# Document Control

| Title | | | |
|---|---|---|---|
| **Antibiotic Guidelines for Urinary Tract Infection in Pregnancy (including asymptomatic bacteriuria)** | | | |
| **Author** | | | **Author's job title**<br>Consultant Medical Microbiologist<br>Consultant Obstetrician<br>Midwife<br>Midwife |
| **Directorate**<br>Obstetrics and Gynaecology | | | **Department**<br>Maternity |
| **Version** | **Date Issued** | **Status** | **Comment / Changes / Approval** |
| 0.1 | Nov 2011 | Draft | First draft for consultation |
| 0.2 | Nov 2011 | Draft | Minor changes to titles and format. |
| 0.3 | Jan 2012 | Draft | Consultation with Maternity Guideline Group. Change to title. Reinsertion of section 6 from previous guideline (management of sepsis). |
| 0.4 | Feb 2012 | Draft | Minor changes after review in AWG. |
| 0.5 | Mar 2012 | Draft | Addition of guidelines for C section prophylaxis |
| 1.0 | Mar 2012 | Final | Ratified by DTG on 8th March 2012. |
| 1.1 | Jun 2012 | Revision | Minor amendment by Corporate Governance to header and footer, table of contents, document control report and added hyperlinks. |
| 1.2 | Sep 2014 | Revision | Guidance separated by indication, |
| 2.0 | Dec 2014 | Revision | Review of updated CG62 NICE guidance, and PHE guidance on management of infection. Change duration to 7 days for all antibiotics. Removal of trimester specific guidance. Change nitrofurantoin to first line on the basis of sensitivity data. |
| 2.1 | Jan 2015 | Revision | Amended after submission to DTG. Addition of trimester-specific guidance split UTI guidance by upper and lower UTI. Nitrofurantoin warning sentence added. |
| 3.0 | Feb 2015 | Final | Upper and lower UTI retitled cystitis and UTI systemic symptoms. |
| 3.1 | Jan 2018 | Revision | References reviewed and updated, guideline put into new Trust template. |
| 4.0 | Jul 2018 | Final | Approved by maternity specialist governance forum |
| 5.0 | Feb 2019 | Final | Re-reviewed by Consultant Obstetrician, addition of roles and responsibilities of midwives, addition of information about risks of untreated UTI added. Clarification of urine dipstick use in pregnancy. Co-amoxiclav IV for |

| | | | |
|---|---|---|---|
| | | | pyelonephritis changed to cefuroxime to match RD+E. Submitted to DTC for final approval. Approved 16th May 2019. |

| | |
|---|---|
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| **Lead Director**<br>Director of Medicine | |
| **Superseded Documents**<br>UTI in pregnancy ver 2.2 130215 | |

| **Issue Date** | **Review Date** | **Review Cycle** |
|---|---|---|
| Feb 2019 | Feb 2022 | Three years |

**Consulted with the following stakeholders:**

- Antibiotic Working Group
- Drug and Therapeutics Group
- Consultant Obstetricians

**Approval and Review Process**

- Antibiotic Working Group
- Drug & Therapeutics Group
-

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| **Policy categories for Trust's internal website (Bob)** | **Tags for Trust's internal website (Bob)** |
|---|---|
| Pharmacy, Microbiology, Obstetrics | Urinary tract infection, asymptomatic bacteriuria, obstetric infection, UTI, pregnancy |

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# 1. Purpose

**1.1.** This document sets out Northern Devon Healthcare NHS Trust's best practice guidelines for appropriate microbiological investigation and antimicrobial prescribing in pregnant female patients with urinary tract infection, or bacteriuria.

**1.2.** This guideline applies to all pregnant female patients. See separate guidance for paediatric patients and non-pregnant patients.

**1.3.** Non-compliance with this guideline may be for valid clinical reasons only. The reason(s) for non-compliance must be documented clearly in the patient's notes.

**1.4.** This guideline is primarily aimed at all prescribing teams but other staff (e.g. nursing staff, pharmacists) may need to familiarise themselves with some aspects of the guideline.

**1.5.** Implementation of this guideline will ensure that:

- Urinary tract infection and bacteriuria is managed according to current evidence and standards of practice in the wider healthcare community.
- A standard of care is specified to facilitate a consistent approach between obstetrics, microbiology and pharmacy in terms of patient management, specimen processing and drug availability.

# 2. Definitions and Abbreviations

**2.1.** Asymptomatic bacteriuria

- Persistent colonisation of the urinary tract by significant numbers of organisms in women (greater than 1 x $10^5$ colony-forming units [CFU] / mL) without clinical symptoms of urinary tract infection

**2.2.** Acute cystitis

- Lower urinary tract symptoms such as dysuria, urinary frequency nocturia, haematuria and supra-pubic discomfort in afebrile women with no evidence of systemic illness. May be bacterial, chemical or trauma induced. For the purposes of this guideline, only bacterial cystitis will be discussed.

**2.3.** Pyelonephritis

- Significant bacteriuria in the presence of systemic illness and symptoms such as flank / renal angle pain, pyrexia, rigors, nausea and vomiting.

**2.4.** ASB – asymptomatic bacteriuria

**2.5.** UTI – urinary tract infection

**2.6.** GBS – Group B *Streptococci*

**2.7.** (M)C&S – (microscopy,) culture and sensitivity

**2.8.** MSU – mid-stream urine sample

# 3. Responsibilities

**3.1.** Community midwives are responsible for

- Ensuring that women understand how to collect mid-stream urine sample.
- Ensuring that all pregnant women are screened for asymptomatic bacteriuria at booking visit and refer to consultant antenatal clinic if screen positive.

**3.2.** Consultant microbiologists, antibiotic pharmacists, obstetricians and midwives are responsible for working in partnership within the multidisciplinary team.

**3.3.** Responsibility for education and training lies with the Lead Consultant Microbiologist for Antibiotic Stewardship. It will be provided through formal study days and informal training on the ward.

**3.4.** The author will be responsible for ensuring the guidelines are reviewed and revisions approved by the Drug and Therapeutics Group in accordance with the Document Control Report.

**3.5.** All versions of these guidelines will be archived in electronic format by the author within the Antibiotic Stewardship policy archive.

**3.6.** Any revisions to the final document will be recorded on the Document Control Report.

**3.7.** To obtain a copy of the archived guidelines, contact should be made with the author.

**3.8.** Monitoring of implementation, effectiveness and compliance with these guidelines will be the responsibility of the Lead Clinician for Antibiotic Stewardship. Where non-compliance is found, the reasons for this must have been documented in the patient's medical notes.

## Role of Antibiotic Working Group (AWG)

**3.9.** The AWG is responsible for:

- Leading antibiotic guideline development and review within Northern Devon Healthcare Trust
- Involving all relevant stakeholders in guideline development and review

# 4. Contacts

## 4.1. Contact numbers:

- Obstetric Consultant on call — Via switchboard
- Obstetric SHO on call — Bleep 299
- Microbiologist — Bleep 193. Via switchboard out of hours.
- Antibiotic Pharmacist — Bleep 029 (Mon-Fri only)

# 5. General Principles of Urinary Tract Infections in Pregnancy

Significant bacteriuria in pregnancy is common and a serious cause of maternal and perinatal morbidity and mortality. Bacteriuria in pregnancy is associated with increased risk of anaemia, pre-eclampsia, chorioamnionitis, pre-term delivery and post-partum endometritis in the mother. Foetal and infant risks include foetal growth restriction, pre-term delivery, stillbirth, perinatal mortality, mental retardation and developmental delay – it is postulated that direct bacterial endotoxin damage, in combination with cerebral hypoperfusion is responsible.

