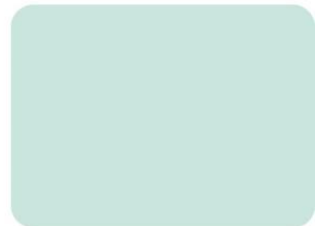
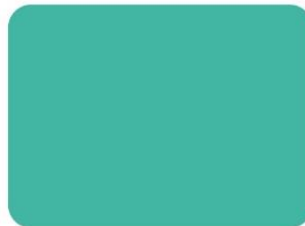
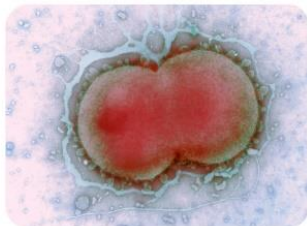
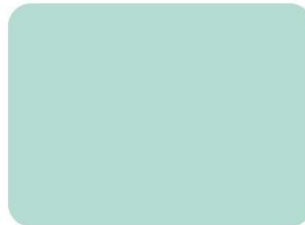
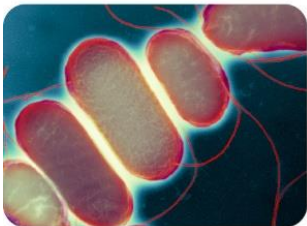
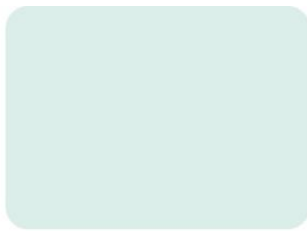
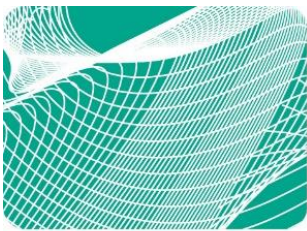




UK Health
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UK Standards for Microbiology Investigations

Investigation of urine



Acknowledgments

UK Standards for Microbiology Investigations (UK SMIs) are developed under the auspices of UKHSA working in partnership with the partner organisations whose logos are displayed below and listed on [the UK SMI website](#). UK SMIs are developed, reviewed and revised by various working groups which are overseen by a [steering committee](#).

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Amendment table

Each UK SMI document has an individual record of amendments. The amendments are listed on this page. The amendment history is available from standards@ukhsa.gov.uk.

Any alterations to this document should be controlled in accordance with the local document control process.

Amendment number/date	19/05.12.25
Issue number discarded	8.7
Insert issue number	8.8
Section(s) involved	Amendment
Whole document.	<p>This is an administrative point change.</p> <p>The content of this UK SMI document has not changed.</p> <p>The last scientific and clinical review was conducted on 11/01/2019.</p> <p>Hyperlinks throughout document updated to Royal College of Pathologists website.</p> <p>Public Health England replaced with UK Health Security Agency throughout the document, including the updated Royal Coat of Arms.</p> <p>Partner organisation logos updated.</p> <p>Broken links to devolved administrations replaced.</p> <p>References to NICE accreditation removed.</p> <p>Scope and Purpose replaced with General and Scientific information to align with current UK SMI template.</p>

Amendment no/date.	18/11.01.19
Issue no. discarded.	8.6
Insert issue no.	8.7
Section(s) involved	Amendment
Section 4.7.1 Antimicrobial susceptibility testing and reporting table	A comment was added for Tazobactam which should not be tested or reported for <i>Acinetobacter spp.</i>

Amendment no/date.	17/07.08.18
Issue no. discarded.	8.5
Insert issue no.	8.6
Section(s) involved	Amendment
Section 2.2 Optimal time and method of collection.	Removed recommendation for periurethral cleaning in mid-stream urine (MSU) collection.

Amendment no/date.	16/01.05.18
Issue no. discarded.	8.4
Insert issue no.	8.5
Section(s) involved	Amendment
Section 5.2 Culture.	Typo amended in text.

Amendment no/date.	15/16.08.17
Issue no. discarded.	8.3
Insert issue no.	8.4
Section(s) involved	Amendment
Page 19 Interpretation of culture.	Bacteria levels have been corrected.

