-forming units/mL with 2 or more organisms may indicate contamination rather than bacteriuria.

Acute cystitis

In addition to MSSU, clinical diagnosis is based on symptoms such as:

- Dysuria, urinary frequency and urgency, strangury
- Lower abdominal pain or supra-pubic pain without fever
- Pyuria
- Haematuria

Pyelonephritis

Pyelonephritis usually presents as an acute episode. In addition to midstream MSSU, clinical diagnosis should include:

- Full maternal clinical history and examination
- Assessment of fetal wellbeing
- Blood cultures (aerobic and anaerobic)
- Low and high vaginal swabs
- Complete blood picture, renal function test including creatinine, urea and electrolytes
- Urinalysis (women with pyelonephritis often have pyuria or leukocyte casts)

Symptoms include:

- Pyrexia, chills, rigor
- Flank or renal angle pain
- Nausea and vomiting
- Usually dehydration
- Less commonly dysuria, frequency
- Fetal tachycardia may also be present

Treatment

Use susceptibility results to guide treatment of asymptomatic bacteriuria. Confirm infection has resolved with repeat MSSU culture 1-2 weeks after treatment is completed.²

A five day course of oral antibiotic for uncomplicated UTI or asymptomatic bacteraemia is normally sufficient in pregnant women.⁷

Intravenous antibiotic treatment is recommended in all cases of acute pyelonephritis and therapy should be guided by urine culture and sensitivity reports as soon as available.¹²

A minimum of 10-14 days total antibiotics (IV plus oral), is recommended for pyelonephritis in the literature including the <u>e-Therapeutic Guidelines: Antibiotic</u>.¹²



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If the woman is bacteraemic, intravenous antibiotics are recommended for at least 48 hours. Intravenous antibiotics can be switched to oral antibiotics once the patient is afebrile for a minimum of 24 hours, inflammatory markers are settling, repeat blood cultures are negative and patient is clinically improving. Also seek Infectious Diseases advice. Check if appropriate oral step down options are available.¹²

Increase fluid intake (may require intravenous fluids if clinically dehydrated).

Monitor urine output to assess complete emptying of the bladder (assists antimicrobial treatment).

Urinary alkalisers are safe in pregnancy, however they should not be used in combination with nitrofurantoin as it can result in a loss of treatment efficacy.¹²

Asymptomatic bacteriuria (directed therapy based on sensitivities)

Asymptomatic bacteriuria is diagnosed using screening MSSU. Given variable patterns of antimicrobial resistance, treatment should be based on culture and sensitivities recommended in the laboratory report with consideration given to appropriate antibiotics in pregnancy. Women who present with symptoms of acute cystitis or pyelonephritis should be managed as below with empiric therapy commenced.

Acute cystitis (empiric therapy)

The following antibiotic selections are suggested as guidance only, based on the Therapeutic Guidelines: *Urinary tract infection and bacteriuria in pregnancy* (current at 1/3/21) – see <u>e-TG</u> for further information. Prescription of antibiotic therapy will need to be modified using the individual culture and sensitivity results to alter already initiated care where appropriate. Always consider individual women's co-morbidities, and in particular, any drug sensitivities or allergies she may have (always check this before prescribing). You should also keep as up to date as possible with your local hospital or community patterns of antibiotic resistance.

1. Cefalexin 500 mg oral twice daily for 5 days

OR

2. Nitrofurantoin 100 mg oral 6 hourly for 5 days (avoid if close to birth [i.e. after 37 weeks gestation or sooner if early birth is planned] due to possible increased risk of neonatal jaundice and haemolytic anaemia)

OR

- 3. Trimethoprim 300 mg oral daily for 3 days (avoid in first trimester and in pregnant women with established folate deficiency, low dietary folate intake, or for women taking other folate antagonists OR if woman has been treated with trimethoprim in previous 3 months or had trimethoprim-resistant *E. coli* isolate during this time)
- OR if culture and sensitivity shows resistance to the 3 choices above and susceptibility is confirmed, suitable alternatives are:
- 4. Amoxicillin 500mg oral 8 hourly for 5 days
- Amoxicillin + clavulanate 500 + 125 mg oral, twice daily for 5 days (if < 20 weeks of gestation)