Urinary tract infection (UTI) in pregnancy has three principal presentations; asymptomatic bacteriuria, acute cystitis and pyelonephritis. In pregnancy, the overall incidence of UTI is approximately 8%, but around 30% of women with ASB will develop acute cystitis during their pregnancy. All are amenable to investigation and treatment, substantially improving outcome.

## 5.1. Risk factors

- Urinary stasis and reflux, due to physiological changes in the genitourinary tract during pregnancy;
- Presence of glycosuria, amino-aciduria of pregnancy and a fall in urine osmolality favours bacterial proliferation;
- Sexual activity: intercourse can traumatise the urothelium of the distal urethra, resulting in increased bacterial invasion. The vagina can act as a reservoir for gastrointestinal bacteria, facilitating inoculation;
- Concomitant urinary tract anomalies and maternal disease (e.g. diabetes or sickle cell disease)
- Medical interventions during pregnancy such as urethral instrumentation and catheterisation predispose to ascending bacteria and can result in nosocomial infection;
- Role of immune status modification in pregnancy and its effect on pathogenicity remains controversial.

## 5.2. Microbiology

- *Escherichia coli* accounts for 80-90% of infections
- Coagulase negative cocci – *Staphylococcus saprophyticus* is the second-most frequently cultured uropathogen
- Gram negative organisms such as *Proteus mirabilis* and *Klebsiella pneumonia* are also sometimes cultured

- Less frequently isolated, but clinically significant: Gram-positive cocci such as Group B haemolytic *Streptococci, Staphylococcus aureus;* acid-fast *Mycobacterium tuberculosis* (more normally acquired through haematological inoculation rather than via ascending infection); *Chlamydia trachomatis; Neisseria gonorrhoea*
- Non-bacterial organisms: yeasts such as *Candida spp.,* fungi
- Single positive cultures have a low predictive value for ASB (approximately 50% are contaminants).
- Nationally for England, resistance of E. coli (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
  - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
  - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
  - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
  - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%).
  - (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)

## 6. General Management of Urinary Tract Infections in Pregnancy

Pregnant women should be screened for asymptomatic bacteriuria (ASB) by urine culture and treated with appropriate antimicrobials because ASB is a known risk factor for developing pyelonephritis and proceeding to premature delivery.

Active urinary tract infection should be treated promptly on diagnosis – it is not appropriate to wait for culture and sensitivity results in the pregnant population due to risks of developing ascending infection. An MSU must be obtained prior to treatment in order to tailor antibiotic treatment as per the Start Smart Then Focus principles of antibiotic stewardship. Any decision to treat should be re-evaluated once culture and sensitivity reports are available.

Acute cystitis and pyelonephritis demand full assessment and treatment, with early involvement of other specialists in severe or systemic infection. DO NOT use dipstick testing to screen for ASB at first or subsequent visits as it lacks sensitivity.

All women should be reviewed to confirm post-treatment urine sterility for both ASB and active infections.

**Self-care advice:**

Paracetamol can be used to relieve pain and fever

Cranberry juice or other cranberry products are not recommended as there is no good evidence to support their use for treating urinary tract infection.

Although urine alkalization has been traditionally used to relieve the symptoms of urinary tract infection, there is a lack of good evidence to support its use.

**Antibiotic treatment:**

Experts recommend that the choice of antibiotic for empirical treatment should take into account local rates of resistance in uropathogens.

A 7-day course for uncomplicated UTI and eradication of ASB is supported by guidance issued by the Health Protection Agency, based on expert consensus.

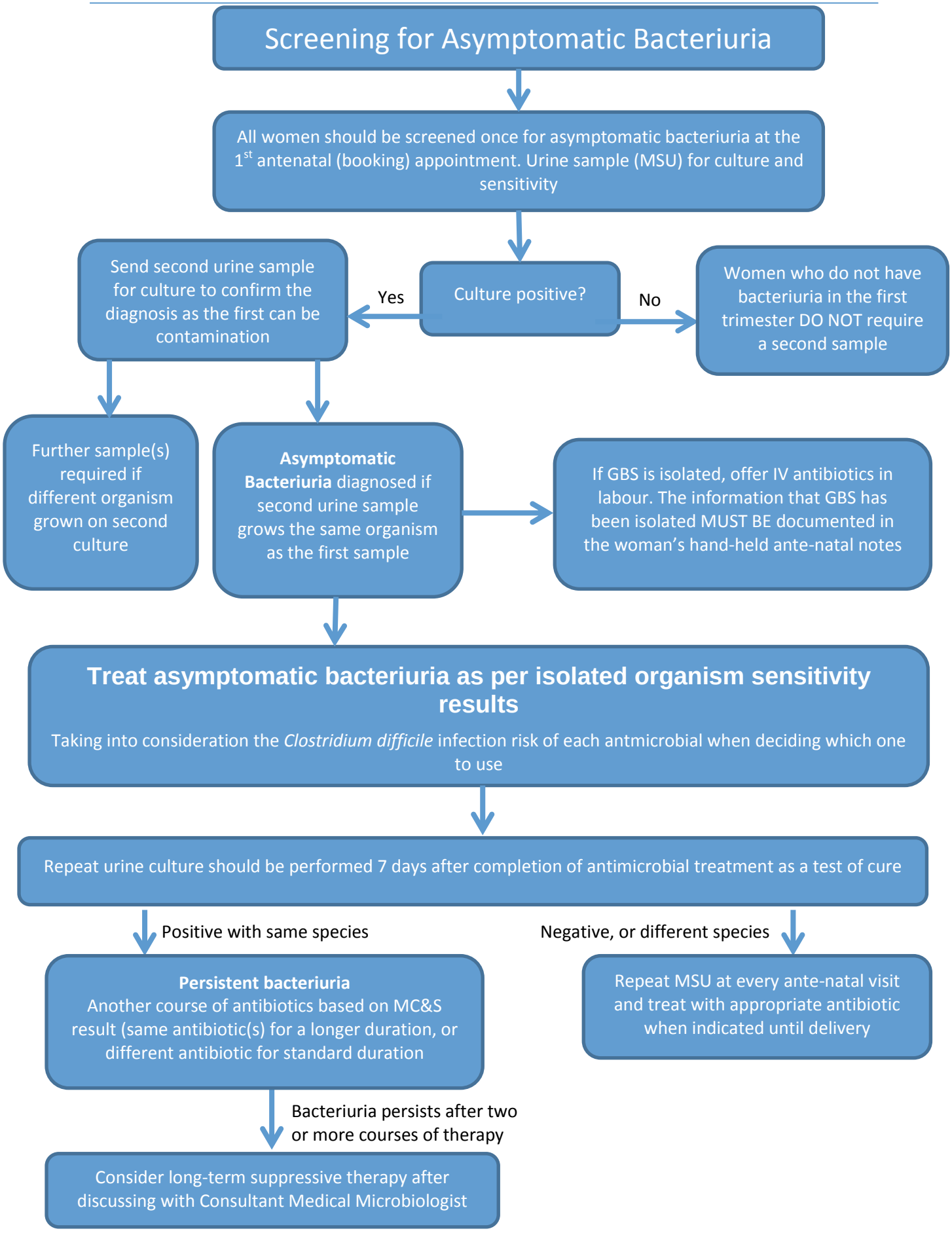
For antibiotic prescribing in North Devon, see below :

