Urinary tract infections in the community

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ABSTRACT

Urinary tract infections (UTIs) are defined as significant bacteriuria in the setting of symptoms of cystitis/pyelonephritis. Urine dipstick is diagnostic in most cases. Urinalysis and Microscopy (U&M) and Culture and Sensitivity (C&S) prior to starting antibiotic therapy is indicated for the diagnosis and as an aid to the correct management of UTIs in certain settings. Antibiotics to treat UTIs must be carefully chosen and their prescribed duration depends on the type of UTI. Over-the-counter products for the treatment and prevention of UTIs are available: these include cranberry products and potassium citrate. Recurrent UTIs in females, UTIs in catheterized men, pyelonephritis and UTIs with unusual organisms require further investigation.

Keywords/ phrases: urinary tract infections; cystitis; bacteriuria; pyelonephritis

INTRODUCTION

Urinary tract infections (UTIs) are defined as significant bacteriuria in the setting of symptoms of cystitis or pyelonephritis (Health Protection Agency, 2006).

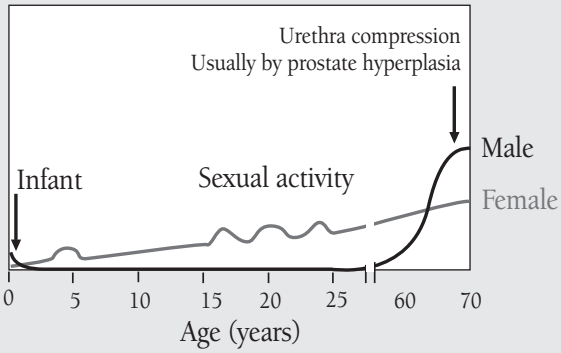
Asymptomatic bacteriuria is a laboratory diagnosis. In women it is present when there are two consecutive specimens with an isolation of 100,000 cfu/mL of single bacterial species (cfu is colony forming units; mL is millilitre) (Health Protection Agency, 2006). In men it is diagnosed when there is one specimen with an isolation of 100,000 cfu/mL of single bacterial species is present (Health Protection Agency, 2006). The diagnosis in catheterized patients is done when a specimen with an isolation of 100cfu/mL of single bacterial species is present (Health Protection Agency, 2006).

The epidemiology is shown in Figure 1. It is relatively common in infancy. With the advent of sexual activity, it is commoner in females than in males. However with the advent of benign prostate hypertrophy it becomes more common in males.

PREDISPOSING FACTORS

A number of predisposing factors make the occurrence of a urinary tract infection more possible. Being female makes a UTI more likely. Urinary stasis is a major determinant. This can be due to obstruction to flow of urine e.g. a person might be too busy to empty the bladder, the presence of urinary stones or bladder tumours, enlargement of the prostate, the effect of pregnancy, after anaesthesia and after major surgery.

Figure 1: Epidemiology (University of South Carolina, 2011)



Other predisposing factors are sexual intercourse, menopause, instrumentation of the urinary tract, anomalies of the urinary tract, constipation in both children and the elderly and poor perineal hygiene in the elderly. Patients with diabetes are more prone to UTIs.

PATHOGENS INVOLVED

In cystitis or in pyelonephritis a number of pathogens can be involved. Some are more common than others. The commonest cause is *Escherichia coli* (Mifsud, 2013). *Proteus* species are associated with renal stones. *Staphylococcus saprophyticus* is associated with UTIs in young women. Other common pathogens are *Klebsiella pneumonia, Pseudomonas aeruginosa*, *Enterobacter* species and *Enterococcus fecalis.* Other pathogens are uncommonly encountered: Adenovirus types 1-47, *Mycobacterium tuberculosis, Leptospira interrogans, Schistosoma* species and *Candida albicans. Candida albicans* is associated with UTIs in people with diabetes and in people who are immunocompromised. Cystitis originates primarily from pathogens in the bowel flora. The infection then ascends to the urinary tract: this mechanism is the most common, especially in females.

At times General Practitioners/Family Doctors need to distinguish the presence of urethritis. This is characterized by dysuria without suprapubic discomfort. Urethritis makes a General Practitioner/Family Doctor think of a Sexually Transmitted Infection. Here the common organisms are *Chlamydia trachomatis* (which gives sterile pyuria in the sexually active), *Ureaplasma urealyticum*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*.