Amendment no/date.	14/07.08.17
Issue no. discarded.	8.2
Insert issue no.	8.3
Section(s) involved	Amendment
Page 14 Organisms implicated in UTI.	Spelling error corrected.
Page 14 Organisms implicated in UTI.	Reorganisation of some text.

Amendment no/date.	13/06.06.17
Issue no. discarded.	8.1
Insert issue no.	8.2
Section(s) involved	Amendment
Introduction.	Definition of pyuria added and referenced.
Appendix 2.	Formula and definitions updated.

Amendment no/date.	12/06.09.16
Issue no. discarded.	8
Insert issue no.	8.1
Section(s) involved	Amendment
Types of urine specimen and collection.	Spelling error corrected.

Amendment no/date.	11/15.08.16
Issue no. discarded.	7.2
Insert issue no.	8
Section(s) involved	Amendment
Introduction.	<p>This has been expanded to include pyuria, haematuria, and Candida species.</p> <p>The section has been streamlined to make it easier to find information that relates to men and women.</p> <p>Healthcare associated UTI has now been changed to 'Catheterisation'.</p> <p>The section on semi-automated methods has been expanded to include more systems.</p> <p>Legionella urinary antigen detection has been added to the document.</p> <p>Screening for <i>Neisseria gonorrhoea</i> has been added.</p>

Investigation of urine

Technical information/limitations.	<p>“Transport of urine specimens” section has been expanded.</p> <p>Section on “Validation and verification” has been added.</p> <p>Section on “Carry over contamination” has been added.</p>
Antimicrobial susceptibility testing.	<p>This section has been expanded and now includes a reporting table.</p>
Reporting procedure.	<p>Two new sections have been added to this;</p> <p>“Microscopy or chemical screening reporting times” and “Urine for antigen testing”.</p> <p>Note for <i>T. hominis</i> removed.</p>

1 General information

[View general information](#) related to UK SMIs.

2 Scientific information

[View scientific information](#) related to UK SMIs.

3 Scope of document

Type of specimen

Bag urine, pad urine, catheter urine, prostate massage/secretions, clean catch urine, suprapubic aspirate, cystoscopy urine, ureteric urine, ileal conduit urine, urostomy urine, mid-stream urine, nephrostomy urine

This UK SMI describes the processing and bacteriological investigation of urine samples. These include mid-stream and clean catch specimens and those collected via bag, ileal conduit, ureter, catheter, urostomy, nephrostomy, cystoscopy, supra pubic aspirate, prostate massage/secretions, and pad urine.

This UK SMI does not describe in detail semi-automated systems such as urine analysers which should be validated and used in accordance with manufacturers' instructions. Due regard should be taken of various groups including pregnant women, children, men and all patients who are immunocompromised.

This UK SMI also covers the detection of Legionella urinary antigens.

This UK SMI should be used in conjunction with other UK SMIs.

4 Introduction

4.1 Urinary tract infection

Urinary tract infection (UTI) results from the presence and multiplication of microorganisms, in one or more structures of the urinary tract, with associated tissue invasion¹. This can give rise to a wide variety of clinical syndromes. These include acute and chronic pyelonephritis (kidney and renal pelvis), cystitis (bladder), urethritis (urethra), epididymitis (epididymis) and prostatitis (prostate gland). Infection may spread to surrounding tissues (eg perinephric abscess) or to the bloodstream.

Protection against infection is normally given by the constant flow of urine and regular bladder emptying. Urine is a poor culture medium for many bacteria due to its acidity, high urea concentration and variable osmolality and, in men, possibly partly as a result of antibacterial activity of prostatic secretions².

The following is a list of terms used in UTI:

Bacteriuria³

Bacteriuria implies that bacteria are present and may be cultured from urine. The patient may or may not be symptomatic.

Pyuria is defined as the presence of 10 or more white blood cells per cubic millimetre in a urine specimen, 3 or more white cells per high-power field of unspun urine, a positive result on Gram's staining of an unspun urine specimen, or a urinary dipstick test that is positive for leucocyte esterase⁴. It is most commonly associated with a bacterial urinary tract infection in the upper or lower urinary tract. Pyuria may be present in septic patients, or in older patients with pneumonia⁵.