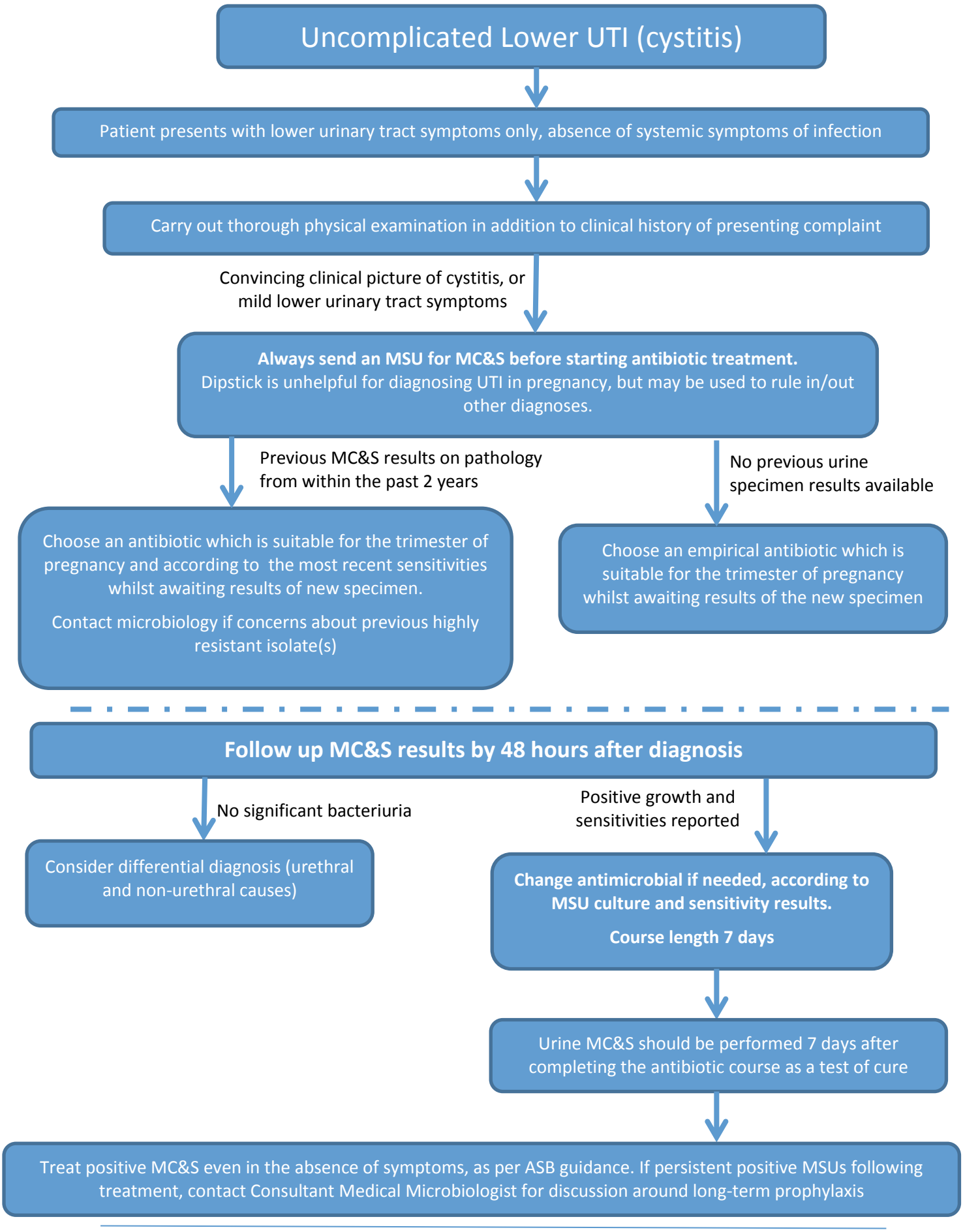
<table>
<tr><td colspan="2">Asymptomatic Bacteriuria</td></tr>
<tr><td colspan="2">Treat as per isolated organism sensitivity results<br>➢ Empirical therapy has no place in the treatment of ASB. Treatment courses are usually 7 days, and urine culture should be performed 7 days after completion of treatment as a test of cure.</td></tr>
<tr><td colspan="2">Uncomplicated Lower UTI (cystitis)</td></tr>
<tr><td>First line for cystitis<br><br>Nitrofurantoin 50mg QDS PO or 100mg MR BD PO for 7 days<br><br>Not contraindicated in any trimester, but avoid at term. Use with caution in patients with underlying chronic lung conditions.</td><td>Second line for cystitis<br><br>Cefalexin 500mg QDS PO for 7 days<br><br>Not contraindicated in any trimester</td></tr>
<tr><td colspan="2">Pyelonephritis (Upper UTI) in Pregnant Women</td></tr>
<tr><td>Intravenous Empirical Treatment First Line<br><br>Cefuroxime 750mg TDS IV<br><br>Not contra-indicated in any trimester of pregnancy<br><br>If severe sepsis, consider adding Gentamicin IV (dose according to Trust protocol)</td><td>Intravenous Empirical Treatment Second Line (penicillin allergy)<br><br>Consider following oral treatment guidelines as below<br><br>Plus<br><br>Gentamicin IV (dose according to Trust protocol)</td></tr>
<tr><td colspan="2">Treat until afebrile for 24 hours, then step down treatment to oral antibiotic only. Use culture results to determine appropriate antibiotics, and take into account the trimester of the pregnancy when choosing treatment.</td></tr>
<tr><td>Oral switch empirical treatment</td><td>Oral switch empirical treatment</td></tr>
</table>