At times a UTI is the result of a blood-borne infection. In this case the culprit organisms are *Mycobacterium tuberculosis*, *Leptospira interrogans* and *Salmonella*.

CLINICAL FEATURES

The clinical features help to distinguish between an acute cystitis and a pyelonephritis. This in turn impacts on the management options.

The clinical features of an acute cystitis are dysuria, urinary frequency, urgency, suprapubic pain and tenderness and haematuria. In the elderly confusion and/or incontinence can be the presenting clinical features of acute cystitis. In children acute cystitis can present with fever, anorexia, lethargy, irritability, failure to thrive, abdominal pain and vomiting. Haemorrhagic cystitis is additionally characterised by macroscopic haematuria. However, apart from bacterial infection and adenovirus type 1-47 infection there are other causes of haemorrhagic cystitis. The latter include bladder stones, schistosomiasis, after radiation therapy, cancer chemotherapy and immunosuppressive medication.

The clinical features of pyelonephritis include flank pain/back pain and fever (these features are indicative of both bacteraemia and of kidney involvement), nausea, vomiting and chills.

Owing to the many natural defences to infection of the urinary tract in males, UTIs in males are considered to be complicated. This is because they are more likely to be associated with anatomical abnormalities, requiring surgical intervention to prevent sequelae. Imaging studies in males are to be considered in patients with diabetes, in patients with polycystic kidneys, in patients with tuberculosis and in patients with a history of kidney stones.

COMPLICATIONS OF UTIs

Patients with UTIs at times present to the consulting room afraid of some of the possible complications. These include bacteraemia, chronic pyelonephritis, kidney abscess, septicaemia and eventually death. UTIs are particularly important in infants and children < 4 years due to the association with vesico-ureteric reflux; and renal scarring (National Institute for Health and Care Excellence (NICE) Guidelines, 2007). Renal scarring leads to reflux nephropathy with associated eventual hypertension and renal failure.

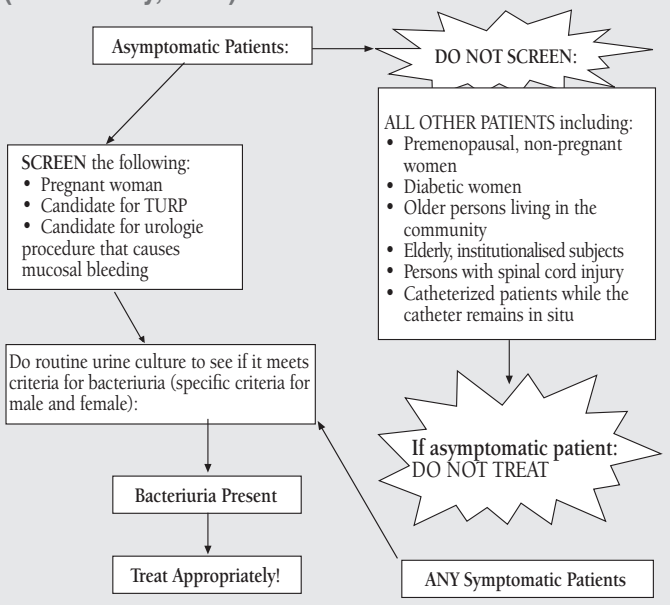
INVESTIGATIONS

The investigations start at the clinic. The physical appearance of the urine sample gives an indication of what may be going on. A urine sample that looks cloudy is strongly suggestive of a bacterial UTI. A red sample points to the presence of haematuria and the cause of this is to be defined.

The investigation of a urine sample demands a 'clean-catch' urine specimen. This would need careful cleansing of the perineal area, removal of skin that is in the way, and the collection of a mid-stream specimen.

The next step is the dipstick analysis. A combination of classical clinical features and the result of dipstick analysis are enough for a diagnosis of UTI in healthy adult women. The nitrite test points towards enterobactericeae if positive. The leucocyte-esterase test detects intact and lysed leucocytes; this needs contact time with bacteria (hence ideally the first morning

Figure 2: Asymptomatic Bacteriuria (Chowdhury, 2012)



specimen should be used). The pH is important as it may assist in choice of antibiotic: a high urinary pH may be indicative of a pathogen that produces urease enzymes, e.g. *Proteus* or *Serratia*, which are intrinsically resistant to nitrofurantoin. Nitrofurantion should not be prescribed for infections characterised with a urine pH >7. Other tests in the dipstick analysis are for protein and blood.