Other conditions that could cause pyuria are infections (such as that caused by *C. trachomatis*, *N. gonorrhoeae*, or herpes simplex virus and occasionally in women with vaginitis caused by *T. vaginalis* or candida infections), pyelonephritis, papillary necrosis, diabetes, renal tuberculosis, renal stones, Kawasaki disease and cancer⁶.

Sterile Pyuria (ie no growth on routine culture media and the persistent presence of white blood cells in the urine) may be the result of many factors including: a result of prior treatment with antimicrobial agents; catheterisation; calculi (stones); or bladder neoplasms. Other conditions which may lead to sterile pyuria include genital tract infection; sexually transmitted diseases, eg *C. trachomatis* or an infection with a fastidious organism^{7,8}. Renal tuberculosis may also be implicated in sterile pyuria but is uncommon, although should be considered if clinically indicated (eg in high risk populations)⁹.

Haematuria¹⁰ – Haematuria is observed in patients with acute cystitis, but is rarely seen in association with other dysuric syndromes. Finding 1–2 red blood cells (RBCs)/high power field is not considered to be abnormal. Haematuria may be caused by non-infective pathological conditions of the urinary tract or by renal mycobacterial infection, with or without associated pyuria. Apparent haematuria may be the result of menstruation. Differentiation of dysmorphic RBCs to determine those of glomerular origin is sometimes requested by specialist units, although its reliability is disputed^{11,12}. RBC lysis may occur in hypertonic and hypotonic urine, rendering them undetectable by microscopy.

Symptomatic patients

Symptomatic patients may be bacteriuric or abacteriuric. Symptoms in children and the elderly, when present, may be non-specific and difficult to interpret.

Frequency

The average bladder capacity is about 500mL. Significant reduction in capacity accompanies acute inflammation which can lead to an increase in the frequency of micturition.

Dysuria

Dysuria is painful and difficult micturition.

Urgency

Urgency is a strong desire to empty the bladder, which can lead to incontinence.

Nocturia

Nocturia is waking in the night one or more times to void the bladder^{13,14}. Nocturnal enuresis is the involuntary voiding of urine during sleep, ie bed-wetting.

Incontinence

Incontinence is the involuntary leakage of urine. The commonest form of this is stress incontinence where leakage accompanies an increase in intra-abdominal pressure due to sneezing, coughing or laughing. Overflow or dribbling incontinence accompanies an overfilled bladder.

Renal colic

This is characterised by very severe cramping pain resulting from distension of the ureter and pelvis above an obstruction such as a renal stone. Often accompanied by frequency and urgency.

4.2 Clinical manifestations of UTI

Asymptomatic bacteriuria and candiduria

Asymptomatic bacteriuria is common in several patient groups, particularly the elderly, pregnant women, transplant patients and diabetic patients¹⁵⁻¹⁷.

Acute urethral syndrome

Acute urethral syndrome occurs in women with acute lower urinary tract symptoms with either a low bacterial count or without demonstrable bacteriuria or vulvovaginal infection^{7,18}. The condition can also occur in men but is not well studied¹⁹.

Uncomplicated UTI

Uncomplicated UTI occurs in otherwise healthy individuals. There are no underlying structural or neurological lesions of the urinary tract, and no other systemic diseases predisposing the host to bacterial infection. Recurrences are usually reinfections with organisms ascending via the urethra.

Acute uncomplicated cystitis

Acute uncomplicated cystitis condition usually occurs in young women. It has an abrupt onset and produces severe symptoms which are usually accompanied by pyuria and bacteriuria. Uncomplicated cystitis can occur in some men²⁰.

Complicated UTI

Complicated UTI occurs in patients in whom there may be residual inflammatory changes following recurrent infection or instrumentation, obstruction, stones, or anatomical or physiological abnormalities or pathological lesions. These interfere with drainage of urine in part of the tract which encourages prolonged colonisation. Relapses with the same organism may occur.