Note: Whilst both the 7 year¹³ and 11 year¹⁴ follow-up of the ORACLE II trial¹⁵ showed no difference in functional impairment or educational attainment in children who had been treated with erythromycin or amoxicillin / clavulanate, the trial itself showed a significant association with proven necrotising enterocolitis in neonates (1.8% with amoxicillin / clavulanate compared to 0.7% with no amoxicillin / clavulanate [p = 0.0005]). Thus, it is recommended that amoxicillin / clavulanate is only used if no alternative treatment is available.^{13,14,15}

• Repeat MSSU 1-2 weeks after completion of treatment



Pyelonephritis

Admit for antimicrobial treatment for a minimum of 48 hours intravenous therapy. Administer intravenous fluids and monitor urine output, as dehydration is common.

Cooling blankets and antipyretics can be used to alleviate pyrexia as required.

Monitor for signs of preterm labour and treat accordingly (For further information refer to the *Preterm labour* PPG available at <u>www.sahealth.sa.gov.au/perinatal</u>).

Repeat MSSU 1-2 weeks after completion of treatment.

Parenteral treatment should be continued until the woman is afebrile for a minimum of 24 hours:

- Amoxicillin 2 g IV every 6 hours AND Gentamicin 5 mg/kg IV once a day
- OR 2. Ampicillin 2 g IV every 6 hours AND

Gentamicin 5 mg/kg IV once a day

Note: If gentamicin is contraindicated, as monotherapy use:

- 1. Ceftriaxone 1 g IV daily OR
- 2. Cefotaxime 1 g IV 8 hourly
 - **Note:** Does not provide cover for *pseudomonas*, *enterococcus*, *staphylococcal* infections or *ESBL* organisms

Note: In women with penicillin hypersensitivity, use gentamicin (as above) as a single drug for empirical therapy. However, it is safe to use most cephalosporins in women with non-severe penicillin hypersensitivity.

For further information on management of women reporting penicillin hypersensitivity where a beta-lactam antibiotic is the preferred option or on gentamicin use in pregnancy, see *Antibiotics in the Peripartum Period* PPG available at <u>www.sahealth.sa.gov.au/perinatal.</u>

As soon as clinically indicated, based on susceptibilities, switch to oral antibiotics (see *Guidance for antimicrobial intravenous to oral switch* information available in the <u>e-TG</u>). A minimum of 10-14 days total antibiotics (IV plus oral), is recommended for pyelonephritis¹²:

- 1. Cefalexin 500 mg oral every 6 hours **OR**
- 2. Amoxicillin 500 mg oral every 8 hours OR
- Trimethoprim 300 mg oral once a day (avoid in first trimester and in pregnant women with established folate deficiency, low dietary folate intake, or for women taking other folate antagonists)
 OR
- 4. Amoxicillin + clavulanate 875 + 125 mg oral 12 hourly (if < 20 weeks of gestation)

Note: In view of the ORACLE II trial¹⁵, which showed an associated increase in necrotising enterocolitis, it is recommended that amoxicillin / clavulanate is only used if no alternative treatment is available.



Recurrent UTI and bacteriuria in pregnancy

Recurrent UTI is diagnosed when women have two (2) or more confirmed UTIs in pregnancy.

- Treat an acute episode of recurrent UTI as for cystitis or pyelonephritis (as above) by commencing empiric therapy and adjusting once bacterial sensitivity is known
- Repeat MSSU at every visit
- Exclude urinary tract anomalies

Antibiotic prophylaxis

Consider giving antibiotic prophylaxis after 2 or more separate episodes of acute cystitis or asymptomatic bacteriuria with risk factors for pyelonephritis (e.g. immune compromise, urinary tract anomalies, diabetes).

- 1. Cefalexin 250 mg oral at night for the remainder of the pregnancy **OR**
- 2. Nitrofurantoin 50 mg oral at night (avoid if close to birth [i.e. after 37 weeks or sooner if early birth is planned] due to possible increased risk of neonatal jaundice and haemolytic anaemia)



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