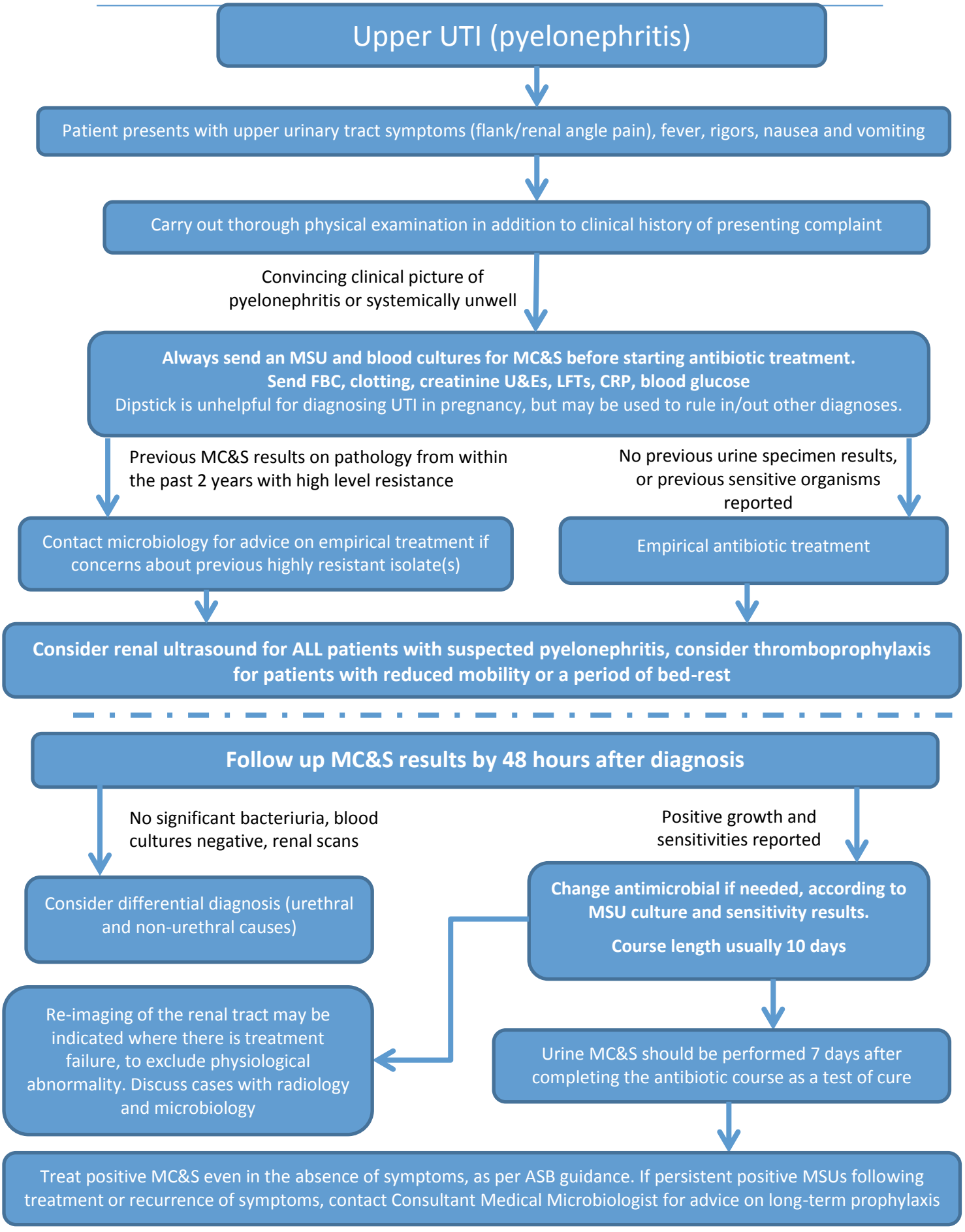
| First Line | Second Line (penicillin allergy) |
|---|---|
| **Cefalexin 500mg QDS PO**, usually for total 10 days including parenteral treatment<br><br>*Not contraindicated in any trimester* | **Trimethoprim 200mg BD PO**, usually for total 10 days including parenteral treatment<br><br>*Women in the first trimester should not routinely be given trimethoprim, unless on the advice of a Consultant Obstetrician, and should be given folate concurrently.*<br><br>***NB. Nitrofurantoin is only suitable for treating simple cystitis, and is not a suitable oral switch for pyelonephritis or upper UTI.*** |

**NB. The following advice should be taken into account when considering which antibiotic agent(s) to treat with:**

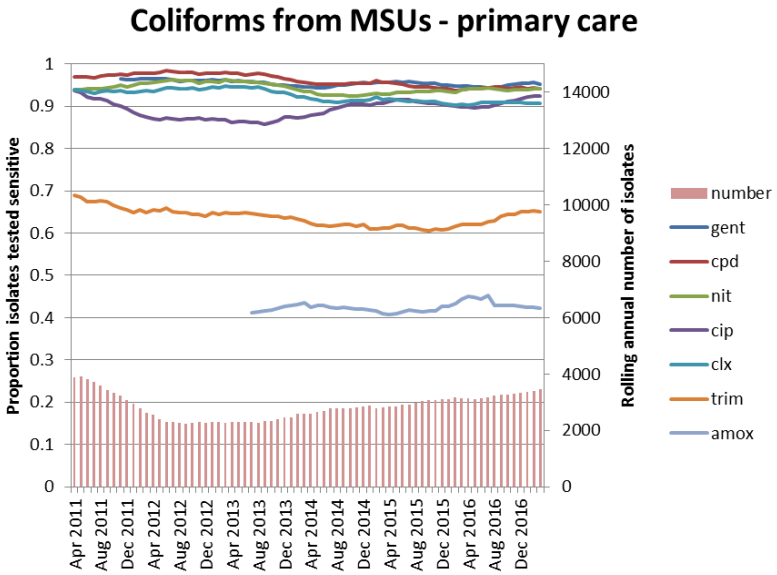
- **Trimethoprim** is not contraindicated in the 2nd and 3rd trimesters of pregnancy, if required on the basis of sensitivity results. Women in the 1st trimester should not routinely be given trimethoprim unless on the advice of a Consultant Obstetrician, as it is a folate antagonist.
- **Nitrofurantoin** should be used with caution in patients who have underlying chronic lung conditions. It should be avoided at term in pregnant women. NB. This antibiotic only treats lower UTI, and does not penetrate into the upper urinary tract.
- **Quinolones** should be avoided unless there are no other effective treatment options available, and prescribed only with the authority of a consultant obstetrician who can make teratology referrals.
- **Tetracyclines** should be avoided unless there are no other effective treatment options available, and prescribed only with the authority of a consultant obstetrician who can make teratology referrals. There is some evidence that prescribing in the first trimester is lower risk, but this should only be undertaken with appropriate teratology and obstetrician support.
- **Other antibiotics** – consult the BNF and summary of product characteristics to assess risk. If no information or advice therein, contact a Pharmacist for advice before prescribing.


Screening for Asymptomatic Bacteriuria
All women should be screened once for asymptomatic bacteriuria at the 1st antenatal (booking) appointment. Urine sample (MSU) for culture and sensitivity
Culture positive?
Yes
Send second urine sample for culture to confirm the diagnosis as the first can be contamination
No
Women who do not have bacteriuria in the first trimester DO NOT require a second sample
Further sample(s) required if different organism grown on second culture
Asymptomatic Bacteriuria diagnosed if second urine sample grows the same organism as the first sample
If GBS is isolated, offer IV antibiotics in labour. The information that GBS has been isolated MUST BE documented in the woman's hand-held ante-natal notes
Treat asymptomatic bacteriuria as per isolated organism sensitivity results
Taking into consideration the Clostridium difficile infection risk of each antmicrobial when deciding which one to use
Repeat urine culture should be performed 7 days after completion of antimicrobial treatment as a test of cure
Positive with same species
Negative, or different species
Persistent bacteriuria
Another course of antibiotics based on MC&S result (same antibiotic(s) for a longer duration, or different antibiotic for standard duration
Repeat MSU at every ante-natal visit and treat with appropriate antibiotic when indicated until delivery
Bacteriuria persists after two or more courses of therapy
Consider long-term suppressive therapy after discussing with Consultant Medical Microbiologist