The following are examples of complicated UTI:

Acute pyelonephritis (pyelitis) – An inflammatory process of the kidneys and adjacent structures. Symptoms include loin, low back or abdominal pain and fever. Symptoms of cystitis may also be present. Severity ranges from mild disease to full blown Gram negative sepsis.

Chronic pyelonephritis (chronic interstitial nephritis, or reflux nephropathy) –

Controversy exists over the definition and cause of this syndrome. It is the second most common cause of end-stage renal failure. It is thought to be a result of renal damage caused by UTI in infants and children with vesicoureteric reflux, or by obstructive uropathy in adults. However, it is still unclear whether recurrent infection causes progressive kidney damage.

Perinephric abscess – A complication of UTI, although uncommon, that affects patients with one or more anatomical or physiological abnormalities. The abscess may be confined to the perinephric space or extend into adjacent structures. Pyuria, with or without positive culture, is seen on examination of urine, but is not always present. Causative organisms are usually Gram negative bacilli but can also be staphylococci or *Candida* species. Mixed infections have also been reported.

Prostatitis^{21,22} – An inflammatory condition of the prostate gland that occurs in a variety of different forms, some involving infection. Routes of infection of the prostate include ascending urethral infection, reflux of infected urine into the prostatic ducts that empty into the posterior urethra, invasion of rectal bacteria by direct extension, or by lymphatic or haematogenous spread.

Types of prostatitis include:

- **acute bacterial prostatitis** – An abrupt, febrile illness with marked constitutional and genitourinary symptoms.
- **chronic bacterial prostatitis** – Relapsing and recurrent UTIs, caused by the organisms persisting in the prostatic secretions despite antimicrobial therapy. The method of Meares and Stamey compares white blood cell (WBC) and bacterial counts of urethral, mid-stream and post-prostatic massage urine specimens, and expressed prostatic secretions (EPS)²³. Prostatic massage should not be undertaken in patients with acute prostatitis because of the risk of precipitating bacteraemia. All specimens are taken at the same time and processed immediately²³. Chronic bacterial prostatitis is less common than non-bacterial prostatitis. Bacterial prostatitis is associated with UTI. Organisms responsible are similar to those that cause UTI.

Pyonephrosis – The bacterial infection of an obstructed ureter which fills with pus. This may follow surgical intervention. Diagnosis is made from blood culture or pus drained from the kidney.

Renal abscesses – Localised in the renal cortex and may occur as a result of bacteraemia. Pyuria may also be present, but urine culture is usually negative. Renal abscesses are increasingly being seen as complications of acute pyelonephritis caused by Gram negative bacilli. The rare condition of emphysematous pyelonephritis, which results in multifocal intrarenal abscesses and gas formation within the renal parenchyma, is usually seen in diabetic patients or as a complication of renal stones. *Escherichia coli* is the commonest cause.

Urethritis – Common in both male and female patients and is often associated with UTI or occasionally with bacterial prostatitis.

In men, urethritis is commonly caused by sexually transmitted diseases and is associated with urethral discharge. The main organisms responsible are: *Neisseria gonorrhoeae* (gonococcal urethritis), *Chlamydia trachomatis* and *Mycoplasma genitalium* (non-gonococcal urethritis or NGU).

In female patients the condition may appear as acute urethral syndrome or urethrocystitis caused by Enterobacterales, *Staphylococcus saprophyticus*, and less commonly by *C. trachomatis* and *N. gonorrhoeae*.

4.3 Incidence of UTI

The incidence of UTIs is influenced by age, sex or by predisposing factors that may impair the wide variety of normal host defence mechanisms².

Children

UTI is a common bacterial infection that causes illness in children, in whom it may be difficult to diagnose as the presenting symptoms are often non-specific^{24,25}. In children, the condition is often associated with renal tract abnormalities and is most common in males in the first three months of life as a result of congenital abnormalities. In older children, females are more commonly affected. Infection in pre-school boys is often associated with renal tract abnormality. Failure to diagnose and treat UTI quickly and effectively may result in renal scarring and ultimately loss of function. The phenomenon of vesicoureteric reflux, while predisposing children to UTI, may also be caused by UTI²⁶⁻²⁹.

