Derbyshire Medicines Management UPDATE
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Derbyshire Medicines Management Prescribing and Guidelines
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To be reviewed again in May 2020

Diagnosis & management of lower UTI – an update on current issues

As antibiotic resistance & E. coli bacteraemias are ↑ in the community, use nitrofurantoin first line, always give safety net & self-care advice, & consider risks for resistance (as below). Give TARGET UTI leaflet, & refer to PHE UTI guidance for diagnostic information

Consider whether urine culture is needed (*as urine submissions to microbiology labs vary greatly*).

- **Do not send urines for culture in asymptomatic patients unless antenatal**
- **Elderly - only sample if: ≥ 2 signs of infection (*especially dysuria, pyrexia >38° or new incontinence*).**
- **Acute uncomplicated UTI in adult women (non-pregnant) – routine urine culture is unnecessary**

However, urine culture is needed if risk of ↑ resistance & other patients (*please see further details in sections below).*

Concerns that UTIs are being over-diagnosed *(as too few symptoms)* & thus treated unnecessarily

Need ≥ 3 typical symptoms of UTI *(i.e. dysuria; urgency; frequency, polyuria; suprapubic tenderness; haematuria)*
in order to give empirical antibiotic treatment in acute uncomplicated UTI in adult women (non pregnant).

Risks for ↑ resistance include:*>65yrs; - care home resident; - recurrent UTI; - previous resistant organism in urine; - treatment failures; - hospitalisation >7days in last 6 months; - recent travel to country with ↑ antimicrob. resistance.*

Catheter in situ (NICE & SIGN **– dipstick tests are not useful in catheterised patients**
- Antibiotics will not eradicate asymptomatic bacteriuria; only treat if systemically unwell or pyelonephritis likely.
- Do not use prophylactic antibiotics for catheter changes - unless history of catheter-change assoc. UTI / trauma.
- Patients should have a catheter passport (*giving details of catheterisation)* - check details with local continence team.

Acute uncomplicated UTI - adult women non-pregnant

(generally self-limiting and resolve without treatment).

- Routine urine culture is **un**necessary.
- Use symptoms & dipstick tests *(as req.)* to diagnose UTI (& ↓*antibiotic use & lab tests*) - **See page 2 for more details**
- 50% of women with symptoms of UTI have negative culture (symptoms are due to inflammation of urethra).

Lab test - culture & sensitivity should be done in:

- **Pregnancy:** If symptomatic, for investigation of positive UTI, and at first antenatal visit, as asymptomatic bacteriuria *is associated with pyelonephritis and premature delivery.*
- Suspected **UTI** in **children**, any sick child & every young child with unexplained fever - if <3m, refer urgently for assessment
- Suspected **pyelonephritis** *(temp ≥ 39.4; rigors; nausea; vomiting; diarrhoea; loin pain; or tenderness).*
- Suspected **UTI** in **men:** consider prostatitis (**or** *if mild / non-specific symptoms, use negative dipstick to exclude UTI)*
- **Catheterised** patients: only if features of systemic infection *as asymptomatic bacteriuria is usual & treatment not needed.* Thus, dipstick tests are **not** useful in catheterised patients.
- **Failed antibiotic treatment or persistent symptoms or recurrent UTI.**
- Community **multi-resistant *E.coli*** with Extended spectrum Beta-lactamase enzymes are ↑, so perform culture in all treatment failures. ESBLs are multi-resistant but can be sensitive to nitrofurantoin, pivmecillinam, **or** fosfomycin.
  Note Fosfomycin can be used but only as advised by C&S results or microbiology. See local **Fosfomycin** guidance and local **Management & Treatment of Infections Guidance**
- **abnormalities of genitourinary tract**
- **renal impairment** - *see* local '**UTI in CKD guidance**'
- **immunosuppression** (CKS) *e.g. poorly controlled diabetes mellitus or receiving immunosuppressants.*

Older people (>65 yrs)

- Asymptomatic bacteriuria in elderly is v common not related to ↑ morbidity /mortality- do **not** treat
- Investigation & treatment will ↑ side effects, medicalise the condition & ↑ antibiotic resistance
- Only sample if: **≥2** signs of infection. Do **not** send a sample in **a**symptomatic elderly with **+ve** dipsticks.

Empirical treatment of UTIs (non-pregnancy)

Uncomplicated UTIs *(lower UTIs, no fever / flank pain).*

- Nitrofurantoin 100mg m/r bd (1st line). If fever use alternative (do **not use** if suspect **upper** UTI-see local guidance: 'Tmt of Infections').

- Trimethoprim 200mg bd – if low risk of resistance

If first line unsuitable:

- Pivmecillinam 400mg stat, then 200mg tds x 3 days
[Note. 400mg tds – ***only if high*** *resistance risk].*

- Amoxicillin 500mg tds (***only if*** *organism is susceptible*).