The subsequent tool in the investigation portfolio is many a time a urine culture. Once again a 'clean-catch' specimen is warranted. The indications for a urine culture are: a man with symptoms of UTI, a child with possible UTI, a suspected UTI in pregnancy, a suspected UTI in a patient with abnormal urinary tract, a suspected UTI in a patient with renal impairment, in cases of suspected pyelonephritis, in cases of unresolved, relapse or recurrent infection, in patients who are immunosuppressed and when instrumentation of the urinary tract was recently performed.

DIAGNOSIS

Dipstick analysis results provide General Practitioners/ Family Doctors with a diagnosis in a number of occasions (Table 2).

Together with a urine culture a sample is usually sent for urine microscopy. A 'clean-catch' specimen is warranted. The sample is examined as a wet preparation to detect the presence of significant pyuria (white blood cells $\geq 10^7$ cells/ml of urine), red blood cells, epithelial cells (an indication of perineal contamination), yeast cells, *Trichomonas vaginalis* trophozoites, *Schistosoma haematobium* eggs, crystals and casts.

For the diagnosis of a UTI, a urine mid-stream specimen of urine (MSU) for culture and sensitivity (C&S) has to be taken prior to starting the patient on any antibiotic treatment. A UTI is diagnosed when a symptomatic patient has a urine MSU C&S of $\geq 10^5$ CFU bacteria/ml of urine (Simon, Everitt and Kendrick, 2006). This amount i.e. $\geq 10^5$ CFU bacteria/ml of urine denotes a significant bacteriuria. If the bacteria specimen grown is *Escherichia coli* or *Staphylococcus saprophyticus* at $\geq 10^3$ CFU bacterial/ml of urine, this is enough for diagnosis of significant bacteriuria (Health Protection Agency, 2006). If the amount is $< 10^4$ CFU bacteria/ml of urine or there are more than one bacterial type, this is indicative of bacterial contamination (Health Protection Agency, 2006).

In a UTI an MSU C&S will show pyuria, bacteriuria and nitrates. If in an MSU C&S shows pyuria without bacteriuria this signifies inflammation whereas bacteriuria without pyuria signifies colonization. Causes of the above are tabulated in Table 3.

A UTI is defined as a significant bacteriuria in a symptomatic patient. There will be instances where a significant bacteriuria will be found in an asymptomatic patient when screening with MSU C&S in done. Asymptomatic screening is only warranted in the categories of patients listed in Figure 2. If significant bacteriuria is found in one of these patients, they should be treated appropriately as is shown in Figure 2. All other asymptomatic patients should not be routinely screened.