Confirmation of UTI in children is dependent on the quality of the specimen, which is often difficult to obtain cleanly. The probability of UTI is increased by the isolation of the same organism from two specimens.

Colony counts of $\geq 10^6$ cfu/L (10^3 cfu/mL) of a single species may be diagnostic of UTI in voided urine. Generally, a pure growth of between 10^7 - 10^8 cfu/L (10^4 - 10^5 cfu/mL) is indicative of UTI in a carefully taken specimen.

Negative cultures or growth of $<10^7$ cfu/L ($<10^4$ cfu/mL) from bag urine may be diagnostically useful. Counts of $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) should be confirmed by culture of a more reliable specimen, either a single urethral catheter specimen or, preferably, an SPA.

Bacteriuria usually exceeds $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) in SPAs from children with acute UTI, although any growth is potentially significant.

Adults

Women

The incidence of UTI is highest in young women. Around 10–20% of women will experience a symptomatic UTI at some time. In acutely symptomatic women, UTI may be associated with counts of a single isolate as low as 10^5 cfu/L (10^2 cfu/mL) in voided urine^{30,31}. Interpretation of culture results must be made with care however, and take into account factors such as age and storage of specimen, level of contamination indicated by SECs, and the sensitivity of the method.

Growths of $<10^8$ cfu/L ($<10^5$ cfu/mL) in asymptomatic, non-pregnant women are rarely persistent and usually represent contamination.

Men

Most infections in adult men are complicated and related to abnormalities of the urinary tract, although a low incidence occurs spontaneously in otherwise healthy young men.

Counts as low as 10^6 cfu/L (10^3 cfu/mL) of a pure or predominant organism have been shown to be significant in voided urine from men³². Where there is evidence of contamination, a carefully collected repeat specimen should be examined.

Diagnosis of prostatitis may be achieved by comparing the levels of pyuria in sequential specimens taken in association with prostatic massage²³. If the level of pyuria after prostatic massage is 10 times that of the initial urine, then bacterial prostatitis is likely. More than 15 WBCs per high power field in expressed prostatic secretions is considered abnormal, even if the WBCs in the urethral and bladder urine are within the normal range.

The elderly

UTI incidence increases with age for both sexes and is one of the most common infections associated with this age group³³⁻³⁵. It is estimated that 10% of males and 20% of females over the age of 80 have asymptomatic bacteriuria³⁶. Underlying health issues can make this condition particularly difficult to diagnosis and prone to resistant strains. According to some, no treatment is indicated for asymptomatic patients except before invasive genitourinary procedures.

Pregnancy

Studies in the UK have shown that asymptomatic bacteriuria (persistent colonisation of the urinary tract without urinary symptoms) occurs in 4% of pregnant women³⁷. Unless detected and treated early, there is an increased risk of preterm birth and pyelonephritis affecting maternal and fetal outcome. In about 30% of patients acute pyelonephritis occurs, especially at the time of delivery^{38,39}. It has been reported that 20–40% of pregnant women with untreated bacteriuria will develop pyelonephritis³⁸.

In pregnancy, routine and sensitive urinary screening programmes are essential for the detection of bacteriuria in pregnancy. The screening can be done by mid-stream urine culture early in pregnancy. The presence of $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) in asymptomatic, pregnant women indicates infection but should be confirmed in a repeat sample⁴⁰.

Diabetes

Women with diabetes have a higher incidence of asymptomatic bacteriuria than those without^{41,42}. There is no difference in the prevalence of bacteriuria between men with diabetes, and men without diabetes⁴². There is a debate as to whether factors such as glycosuria, age or instrumentation are contributory to the high prevalence of UTI, but bladder dysfunction as a result of diabetic neuropathy may be the major predisposing factor⁴¹. The relative incidences of symptomatic infection in patients with or without diabetes remain unclear but, when they do occur, UTIs tend to be more severe in patients with diabetes^{43,44}.

Neuromuscular disorders

Patients with impaired bladder innervation as a result of congenital or acquired disorders (spina bifida, spinal cord injury) are at increased risk of UTI and it can be a significant cause of death⁴⁵. This may be due to impaired function of the bladder leading to incomplete emptying, or an increased requirement for instrumentation of the urinary tract to assist voiding.