- Treat for: 3 days in women *(all ages);* & 7 days in men

If ↑ resistance risk: Fosfomycin - only if advised by microb. or via C&S report (*if it is the only suitable option available).*
Women & men: 3g stat. Men: a 2nd 3g stat on day 3 (unlicensed)

- **Use urine dipstick** to guide treatment for women with mild or ≤ 2 symptoms of UTI – see next page
- **Perform culture & senstivity** in: treatment failure; pregnancy; children; men etc – *as per details on this page*
- **In >65 yrs - do not treat asymptomatic bacteriuria**
- **Community multi resistant E. coli (with ESBLs) are ↑** *thus, perform cultures in all treatment failures*
- **Co-amoxiclav has ↑ risk of C *difficile*** ***(only use if culture confirms susceptibility & other agents are C/I)***
- **Cephalosporins have ↑ risk of C *difficile* – *do not use cefalexin first line as empirical treatment***
- **See**: Fosfomycin guidance **- *See BNF cautions & C/Is*** *(all*

Note - in sexually active young men & women with urinary symptoms, consider Chlamydia

This update is based on PHE Primary Care Guidance: 'Management and Treatment of Common Infections' (March 18); and Diagnosis of UTIs by PHE (Updated, May 18) https://www.gov.uk/government/publications/urinary-tract-infection-diagnosis (includes all references)

Empirical treatment of UTIs in pregnancy PHE Managing Infections Guidance in Primary Care (PHE, March.2018).

Send MSU for culture and start antibiotics in all with a significant positive culture, even if asymptomatic

- **1st line - Nitrofurantoin** 100mg m/r bd for 7 days (except *at term in pregnancy, or if G6PD deficient*).
- **2nd line - Trimethoprim** 200mg bd (off label) for 7 days (except *in 1st trimester pregnancy*).
- **3rd line - Cefalexin** 500mg bd for 7 days [*PHE considers cefalexin as 3rd line. Also has ↑risk of C difficile].*
  [Note. Pivmecillinam – manufacturer advises to **avoid** its use in pregnancy, as per details in BNF]

Acute uncomplicated UTI in adult symptomatic women, <65yrs, (non- pregnant).

ASSESS SYMPTOMS - do not culture routinely. Consider Chlamydia, as appropriate.

Severe or ≥ 3 typical UTI symptoms
dysuria; urgency; frequency, polyuria; suprapubic tenderness; haematuria

— **AND** —

No vaginal discharge or irritation [*If present need to explore other diagnoses e.g. STIs, vulvovaginitis (due to candida),etc]*

→ **No dipstick/culture needed**
90% culture positive
Give empirical antibiotic treatment.

Mild or ≤ 2 symptoms of UTI
(as above)

→ Cloudy urine Do dipstick test with nitrite**- *to guide treatment**
*- reading test **wait** for recommended time*

If urine is **not** cloudy (& mild or ≤ 2 symptoms) 97% NPV. Do NOT treat (*unless other risk factors for infection*). Consider other diagnosis

Positive nitrite, **&** blood **&** leucocytes- **92% PPV** **or Positive nitrite alone**	**Negative:** -nitrite; -leucocytes; **&** blood **76% NPV**	**negative** nitrite **positive** leucocyte	**negative** nitrite & leucocyte **positive blood or protein**
Probable UTI	**UTI unlikely** Consider other diagnosis	*UTI **or** other diagnosis **equally likely*** Review time of specimen (morning is most reliable)	UTI **unlikely** Consider other diagnosis Reassure & give advice on managing symptoms
Treat with first line antibiotics - on local guidance	Reassure & give advice on management of symptoms.	Treat if severe symptoms or consider delayed script **& send urine for culture**	**Key: PPV= +ve Predictive Value** **NPV= -ve Predictive Value**

For further details, see: UTI guidance by PHE https://www.gov.uk/government/publications/urinary-tract-infection-diagnosis

Important As multi-resistant E. coli & bacteraemias are↑ in community, always safety net & consider risks for↑ resistance including: >65yrs; - care home resident; - recurrent UTI; - previous resistant organism in urine; - treatment failures; - hospitalisation >7days in last 6 months; - recent travel to country with ↑ antimicrobial resistance. See p4 for more details.

***** Note. Due to the risk of false negatives with dipsticks, it is generally advised to limit their use to situations when the diagnosis is not straightforward e.g. one or two mild symptoms but with cloudy urine (as above).

Nitrite is produced by the action of bacterial nitrate reductase in urine. As contact time between bacteria and urine is needed, morning specimens are most reliable. Leucocyte esterase detects intact and lysed leucocytes produced in inflammation. Haematuria and proteinuria occur in UTI but are also present in other conditions. When reading test **WAIT for the time recommended by manufacturer.