Uncomplicated Lower UTI (cystitis)
Patient presents with lower urinary tract symptoms only, absence of systemic symptoms of infection
Carry out thorough physical examination in addition to clinical history of presenting complaint
Convincing clinical picture of cystitis, or mild lower urinary tract symptoms
Always send an MSU for MC&S before starting antibiotic treatment.
Dipstick is unhelpful for diagnosing UTI in pregnancy, but may be used to rule in/out other diagnoses.
Previous MC&S results on pathology from within the past 2 years
No previous urine specimen results available
Choose an antibiotic which is suitable for the trimester of pregnancy and according to the most recent sensitivities whilst awaiting results of new specimen.
Contact microbiology if concerns about previous highly resistant isolate(s)
Choose an empirical antibiotic which is suitable for the trimester of pregnancy whilst awaiting results of the new specimen
Follow up MC&S results by 48 hours after diagnosis
No significant bacteriuria
Positive growth and sensitivities reported
Consider differential diagnosis (urethral and non-urethral causes)
Change antimicrobial if needed, according to MSU culture and sensitivity results.
Course length 7 days
Urine MC&S should be performed 7 days after completing the antibiotic course as a test of cure
Treat positive MC&S even in the absence of symptoms, as per ASB guidance. If persistent positive MSUs following treatment, contact Consultant Medical Microbiologist for discussion around long-term prophylaxis


Upper UTI (pyelonephritis)
Patient presents with upper urinary tract symptoms (flank/renal angle pain), fever, rigors, nausea and vomiting
Carry out thorough physical examination in addition to clinical history of presenting complaint
Convincing clinical picture of pyelonephritis or systemically unwell
Always send an MSU and blood cultures for MC&S before starting antibiotic treatment.
Send FBC, clotting, creatinine U&Es, LFTs, CRP, blood glucose
Dipstick is unhelpful for diagnosing UTI in pregnancy, but may be used to rule in/out other diagnoses.
Previous MC&S results on pathology from within the past 2 years with high level resistance
No previous urine specimen results, or previous sensitive organisms reported
Contact microbiology for advice on empirical treatment if concerns about previous highly resistant isolate(s)
Empirical antibiotic treatment
Consider renal ultrasound for ALL patients with suspected pyelonephritis, consider thromboprophylaxis for patients with reduced mobility or a period of bed-rest
Follow up MC&S results by 48 hours after diagnosis
No significant bacteriuria, blood cultures negative, renal scans
Positive growth and sensitivities reported
Consider differential diagnosis (urethral and non-urethral causes)
Change antimicrobial if needed, according to MSU culture and sensitivity results.
Course length usually 10 days
Re-imaging of the renal tract may be indicated where there is treatment failure, to exclude physiological abnormality. Discuss cases with radiology and microbiology
Urine MC&S should be performed 7 days after completing the antibiotic course as a test of cure
Treat positive MC&S even in the absence of symptoms, as per ASB guidance. If persistent positive MSUs following treatment or recurrence of symptoms, contact Consultant Medical Microbiologist for advice on long-term prophylaxis

6.1. Local epidemiology of urine cultures from primary care




6.2. Asymptomatic bacteriuria should be confirmed with repeat culture

Data from 2011 to 2018 on antenatal urines and reproducibility in North Devon :

| | **Total** |
|---|---|
| N | **2228** |
| Positive (%) | **184/2228** |
| Repeated (%) | **131/184** |
| Reproduced (%) | **50/131** |

6.3. Specific recommendations : See appendix 1

6.4. Management Algorithm for Asymptomatic Bacteriuria

# 7. Monitoring Compliance with and the Effectiveness of the Guideline

## Suggested audit criteria

7.1. The following could be used:

- Percentage of women who get a screening sample of urine sent at booking
- Percentage of women who are prescribed antibiotics for ASB

**Process for Implementation and Monitoring Compliance and Effectiveness**

7.2. Incidents involving urological infection in pregnancy should be reported according to the Trust's Incident Reporting Policy. Critical incident reports relating to urological infection in pregnancy will be collated by the Antibiotic Pharmacist. Results will be reported on an annual basis to the Drug and Therapeutics Group.

# 8. Equality Impact Assessment

8.1. The author must include the Equality Impact Assessment Table and identify whether the policy has a positive or negative impact on any of the groups listed. The Author must make comment on how the policy makes this impact.

**Table 1: Equality impact Assessment**

| Group | Positive Impact | Negative Impact | No Impact | **Comment** |
|---|---|---|---|---|
| Age | X | | | Separate guidance for paediatrics |
| Disability | | | X | |
| Gender | | | X | |
| Gender Reassignment | | | X | |
| Human Rights (rights to privacy, dignity, liberty and non-degrading treatment) | | | X | |
| Marriage and civil partnership | | | X | |
| Pregnancy | X | | | Treatment advice specifically for this patient group |
| Maternity and Breastfeeding | | X | | Some treatments may be excreted in breast milk. Discuss on a case-by-case basis with Paediatricians and Pharmacy for advice. |
| Race (ethnic origin) | | | X | |
| Religion (or belief) | | | X | |

# 9. References

9.1. Up to Date – UTI in Pregnancy and Pyelonephritis in Pregnancy articles, via library links on BOB.

9.2. Hill, JB; Sheffield, JS; McIntire, DD; Wendel, GD. 2005. Acute Pyelonephritis in Pregnancy. Obstetrics and Gynaecology vol 105:1;18-23. https://journals.lww.com/greenjournal/Fulltext/2005/01000/Acute_Pyelonephritis_in_Pregnancy.5.aspx

9.3. British National Formulary, via www.medicinescomplete.com/mc

**9.4.** Green Top Guideline No. 36: Group B Streptococcal Disease, Early-onset. Royal College of Obstetricians and Gynaecologists. 2017.

**9.5.** SIGN. 2012. SIGN 88: Management of suspected bacterial urinary tract infection in adults. http://www.sign.ac.uk/sign-88-management-of-suspected-bacterial-urinary-tract-infection-in-adults.html

**9.6.** NICE Clinical Knowledge Summaries. 2015. Urinary tract infection (lower) – women. Scenario: Asymptomatic bacteriuria in pregnancy. https://cks.nice.org.uk/urinary-tract-infection-lower-women#!scenario:4

**9.7.** NICE Clinical Knowledge Summaries. 2019. Pyelonephritis – acute. https://cks.nice.org.uk/pyelonephritis-acute#!scenario

**9.8.** Widmer M, Lopez I, Gülmezoglu A, Mignini L, Roganti A. Duration of treatment for asymptomatic bacteriuria during pregnancy. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD000491. DOI: 10.1002/14651858.CD000491.pub3

**9.9.** Widmer M, Lopez I, Gülmezoglu A, Mignini L, Roganti A. Duration of treatment for asymptomatic bacteriuria during pregnancy. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD000491. DOI: 10.1002/14651858.CD000491.pub3

**9.10.** McCormick T, Ashe R.G, Kearney P.M. 2008. Urinary Tract Infection in Pregnancy. The Obstetrician and Gynaecologist. 10:156-162

**9.11.** UK National Screening Committee. 25 April 2012. Asymptomatic Bacteriuria Screening in Pregnancy Policy Position Statement

**9.12.** Royal Devon and Exeter NHS Foundation Trust Antimicrobial Stewardship Group. 2018. Obstetrics Antibiotics Guidelines. Via RxGuidelines app online https://webview.rx-guidelines.com/Viewing/Index/171#VTRjQQyz9W (accessed 15/03/2019)

## 10. Associated Documentation

- Incident reporting policy
- Antibiotic guidelines for management of maternal sepsis
- Antibiotic prescribing policy
- Penicillin allergy policy
- Antibiotic guidelines for Caesarean section
- Prevention of Neonatal Group B *Streptococcal* Infection

# 11. Appendix 1 – Asymptomatic Bacteriuria (ASB)

## 11.1. Name of guideline on app

UTI in pregnancy

## 11.2. Location on app

Secondary Care
Adult Treatment
Obstetric
UTI in Pregnancy
Asymptomatic Bacteriuria (ASB)

## 11.3. Header

Dipsticks have no role in the diagnosis of asymptomatic bacteriuria in pregnant women.