Renal transplantation⁴⁶⁻⁴⁸

Most infections occur soon after transplantation, usually as a result of catheterisation, the presence of a ureteric drainage tube, or a previous UTI whilst on dialysis. Less commonly, infection may be introduced via the donor kidney.

Immunosuppression

Overall the incidence of UTI is not higher in patients who are immunocompromised compared with those who are not. The exceptions to this include patients who are diabetic or have undergone renal transplants⁴⁹. There have also been studies that suggest that men who are suffering from acquired immunodeficiency syndrome (AIDS) may also be at increased risk from bacteruria, and symptomatic UTI; with severe episodes resulting in bloodstream infection and death being reported⁵⁰. However, because of long-term antibiotic use for other infections, UTI in such patients is often due to more unusual or resistant organisms. Steroid treatment may induce reactivation of tuberculosis of the urinary tract.

Catheterisation

Catheter acquired urinary tract infections is one of the most common health care acquired infections⁵¹. However samples from patients with indwelling catheters may not accurately reflect the true bladder pathogen and often contains several bacterial species. Culture results should be interpreted with caution. The criteria have not been established for differentiating asymptomatic colonisation of the urinary tract from symptomatic infection⁵². Urine cultures may not reflect bladder bacteriuria because sampled organisms may have arisen from biofilms on the inner surface of the catheter⁵³. Therefore the quality of the specimen collected and clinical circumstances in the individual patient are critical in the interpretation of bacterial counts. In carefully collected specimens, taken under controlled study conditions in short term catheterised patients, counts of $<10^8$ cfu/L ($<10^5$ cfu/mL) have been shown to be significant⁵⁴. In specimens of unknown quality and those from long term-catheterised patients, interpretation of significance on the basis of bacterial counts alone may be impossible. Significance of isolates and reporting of sensitivities may be indicated in certain groups – such as urology or post-operative patients, especially if future operative intervention is planned on the urinary tract.

Bacterial counts from catheterised patients may be affected by the administration of medication or fluids that increase urine flow, rapid transit of urine from the catheterised bladder, or colonisation with relatively slow growing organisms such as *Candida* species⁵⁵.

Catheterisation is occasionally used to collect a contamination free sample ('in and out') when any bacterial growth is significant. Specimens from patients with intermittent self-catheterisation should be treated as mid-stream urine.

4.4 Organisms implicated in UTI

Acute, uncomplicated UTIs

Acute, uncomplicated UTIs are usually caused by a single bacterial species.

E. coli – is the most common organism involved in UTI. An international survey of mid-stream urine (MSU) samples taken at 252 centres in 17 countries reports that *E. coli* accounts for 77% of isolates⁵⁶.

Only a few serotypes frequently cause UTI. This might reflect their prevalence in the faecal flora, or reflect differences in virulence factors. Certain virulence factors specifically favour the development of pyelonephritis, whereas others favour cystitis or asymptomatic bacteriuria⁵⁷.

Proteus mirabilis – Common in young boys and males, and is associated with renal tract abnormalities, particularly calculi. In hospital patients it may cause chronic infections.

S. saprophyticus – Studies have shown that this organism was found to be responsible for 4% of UTIs. *S. saprophyticus* adheres to uroepithelial cells significantly better than *S. aureus* or other coagulase negative staphylococci.

Other coagulase negative staphylococci – Often considered as urinary contaminants as they are part of the normal perineal flora.

Streptococci – Rarely cause uncomplicated UTI, although Lancefield Group B streptococci may cause infection in some women. Enterococci may occasionally cause uncomplicated UTI.

***Candida* species** - is associated with indwelling catheters but may also be present as contamination from the genital tract. *Candida albicans* is the most frequently isolated species.

Complicated UTIs

Complicated UTIs which occur in the abnormal or catheterised urinary tract are caused by a variety of organisms, many of them with increased antimicrobial resistance as a result of the prolonged use of antibiotics.