For further info. on UTIs: www.rcgp.org.uk/targetantibiotics (useful patient leaflets). Guidance: - Urinary tract infection - children - NICE CKS - **Urinary tract infection** (lower) - **women** - NICE **CKS** - **Urinary tract infection** (lower) - **men** - NICE **CKS** - **PHE UTI** (diagnosis details).

Sampling

- In men & women, the specimen should be mid-stream.
  In *women: cleansing with water & holding labia apart are not essential. Cleansing with antiseptic - leads to false negatives.*
- People with catheters: using aseptic technique, drain a few ml of urine, then collect a sample from catheter sampling port
- In toddlers: clean catch urine using potties washed in hot water (60°C) with washing up liquid are suitable.
- In infants: clean catch urine is preferable; a collection pad in nappy may be used but ↓ accuracy. Bag urines have ↓ comfort

Storage of samples

Refrigerate samples to prevent bacterial overgrowth (*or use specimen pots containing boric acid*). Samples that are not going to reach microbiology lab within 12 hours should not be sent unless they have been refrigerated or stored in a cool box.

How to interpret a culture result?

- *Culture of single organisms ≥ 10^4 colony forming units (CFUs)/mL* - ***Or*** *≥10^5 mixed growth with one predominant organism*
- ***Or*** *Escherichia coli or Staphylococcus saprophyticus significant if ≥10^3 CFU/ml.*

These (as above) usually indicate UTI in patient with urinary symptoms. Higher counts have even higher positive predictive value.

White blood cells:	- White cells ≥ 10^4/mL are considered to represent inflammation - In adults 'no white cells present' indicates no inflammation and ↓ significance of culture - Pregnancy is associated with physiological pyuria
Sterile pyuria:	- Consider *Chlamydia trachomatis* (if 16-24 years), other vaginal infections, other non-culturable organisms, including TB or renal pathology
Epithelial cells or mixed growth:	- Presence indicates perineal contamination, which reduces significance of culture.
Red cells	- May be present in UTI, patients with persistent haematuria post UTI should be referred

Urinary tract infections in adults - NICE quality standard [QS90], June 2015 https://www.nice.org.uk/guidance/qs90

This NICE quality standard covers the management of suspected community-acquired bacterial UTI in adults aged 16 years and over. This includes women who are pregnant, people with indwelling catheters and people with other diseases or medical conditions such as diabetes. For more information see the topic overview

Quality statement 1:

Diagnosing urinary tract infections in adults aged 65 years and over

Adults aged 65 years and over have a full clinical assessment before a diagnosis of a UTI is made.

Rationale

The accuracy of dipstick testing in adults aged 65 years and over can vary. It is therefore important that factors other than the results of dipstick testing are taken into consideration when diagnosing urinary tract infections in older people to ensure appropriate management and avoid unnecessary use of antibiotics.

Quality statement 2:

Diagnosing urinary tract infections in adults with catheters

Healthcare professionals do not use dipstick testing to diagnose urinary tract infections in adults with urinary catheters.

Rationale

Dipstick testing is not an effective method for detecting urinary tract infections in catheterised adults. This is because there is no relationship between the level of pyuria and infection in people with indwelling catheters (the presence of the catheter invariably induces pyuria without the presence of infection). To ensure that urinary tract infections are diagnosed accurately and to avoid false positive results, dipstick testing should not be used.

Quality statement 3:

Referring men with upper urinary tract infections

Men who have symptoms of an upper urinary tract infection are referred for urological investigation.

Rationale

Upper urinary tract infections can indicate the presence of lower urinary tract abnormalities. It is important that men with symptoms of an upper urinary tract infection have urological investigations to ensure that any possible abnormalities are diagnosed and treated

Quality statement 4:

Urine culture for adults with a UTI that does not respond to initial antibiotic treatment

Adults with a urinary tract infection not responding to initial antibiotic treatment have a urine culture.

Rationale

Some urinary tract infections are resistant to initial antibiotic treatment and a urine culture is needed (or a repeat where an initial urine culture was taken) to determine which antibiotic will work against the specific strain of bacteria causing the urinary tract infection. A urine culture is needed to guide a change in antibiotic treatment in people who do not respond to initial treatment with antibiotics.

Quality statement 5:

Antibiotic treatment for asymptomatic adults with catheters and non-pregnant women

Healthcare professionals do not prescribe antibiotics to treat asymptomatic bacteriuria in adults with catheters and non-pregnant women.

Rationale

Antibiotics are not effective for treating asymptomatic bacteriuria in adults with catheters or non-pregnant women. Unnecessary treatment with antibiotics can also increase the resistance of bacteria that cause urinary tract infections, making antibiotics less effective for future use.