All pregnant women should have an MSU sent at 1st antenatal booking for culture and sensitivity

## 11.4. Diagnosis and Differentials [open/closed]

- Asymptomatic bacteriuria is routinely screened for and treated with antibiotics in pregnancy because it is a risk factor for pyelonephritis and premature delivery.
  - Meta-analyses of studies evaluating asymptomatic bacteriuria in pregnancy conclude that there are true associations with preterm delivery and low birthweight.
  - In addition, there are increased risks of preeclampsia, anaemia, chorioamnionitis and postpartum endometritis. Fetal risks include fetal growth restriction, stillbirth, perinatal mortality, mental retardation and developmental delay. It is postulated that direct bacterial endotoxin damage, in combination with cerebral hypoperfusion is responsible.
- All women should be screened for asymptomatic bacteriuria at the 1st antenatal (booking) appointment. Urine sample (MSU) for culture and sensitivity. If initial sample grows mixed bacteria, the woman should be invited back to give a specimen using the Peezy™ MSU collection device
- If Group B Streptococcus (GBS) is isolated, this information must be recorded in the woman's handheld notes. GBS can persist after antibiotic treatment, and is associated with increased risk of neonatal GBS disease, which must be considered as part of the birth plan. See guidelines on management of GBS for further advice on risk assessments.
- Thirty percent of women with asymptomatic bacteriuria will develop acute cystitis during their pregnancy.

- DO NOT use dipstick testing to screen for asymptomatic bacteriuria at first or subsequent visits as it lacks the sensitivity.
- A Cochrane review established that treatment reduces the risk of pyelonephritis in pregnancy and, consequently, the risks of preterm delivery and low birthweight. This review recommends that treatment schedules are directed by urine culture and sensitivity testing and that appropriate antibiotics are continued for at least 7 days.

### 11.5. Always Remember To… [open/closed]

- If bacterial growth is found on a screening MSU, send a second urine sample for culture to confirm diagnosis.
- If the second urine culture grows the same organism, this is classed as asymptomatic bacteriuria.
- If the second urine culture shows a different organism, then further sample(s) will be requested in order to conclusively confirm or rule out asymptomatic bacteriuria.
- Women who do not have bacteriuria in the first trimester should not have repeat urine cultures, unless they have clinical symptoms of UTI.
- Women who have a confirmed bacteriuria and who receive treatment should then be re-screened at each antenatal visit (and treated with appropriate antibiotic therapy when indicated) until delivery, to minimise the risk of developing pyelonephritis.

### 11.6. Watch Out For (red flags)… [open/closed]

- If Group B *Streptococcus* (GBS) is isolated, this information must be recorded in the woman's handheld antenatal notes. GBS can persist after antibiotic treatment, and is associated with increased risk of neonatal GBS disease, which must be considered as part of the birth plan. See guidelines on management of GBS for further advice on risk assessments.

### 11.7. General Interest [closed]

Urinary tract infection (UTI) in pregnancy has three principal presentations; asymptomatic bacteriuria, acute cystitis and pyelonephritis. In pregnancy, the overall incidence of UTI is approximately 8%, but around 30% of women with ASB will develop acute cystitis during their pregnancy. All are amenable to investigation and treatment, substantially improving outcome.

- Risk factors
  - Urinary stasis and reflux, due to physiological changes in the genitourinary tract during pregnancy;
  - Presence of glycosuria, amino-aciduria of pregnancy and a fall in urine osmolality favours bacterial proliferation;
  - Sexual activity: intercourse can traumatise the urothelium of the distal urethra, resulting in increased bacterial invasion. The vagina

can act as a reservoir for gastrointestinal bacteria, facilitating inoculation;
- Concomitant urinary tract anomalies and maternal disease (e.g. diabetes or sickle cell disease)
- Medical interventions during pregnancy such as urethral instrumentation and catheterisation predispose to ascending bacteria and can result in nosocomial infection;
- Role of immune status modification in pregnancy and its effect on pathogenicity remains controversial.

- Microbiology
  - *Escherichia coli* accounts for 80-90% of infections
  - Coagulase negative cocci – *Staphylococcus saprophyticus* is the second-most frequently cultured uropathogen
  - Gram negative organisms such as *Proteus mirabilis* and *Klebsiella pneumonia* are also sometimes cultured
  - Less frequently isolated, but clinically significant: Gram-positive cocci such as Group B haemolytic *Streptococci, Staphylococcus aureus;* acid-fast *Mycobacterium tuberculosis* (more normally acquired through haematological inoculation rather than via ascending infection); *Chlamydia trachomatis; Neisseria gonorrhoea*
  - Non-bacterial organisms: yeasts such as *Candida spp.,* fungi
- Single positive cultures have a low predictive value for ASB (approximately 50% are contaminants).
- Nationally for England, resistance of E. coli (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
  - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
  - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
  - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
  - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%).
  - (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)

### 11.8. Treatment [closed]

## Treat as per isolated organism sensitivity results

- Empirical therapy has no place in the treatment of ASB

Treatment courses are usually 7 days, and urine culture should be performed 7 days after completion of treatment as a test of cure.

NB. The following advice should be taken into account when considering which antibiotic agent(s) to treat with:

- **Trimethoprim** is not contraindicated in the 2nd and 3rd trimesters of pregnancy, if required on the basis of sensitivity results. Women in the 1st trimester should not routinely be given trimethoprim unless on the advice of a Consultant Obstetrician, as it is a folate antagonist.

- **Nitrofurantoin** should be used with caution in patients who have underlying chronic lung conditions. It should be avoided at term in pregnant women. NB. This antibiotic only treats lower UTI, and does not penetrate into the upper urinary tract.
- **Quinolones** should be avoided unless there are no other effective treatment options available, and prescribed only with the authority of a consultant obstetrician who can make teratology referrals.
- **Tetracyclines** should be avoided unless there are no other effective treatment options available, and prescribed only with the authority of a consultant obstetrician who can make teratology referrals. There is some evidence that prescribing in the first trimester is lower risk, but this should only be undertaken with appropriate teratology and obstetrician support.
- **Other antibiotics** – consult the BNF and summary of product characteristics to assess risk. If no information or advice therein, contact a Pharmacist for advice before prescribing.