FURTHER INVESTIGATIONS

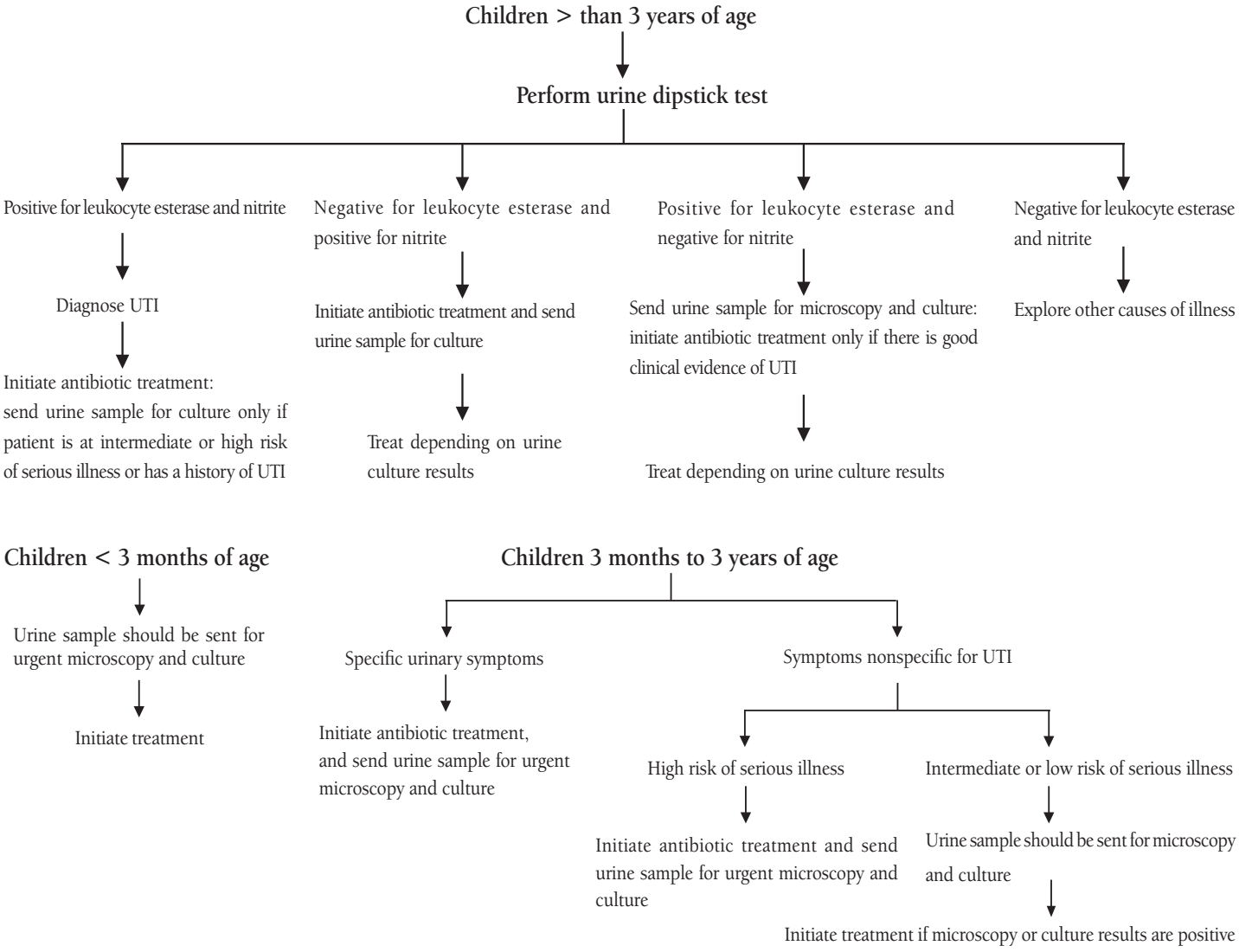
UTIs in uncatheterised males, recurrent UTIs in women, pyelonephritis, where the diagnosis is unclear and in cases where unusual pathogens are grown, require further investigations. These include blood tests for renal profile and possibly a Prostate Specific Antigen test in males. Imaging such as ultrasound (US), computed tomography scan of the kidney, ureter and bladder (CT-KUB), intravenous urogram (IVU), micturating cystourethrogram (MCUG) and dimercaptosuccinic acid scan (DMSA) may be needed.

TREATING UTIs

Over-The-Counter Preparation

Alkalization of urine with products such as **potassium citrate** is used to alleviate symptoms of dysuria; however evidence base is lacking. It should be used with caution in patients suffering from heart failure and hypertension

Diagnosing UTI in children (adapted into table format from NICE Guidelines 2007: Urinary Tract Infections in Children)



because of their high sodium and potassium content as well as patients on potassium sparing diuretics such as angiotensin converting enzyme Inhibitors and angiotensin receptor blockers. It should not be used in combination with nitrofurantoin because the latter needs an acidic pH to work.

Antibiotics

Table 4 shows the UTI cases isolated from the urine samples sent from the community to the Pathology Department of Mater Dei Hospital in the period January to March 2014. It shows what organisms were cultured and their sensitivities to different antibiotics.

First line antibiotics for UTIs are (Mifsud, 2013):

Nitrofurantoin provides consistent efficacy for *Escherichia coli* and *Staphylococcus saprophyticus*. It does not disturb the vaginal flora. It is not advisable for use after 36 weeks' gestation because of the risk of haemolysis if the fetus has glucose-6-phosphate dehydrogenase deficiency.

Beta-Lactam antibiotics including amoxicillin, amoxicillin/clavulanate and cephalosporins are effective but there are hypersensitivity issues.

Quinolones are contraindicated in patients prone to seizure. Tendinitis as a side effect of quinolone use has to be kept in mind. Norfloxacin and ciprofloxacin are particularly useful for upper UTIs and pyelonephritis, but nalidixic acid is not effective against *Pseudomonas*.

Co-trimoxazole: consider hypersensitivity to these drugs and contemporary drug resistance patterns before prescribing such drugs.