E. coli remains the most common isolate. Other frequent isolates include *Klebsiella*, *Enterobacter* and *Proteus* species, *Enterococcus* species (usually associated with instrumentation and catheterisation), and *Pseudomonas aeruginosa* (associated with structural abnormality or permanent urethral catheterisation). *S. aureus* rarely causes infection and is associated with renal abnormality or as a secondary infection to bacteraemia, surgery or catheterisation. It is frequently seen as a contaminant due to perineal carriage. Other coagulase negative Staphylococci may cause complicated infections in patients of both sexes with structural or functional abnormalities of the urinary tract, prostatic calculi or predisposing underlying disease.

4.5 Types of urine specimen and collection

Midstream urine (MSU) and clean-catch urine

MSU and clean catch urines are the most commonly collected specimens and are recommended for routine use. Cleaning the area before sampling makes little difference to contamination rates⁵⁸⁻⁶⁰.

Suprapubic aspirate (SPA)

Suprapubic aspirate (SPA) is seen as the 'gold standard' but is usually reserved for clarification of equivocal results from voided urine in infants and small children. Before SPA is attempted it is preferable to use ultrasound guidance to determine the presence of urine in the bladder²⁴.

Catheter urine (CSU)

'In and out', or intermittent self-catheterisation, samples are occasionally collected to ensure that they are contamination free.

Bag and pad urine

Bag urine is commonly collected from infants and young children, although it should be discouraged as pads are a more comfortable and easier method of collection^{61,62}. Artificially elevated leucocyte counts may be seen as a result of vaginal reflux of urine, recent circumcision or confusion with round epithelial cells found in urine from neonates. Negative cultures provide useful diagnostic information, but significant growth should be confirmed with SPA.

Other specimens

Other specimens obtained during or as a result of surgery include those from ileal conduit, cystoscopy, nephrostomy and urostomy, prostatic massage/secretions. Specimens may also be taken after bladder washout.

4.6 Laboratory investigation of UTI

Laboratory investigation of UTI normally involves microscopy (or an alternative method of measuring cellular components) and quantitative culture (or an alternative non-culture method such as a semi-automated urine analyser) with the use of chemical screening methods in certain instances⁶³.

The three main methods for the detection of UTIs involve culture, non-culture semi-automated systems (eg particle counting, electrical impedance, colorimetric filtration, photometry, bioluminescence, radiometry) and chemical (eg leucocyte esterase, nitrite, protein, and blood detection):

Except in a few patient groups, interpretations of culture results are made with regard to clinical presentation, the presence or absence of pyuria (which are associated with infection) and squamous epithelial cells (SECs) (which indicate contamination).

A reference guide for the diagnosis of UTI is available for use by clinicians⁶⁴. Clinical evaluation of the patient helps the interpretation of laboratory results and assists in the diagnosis of UTI.

Adequate internal control measures are critical, especially when chemical tests are deployed away from the laboratory near to the patient and where culture is not performed on the basis of negative results.

Microscopy

Microscopy is used to identify the presence of white blood cells (WBCs), RBCs, casts, SECs, bacteria and other cellular components in the urine. Semi-quantitative methods using a microtitre tray with an inverted microscope or a disposable counting chamber are recommended for routine use. This UK SMI contains a table of multiplicative factors based on the varying volumes of urine dispensed, the diameter of well and the field of vision diameter (refer to Appendix 1 and 2)⁶⁵.

Microscopy need not be performed on all urine samples where screening for asymptomatic bacteriuria is required (eg antenatal clinic screening) and may be omitted for such indications if in compliance with local protocols. Automated screening systems offer flexible, cost effective alternatives to microscopy⁶³. Microscopy (or an

alternative) is recommended for all symptomatic patient groups, to assist in the interpretation of culture results and the diagnosis of UTI.

Microscopy of uncentrifuged, unstained urine has been used as a method of screening for bacteriuria without the need for culture, but is unreliable to detect counts $<10^7$ colony forming units per litre (cfu/L), ie $<10^4$ colony forming units per millilitre (cfu/mL). The sensitivity increases if the specimen is centrifuged and/or stained⁶⁶.