Quality statement 6:

Antibiotic prophylaxis to prevent catheter-related urinary tract infections

Healthcare professionals do not prescribe antibiotic prophylaxis to adults with long-term indwelling catheters to prevent urinary tract infection unless there is a history of recurrent or severe urinary tract infection.

Rationale

Evidence shows that antibiotic prophylaxis is not effective in preventing symptomatic urinary tract infection in adults with long-term indwelling catheters unless there is a history of recurrent or severe urinary tract infection.

Quality statement 7:

Treatment of recurrent urinary tract infection

Recurrent urinary tract infections are common and it is important that they are managed and prevented effectively.

Key messages on preventing Gram-negative (*E. coli)* bloodstream infections (BSIs). All new details

Preventing healthcare associated Gram-negative (focus on *E. coli)* BSIs: an improvement resource by PHE and NHS Improvement. May 17 https://improvement.nhs.uk/uploads/documents/Gram-negative_IPCresource_pack.pdf

Please see this useful resource (from link above). It includes: background facts and figures on *E. coli* BSIs across England. It explains that the risk is greater among older patients and that most cases (73%) are community onset.

The most common source of infection is **UTI** (45%), followed by unknown (24%), hepatobiliary (14%), other source (11% e.g. skin/soft tissue, intravascular devices, respiratory tract), and gastrointestinal (6%).

It highlights that the most common source of infection is the urogenital tract at 51.2%. Thus targeting UTIs can have a significant impact in reducing the number of these infections.

Please see the different guidance /action that can be taken to reduce *E. coli* BSIs on p 9-11, including the following for urinary tract or catheter associated urinary tract: -bladder scanners; -urinary catheters; -catheter passports; -appropriate recognition and treatment of UTIs.

Please also see **Sepsis: recognition, diagnosis & early management** **https://www.nice.org.uk/guidance/ng51** *Updated: Sept 17*

E. Coli bacteraemias (BSIs)

- Significant numbers occur in patients with a history of repeated UTIs (in the period leading up to the BSI).
- Increased resistance to trimethoprim (treatment should be based on local antibiotic resistance patterns).
- Patients diagnosed with a UTI (especially those with a history of repeated infections) should be subject to a 'safety netting' procedure to ensure that treatment has been effective.

Results of Investigation of E. coli BSIs (ARHAI, 2013)
Only a small proportion of infections were related to urinary catheterisation. Other factors e.g. repeated UTIs (treated by sub-optimal antibiotic prescribing) and dehydration as risk factors for UTIs had a significant impact.

Higher rates of E. coli BSIs in England are in older people (≥75 yrs) at 402.9 & 313.5 reports /100,000 population for males and females respectively, followed by adults (65-74 yrs) at 132.3 & 104.3 reports.

Optimising the management of UTIs, including assessing risk factors for resistance

- Antibiotic resistance and E. coli BSIs are increasing in the community: use nitrofurantoin first line; always give safety net and self-care advice, plus consider risks for resistance.
- Give TARGET UTI patient leaflet – V18 [PDF] [DOC] and refer to PHE UTI guidance for diagnostic information
Diagnosis of urinary tract infections: quick reference guide for primary care

Risk factors for increased resistance include:

- >65yrs; - care-home resident; - Recurrent UTI; - hospitalisation >7 days in last 6 months;
- unresolving urinary symptoms; - recent travel to a country with ↑ resistance; - treatment failures;
- previous UTI resistant to trimethoprim, cephalosporins, or quinolones.

- If risk of resistance: send urine for culture and susceptibilities and safety net
- Community multi-resistant E. coli are ↑, so perform culture in all treatment failures
- Multi-resistant isolates are usually resistant to amoxicillin, co-amoxiclav, cephalosporins & *may also be resistant to trimethoprim & quinolones*. Often susceptible to nitrofurantoin, pivmecillinam & fosfomycin

Pivmecillinam (a penicillin) was introduced as a 2nd line option for lower UTIs. Resistance rate is low and it is less likely to cause C. difficile.

Local Resistance rates (urine samples):
Pivmecillinam 2%; Nitrofurantoin 4%; Trimethoprim 27%; Amoxicillin 51%; Co-amoxiclav 13%; Cefalexin 11%

As trimethoprim resistance is increasing, it is only advised if there is low risk of resistance (e.g. younger female with acute UTI and no risk factors for resistance). Furthermore, as amoxicillin resistance is high, it is not advised for empirical use and should only be used if organism is susceptible.

Note. To obtain a urine sample in people with urinary catheters.

Contact district nurse to change the catheter (if not done within past 7 days and able to change it in the community). The nurse will obtain a CSU (Catheter Specimen of Urine) 'directly from the tubing of the clean catheter' to obtain an uncontaminated sample - preferably prior to commencing antibiotics. Please note that GPs/clinicians should contact the district nurse informing them of the CAUTI (rather than family members taking a urine sample & returning it to the surgery.