Antibiotic duration for UTIs depends on the type of UTI. For example for cystitis 3-5 days of antibiotics is sufficient, while for pyelonephritis up to 14 days of antibiotics may be needed. Complicated UTIs may need more prolonged treatment. Patients with risk factors such as prostatic enlargement, urologic anomaly, resistant

pathogens and recurrent UTIs usually require prolonged treatments and also combination treatments.

PROPHYLAXIS FOR RECURRENT UTIs

Advise patients to drink plenty of water, micturate frequently, double void, void after intercourse, wipe perineum front to back, avoid perfumed soaps/bubble baths and to wear cotton underwear to avoid recurrent UTIs.

Cranberry products are recommended for the prophylaxis of recurrent UTIs in premenopausal women (Health Protection Agency, 2006). Thirty-six mg/day of the active compound proanthocyanindin A is recommended. Cranberry products have not been shown to be effective for the treatment of a UTI and neither is it effective for the prophylaxis of UTIs in postmenopausal or catheterised patients. When suggesting cranberry products for the prophylaxis of UTIs, the interaction with warfarin through cytochrome P 450 is to be kept in mind.

Topical Hormone Replacement Treatment decreases recurrent UTIs in women of all ages(Health Protection Agency, 2006). In men with prostatic enlargement, finasteride and/or doxazocin helps decrease the incidence of recurrent UTIs (Health Protection Agency, 2006).

Recurrent UTIs in adults are defined as three UTIs in 12 months or two UTIs in six months(Health Protection Agency, 2006). In these cases, if symptoms are debilitating for the patient one might consider antibiotic prophylaxis, which is usually taken at night when urine flow is low. Antibiotic prophylaxis is not recommended for more than six months in view of resistance (Mifsud, 2013). Antibiotic prophylaxis is usually not recommended for catheterized patients (Mifsud, 2013).

UTIs IN CHILDREN

UTIs in children have different clinical features depending on the age group of the child. At times diagnosing UTIs in children is a challenge. Table 1 summarises the clinical features of UTIs in children.

One may diagnose UTI in children using the algorithms in Figures 3. The following lists (National Institute for Health and Care Excellence (NICE) Guidelines, 2007) may be used to come to a working diagnosis:

Children with an atypical UTI:

- Are seriously ill
- Have poor urine flow
- Have an abdominal or bladder mass
- Have a raised creatinine
- Have septicaemia
- Fail to respond to suitable antibiotics within 48 hours
- Have non-*E coli* organisms.

Table 1: UTI Features in Children (adapted into table format from NICE Guidelines 2007: Urinary Tract Infections in Children)

Age group		Symptoms and signs		
		Most common		Least common
Infants younger than 3 months		Fever Vomiting Lethargy Irritability	Poor feeding Failure to thrive	Abdominal pain Jaundice Haematuria Offensive urine
Infants and children, 3 months or older	Preverbal	Fever	Abdominal pain Loin tenderness Vomiting Poor feeding	Lethargy Irritability Haematuria Offensive urine
	Verbal	Frequency Dysuria	Dysfunctional voiding Changes to continence Abdominal pain Loin tenderness	Fever Malaise Vomiting Haematuria Offensive urine Cloudy urine

Table 2: Urine Dipstick Interpretation (WCC- white cell count; RBC red blood cells)

Nitrites	WCC	Protein	RBC	Diagnosis
+	±	±	±	Probable UTI: give Antibiotic
-	-	-	-	"Urethral syndrome". Reassure
-	+	±	±	Review sampling time. Treat if symptoms severe and send culture
-	-	±	+	Consider other causes

Table 3: Causes of pyuria without bacteriuria and causes of bacteriuria without pyuria

Pyuria without bacteriuria	Bacteriuria without pyuria
Patient on antimicrobial treatment	Urine contamination
Inadequately treated UTI	
Renal tuberculosis	Childhood UTI
Gonococcal urethritis	
Prostatitis	Bacterial endocarditis
Chlamydia trachomatis	
Leptospirosis	Diabetes Mellitus
Appendicitis	
Schistosomiasis	Enteric Fever
Papillary necrosis	
Interstitial nephritis	
Interstitial cystitis	
Polycystic kidneys	
Renal Stones	
Bladder tumor	
Chemical/Radiation cystitis	

A recurrent UTI is defined as:

- Two or more episodes of UTI with upper UTI
- One episode of UTI with upper UTI plus one or more episodes of lower UTI
- Three or more episodes of UTI with lower UTI.