### 11.9. If No Better… [closed]

- If the first follow-up culture for test of cure is positive for bacterial growth with the same species, this is classed as persistent bacteriuria. Another course of antimicrobial treatment based on susceptibility data should be administered: either the same antibiotic in a longer course, or a different antibiotic in a standard regimen. The woman should again have a urine sample sent at the end of the course for test-of-cure.
- When the bacteriuria has been treated and follow-up MSU at 7 days is negative for growth: At each subsequent antenatal visit, women should have repeat urine cultures to check sterility of urine. Treat as per sensitivity results if urine subsequently becomes positive for bacterial growth.
- If follow-up MSU at 7 days is positive for bacteriuria after two or more courses of therapy, long-term suppressive therapy may be appropriate for the duration of the pregnancy. Discuss suitable regimens with microbiology. See contraindications advice for various antibiotics, in “treatment”.
- Repeated positive samples despite adequate treatment: refer to urology for ultrasound of urinary tract to screen for abnormalities. Contact Microbiology for advice on further treatment.

### 11.10. Other Relevant Guidelines [closed]

GBS Guidelines

Maternal sepsis guidelines

### 11.11. Organisms and Sensitivities [closed]

### 11.12. Version Control [closed]

Antibiotic Guidelines for Urinary Tract Infection in Pregnancy (including asymptomatic bacteriuria) v2 6 031218

# 12. Appendix 2 – Lower Urinary Tract Infection in Pregnant Women

## 12.1. Name of guideline on app

UTI in pregnancy

## 12.2. Location on app

Secondary Care
Adult Treatment
Obstetric
UTI in Pregnancy
Uncomplicated lower UTI (cystitis)

## 12.3. Header

This guideline is for pregnant women presenting with cystitis who are apyrexial and have lower urinary tract symptoms of recent onset only. Dipsticks have no role in the diagnosis of UTI – all pregnant women with suspected UTI should have an MSU sent.

## 12.4. Diagnosis and Differentials [open/closed]

- Presenting symptoms usually the same as in the non-pregnant patient.
  - Acute onset dysuria
  - Urinary urgency and/or frequency
  - Absence of systemic symptoms such as fevers and chills

Prompt treatment is indicated to prevent ascending infection to pyelonephritis and its sequelae, which is more common in the pregnant patient due to physiological changes in pregnancy.

Accurate physical examination is essential to complement a clinical history. A differential diagnosis comprises of urethral: gonococcal and nongonococcal urethritis, nonurethral: vulvo-vaginitis, chemical cystitis

## 12.5. Always Remember To… [open/closed]

- Send MSU for all pregnant women presenting with acute cystitis
- Dipstick is unsuitable for use in diagnosing UTI in pregnant women, but it may help to rule in/out other differential diagnoses
- For patients who present with definite but mild lower urinary tract symptoms, or a convincing clinical picture of cystitis, start empirical treatment as there is a significant risk of ascending UTI from untreated cystitis in the pregnant population.
- The prescriber MUST ensure follow-up of the diagnosis and treatment with MSU results to ensure antimicrobial therapy is tailored according to sensitivities, or stopped if MSU returns no growth and alternative diagnoses considered

- Provide safety-netting advice about red flag symptoms, and information about how to access maternity services out of routine GP hours.
- A test-of-cure MSU should be sent 7 days after the end of the antibiotic course.

### 12.6. Watch Out For (red flags)… [open/closed]

- Flank or loin pain
- Rigors
- Initial treatment failure - primary treatment failures or relapses should be treated with a full 7-day course of a different antimicrobial in accordance with sensitivity testing.
- The possibility of underlying urinary tract pathology should also be considered.

### 12.7. General Interest [closed]

Urinary tract infection (UTI) in pregnancy has three principal presentations; asymptomatic bacteriuria, acute cystitis and pyelonephritis. In pregnancy, the overall incidence of UTI is approximately 8%, but around 30% of women with ASB will develop acute cystitis during their pregnancy. All are amenable to investigation and treatment, substantially improving outcome.

- Risk factors
  - Urinary stasis and reflux, due to physiological changes in the genitourinary tract during pregnancy;
  - Presence of glycosuria, amino-aciduria of pregnancy and a fall in urine osmolality favours bacterial proliferation;
  - Sexual activity: intercourse can traumatise the urothelium of the distal urethra, resulting in increased bacterial invasion. The vagina can act as a reservoir for gastrointestinal bacteria, facilitating inoculation;
  - Concomitant urinary tract anomalies and maternal disease (e.g. diabetes or sickle cell disease)
  - Medical interventions during pregnancy such as urethral instrumentation and catheterisation predispose to ascending bacteria and can result in nosocomial infection;
  - Role of immune status modification in pregnancy and its effect on pathogenicity remains controversial.
- Microbiology
  - *Escherichia coli* accounts for 80-90% of infections
  - Coagulase negative cocci – *Staphylococcus saprophyticus* is the second-most frequently cultured uropathogen
  - Gram negative organisms such as *Proteus mirabilis* and *Klebsiella pneumonia* are also sometimes cultured
  - Less frequently isolated, but clinically significant: Gram-positive cocci such as Group B haemolytic *Streptococci, Staphylococcus aureus;* acid-fast *Mycobacterium tuberculosis* (more normally acquired through haematological inoculation rather than via ascending infection); *Chlamydia trachomatis; Neisseria gonorrhoea*
  - Non-bacterial organisms: yeasts such as *Candida spp.,* fungi

- Single positive cultures have a low predictive value for ASB (approximately 50% are contaminants).
- Nationally for England, resistance of E. coli (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
  - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
  - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
  - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
  - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%).
  - (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)

### 12.8. Treatment [closed]

**First line** for cystitis
**Nitrofurantoin 50mg QDS PO or 100mg MR BD PO** for 7 days
*Not contraindicated in any trimester, but avoid at term. Use with caution in patients with underlying chronic lung conditions.*

**Second line** for cystitis

**Cefalexin 500mg QDS PO** for 7 days
*Not contraindicated in any trimester*

### 12.9. If No Better… [closed]

- Dysuria in pregnant women can be a result of other infectious and non-infectious processes, such as vaginitis or urethritis.
- Sometimes, urinary frequency and urgency may be symptoms of normal pregnancy in the absence of urinary tract infection, which is borne out by absence of bacteriuria in repeat MSUs.
- If not already performed, testing for sexually transmitted infections (such as chlamydia and gonorrhoea) is warranted for pregnant women with dysuria without bacteriuria, or women who have persistent dysuria despite successful treatment of bacteriuria.

### 12.10. Other Relevant Guidelines [closed]

- Maternal sepsis guideline
- GBS guidelines

### 12.11. Organisms and Sensitivities [closed]

### 12.12. Version Control [closed]

Antibiotic Guidelines for Urinary Tract Infection in Pregnancy (including asymptomatic bacteriuria) v2 6 031218

# 13. Appendix 3 – Pyelonephritis (Upper UTI) in Pregnant Women

## 13.1. Name of guideline on app

UTI in pregnancy

## 13.2. Location on app

Secondary Care
Adult Treatment
Obstetric
UTI in Pregnancy
Pyelonephritis (upper UTI) in pregnant women

## 13.3. Header

Pyelonephritis is more common in the 2nd and 3rd trimesters of pregnancy, and in women with history of asymptomatic bacteriuria, recurrent UTI or previous pyelonephritis. Urinalysis to check for pyuria may be useful in determining differential diagnoses, but should not be used as a positive diagnostic test. The risks of preterm labour increase significantly during an episode of acute pyelonephritis.