Table 5 summarizes imaging tests used in children with UTIs

URETHRAL SYNDROME

Fifty per cent of women with symptoms of cystitis have negative bacteriological culture and are said to have urethral syndrome. The aetiology is unknown however it is being linked to chlamydia. Is it associated with cold, stress, sex, nylon underwear and the combined oral contraceptive (COC) pill (Health Protection Agency, 2006). Treatment may include stopping or changing the COC pill, topical oestrogen if post-menopausal or doxycycline 100mg twice daily for 14 days or azithromycin 500mg daily for 6 days. Urethral dilatation/ massage might help (Health Protection Agency, 2006).

INTERSTITIAL CYSTITIS

This condition affects predominantly middle-aged women. It can cause fibrosis of the bladder wall. The symptoms are frequency, urgency and suprapubic pain when the bladder is full. It can be misdiagnosed as recurrent UTI. The MSU C&S shows no bacteriuria. The General Practitioner/Family Doctor may consider referral to urology but there is no satisfactory treatment though antispasmodics, amitriptyline and bladder stretching may help.

Table 4: Local UTI cases January- March 2014: organisms isolated and their sensitivities (table presented by Consultant Virologist Dr. Chris Barbara during Malta College of Family Doctors Continued Medical Education activity of 01.04.2014)

Organism	Escherichia coli	Enterococcus faecalis	Klebsiella oxytoca	Klebsiella pneumoniae	Citrobacter koseri
Cases Isolated 2014 (Jan to Marc)	17	7	2	2	2
	%Sensitive	%Sensitive	%Sensitive	%Sensitive	%Sensitive
Amikacin	100.00		100.00	100.00	100.00
Ampicillin	41.18	100.00	0.00	0.00	
Co-Amoxyclav	82.35		100.00	100.00	100.00
Ceftazidime	94.12		100.00	100.00	100.00
Ciprofloxacin	94.12		100.00	100.00	100.00
Trimeth Sulfa	64.71		100.00	100.00	100.00
Cefotaxime	94.12		100.00	100.00	100.00
Ertapenem	100.00		100.00	100.00	100.00
Cefepime	94.12		100.00	100.00	100.00
Fosfomyain	100.00		100.00	100.00	100.00
Gentamicin	94.12	85.71	100.00	100.00	100.00
Imipenem	100.00	100.00	100.00	100.00	100.00
Meropenem	100.00		100.00	100.00	100.00
Nitrofurantoin	94.12	100.00	0.00	0.00	100.00
Norfloxacin	64.71		100.00	100.00	100.00
Pip/Tazobactan	100.00		100.00	100.00	100.00
Levofloxacin		100.00			
Linezolid		100.00			
Moxifloxacin		100.00			
Quinupristine Dalfopristine		0.00			
Anti-Smith Ab (Sm)		100.00			
Ampicillin/Sulbactam		100.00			
Streptomycin		71.43			
Teicoplanin		100.00			
Tigecycline		100.00			
Vancomycin		100.00			
Other organisms isolated once:	Enterobacter cloacae				
	Proteus vulgaris				
	Citrobacter freundii				

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Table 5: Imaging in children with UTIs (adapted into table format from NICE Guidelines 2007: Urinary Tract Infections in Children). NB: DMSA scan: dimercaptosuccinic acid scan; MCUG: micturating cystourethrogram

5A: Imaging in infants < 6 months of age with UTI

Test	Responds well to treatment within 48 hours	Atypical UTI	Recurrent UTI
Ultrasound during the acute infection	No	Yes	Yes
Ultrasound within six weeks	Yes	No	No
DMSA scan four to six months following the acute infection	No	Yes	Yes
MCUG	No	Yes	Yes

5B: Imaging in children > 6months of age and < 3 years of age

Test	Responds well to treatment within 48 hours	Atypical UTI	Recurrent UTI
Ultrasound during the acute infection	No	Yes	No
Ultrasound within six weeks	No	No	Yes
DMSA scan four to six months following the acute infection	No	Yes	Yes
MCUG	No	No	No

5C: Imaging in children > 3 years of age

Test	Responds well to treatment within 48 hours	Atypical UTI	Recurrent UTI
Ultrasound during the acute infection	No	Yes	No
Ultrasound within six weeks	No	No	Yes
DMSA scan four to six months following the acute infection	No	No	Yes
MCUG	No	No	No

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Competing Interests
None to our knowledge

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