## 13.4. Diagnosis and Differentials [open/closed]

- Prompt recognition and treatment is essential to prevent serious sequelae: If untreated, it can lead to infection of the whole kidney (Pyonephrosis); perinephric abscess, gram-negative septicaemia and septic shock, resulting in multiple organ failure

- Presentation is similar to the non-pregnant patient
  - Flank pain
  - Nausea / vomiting
  - Fever >38$^{o}$C
  - Costovertebral angle tenderness
  - May not have accompanying symptoms of cystitis
  - Foetal tachycardia can also be indicative of systemic infection and the foetus should be assessed as part of any clinical evaluation

- Differential diagnoses
  - Nephrolithiasis – severe pain, fever is uncommon. Stones can be visualised on renal ultrasound
  - Intra-amniotic infection – the following features suggest intra-amniotic infection over pyelonephritis: presentation with premature rupture of membranes, uterine tenderness and/or foul odour of amniotic fluid/vaginal discharge, absence of bacteriuria.
  - Acute abdomen – appendicitis
  - Placental abruption – back pain is prominent when the placenta is on the posterior wall of the uterus. Fever is absent and vaginal bleeding is classically present. Uterus is often firm, and may be

rigid and tender in patients with abruption, but is usually soft in patients with pyelonephritis. Retroplacental haematoma on ultrasound supports diagnosis of abruption.

### 13.5. Always Remember To… [open/closed]

- Send urine sample for culture and sensitivity, preferably prior to first dose of antibiotics
- Send blood cultures x 2 bottles, preferably prior to first dose of antibiotics
- Send blood for U+Es to check for degree of renal injury and any electrolyte disturbances.
- Consider ultrasound of renal tract to look for significant hydronephrosis
- Thromboprophylaxis should be used if the woman has reduced mobility or a period of bed rest.
- Dipstick is unsuitable for use in diagnosing pyelonephritis in pregnant women, but it may help to rule in/out other differential diagnoses

### 13.6. Watch Out For (red flags)… [open/closed]

- Consider severe sepsis if evidence of end-organ dysfunction, e.g. Hypotension, confusion, desaturation or reduced urine output. Follow guidance in Maternal Sepsis guidelines for managing suspected sepsis.

### 13.7. General Interest [closed]

Urinary tract infection (UTI) in pregnancy has three principal presentations; asymptomatic bacteriuria, acute cystitis and pyelonephritis. Acute pyelonephritis occurs in 1-2% of pregnant women.

- Risk factors
  - Urinary stasis and reflux, due to physiological changes in the genitourinary tract during pregnancy;
  - Presence of glycosuria, amino-aciduria of pregnancy and a fall in urine osmolality favours bacterial proliferation;
  - Sexual activity: intercourse can traumatise the urothelium of the distal urethra, resulting in increased bacterial invasion. The vagina can act as a reservoir for gastrointestinal bacteria, facilitating inoculation;
  - Concomitant urinary tract anomalies and maternal disease (e.g. diabetes or sickle cell disease)
  - Medical interventions during pregnancy such as urethral instrumentation and catheterisation predispose to ascending bacteria and can result in nosocomial infection;
  - Role of immune status modification in pregnancy and its effect on pathogenicity remains controversial.
- Microbiology
  - *Escherichia coli* accounts for 80-90% of infections
  - Coagulase negative cocci – *Staphylococcus saprophyticus* is the second-most frequently cultured uropathogen

- Gram negative organisms such as *Proteus mirabilis* and *Klebsiella pneumonia* are also sometimes cultured
- Less frequently isolated, but clinically significant: Gram-positive cocci such as Group B haemolytic *Streptococci, Staphylococcus aureus;* acid-fast *Mycobacterium tuberculosis* (more normally acquired through haematological inoculation rather than via ascending infection); *Chlamydia trachomatis; Neisseria gonorrhoea*
- Non-bacterial organisms: yeasts such as *Candida spp.,* fungi

- Single positive cultures have a low predictive value for ASB (approximately 50% are contaminants).
- Nationally for England, resistance of E. coli (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
  - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
  - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
  - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
  - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%).
  - (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)

### 13.8. Treatment [closed]

Follow culture and sensitivity results to guide antibiotic choices, if available, taking into account the trimester of pregnancy and the time-dependent relative contraindications to some treatments.

**Intravenous Empirical Treatment**

**First Line**

**Cefuroxime 1.5 TDS IV**

*Not contra-indicated in any trimester of pregnancy*

If severe sepsis, consider adding **Gentamicin I**V (dose according to Trust protocol)

**Second Line** (penicillin allergy)

**Consider following oral treatment guidelines as below**

*Plus*

**Gentamicin IV** (dose according to Trust protocol)

Treat until afebrile for 24 hours, then step down treatment to oral antibiotic only. Use culture results to determine appropriate antibiotics, and take into account the trimester of the pregnancy when choosing treatment.

**Oral switch empirical treatment**

**First Line**

**Cefalexin 500mg QDS PO**, usually for 10 days total including parenteral treatment

*Not contraindicated in any trimester*

**Second Line** (penicillin allergy)

**Trimethoprim 200mg BD PO**, usually for 10 days total including parenteral treatment

*Women in the first trimester should not routinely be given trimethoprim, unless on the advice of a Consultant Obstetrician, and should be given folate concurrently.*

***NB. Nitrofurantoin is only suitable for treating simple cystitis, and is not a suitable oral switch for pyelonephritis or upper UTI.***

13.9. If No Better… [closed]

- Ultrasound imaging of renal tract to check for collections and rule out obstruction
- Ultrasound imaging of uterus and foetus to rule out other differential diagnoses
- Ensure urine and blood cultures have been sent
- Recurrent episodes of pyelonephritis may require prophylaxis for the remainder of the pregnancy if other factors have been optimised, but this must be discussed with a Consultant **Microbiologist** on a case-by-case basis.

13.10. Other Relevant Guidelines [closed]

- Maternal sepsis guidelines
- GBS Guidelines

13.11. Organisms and Sensitivities [closed]

13.12. Version Control [closed]

Antibiotic Guidelines for Urinary Tract Infection in Pregnancy (including asymptomatic bacteriuria) v2 6 031218

# 14. Appendix 4 – Recurrent Urinary Tract Infection in Pregnant Women

**14.1.** The exact aetiology is uncertain but re-infection by coliform bacteria from the vaginal reservoir can occur because of sexual activity. Urinary tract anomalies must be excluded, and postpartum evaluation is advisable after several episodes of antenatal infection.

**14.2.** According to three systematic reviews (Guinto et al. 2010, Smaill et al. 2015 and Widmer et al. 2015), continuous courses of antibiotics reduced the number of babies born with a birthweight below 2,500g compared with no treatment (low quality evidence). Single-dose, an intermediate course of 3 to 6 weeks and continuous antibiotics also significantly reduced the incidence of pyelonephritis compared with no treatment (low to moderate quality data).

**14.3.** Although there is no strong evidence on prescribing continuous prophylactic antibiotics long-term, they might be considered for individual patients if the benefit appears to outweigh the risk. Discuss individual patients with the consultant medical microbiologist.