In a carefully taken specimen, significant pyuria correlates well with bacteriuria and symptoms in most patients to suggest a diagnosis of UTI. Significant pyuria is defined as the occurrence of 10^7 or more WBC/L (10^4 WBC/mL), although higher numbers of WBC are often found in healthy asymptomatic women⁶⁷. A level of $>10^8$ WBC/L ($>10^5$ WBC/mL) has been suggested as being more appropriate in discriminating infection.

RBCs - Laboratories should consult with local urologists regarding the reporting of RBCs in urine.

Casts – Casts are cylindrical protein mouldings formed in the renal tubules and often giving clues to renal pathology. Recognition of casts is important in helping to establish the existence of renal disease but is less useful in the differentiation of renal disorders.

Large numbers of hyaline casts are associated with renal disease but may also be found in patients with fever or following strenuous exercise. Cellular and densely granular casts indicate pyelonephritis or glomerulonephritis. RBC casts usually indicate glomerular bleeding and are excreted in large numbers in the acute phase of post-streptococcal nephritis or rapidly progressive nephritis. Less commonly, epithelial cell and fatty casts accompany acute tubular necrosis and nephrotic syndrome.

Crystals – These may be asymptomatic or associated with the formation of urinary tract calculi. Some crystals such as cystine are rarely seen and may indicate an underlying metabolic disease.

Squamous epithelial cells – SECs are a useful indicator of the degree of contamination from the perineal region.

Non-culture methods

Semi-automated methods

Urine analyser systems are expensive and vary in their performance. They are intended to identify red and white blood cells, bacteria, yeasts, epithelial cells, mucus, sperm, crystals and casts (depending on the technology).

Urine analysers may be used to screen for 'negatives' to allow earlier reporting and to facilitate cost-effective processing^{68,69}.

If urine analysers are used as a screening procedure to reduce the number of urine samples set up for culture, then there is a need for a robust validation and the key performance parameter is sensitivity. The cut-off values of the bacterial and WBC counts used to screen out urines can usually be set by individual users using the Sysmex UF-100 demonstrated that they could achieve a high sensitivity (98%) only at the price of reduced specificity (25%) which meant that only 22% of their urines would not be cultured⁷⁰.

Each laboratory should set cut off values to achieve clinically relevant sensitivity and predictive values appropriate for the key local populations (children, pregnant women

and patients who are immunocompromised) and under take appropriate validation and verification.

It may be prudent, regardless of the screening results, to culture all urines from certain patients such as those from children, pregnant women and patients who are immunocompromised. The rationale for this recommendation is that there are more severe consequences in missing infection in children and the potential absence of WBCs in urine from asymptomatic pregnant women or patients who are immunocompromised.

Currently available technologies include the following:

- flow cytometry: this works by measuring electrical impedance (for volume), light scatter (for size) and use of fluorescent dyes (for nuclear and cytoplasmic staining). The particles are characterised using these measurements, and the results are displayed as scattergrams. Sensitivity and specificity results can vary depending on the parameters and cut-offs employed. Cut-off criteria are chosen for an analyser to balance the levels of sensitivity and specificity required according to a local assessment of clinical need⁷¹⁻⁷³.
- particle recognition system: the urine specimen passes through the analyser and a camera captures up to 500 frames per specimen. Each image is classified by size, shape, contrast and texture features. This technology has been shown to be more reliable for identifying cellular components, but less suitable for detection of bacteriuria. For cases that appear to be borderline manual microscopy counts are still needed⁷⁴⁻⁷⁶.
- microscopic urine sediment analysis: the autoanalyzer will homogenize the specimen and transfer it to a single use cuvette (volume aspirated: 2.0 ml, volume examined: 2.2 µl) which are centrifuge for few seconds. Afterwards, whole-field high definition images are obtained (15 per sample) and the software (Auto Image Evaluation Module AIEM) performs a morphological analysis of the particles, allowing them to be counted and classified⁷⁷.

Chemical screening tests

Non-culture chemical screening tests may be used for screening negative urines according to selected criteria⁷⁸⁻⁸¹. Most chemical tests are available commercially as dipsticks and are quick and easy to use. Reading colour changes in dipstick strips using colorimetric measurement is preferred, as results are more reliable and reproducible, and free from observer error, particularly if an automated reading system is used^{82,83}. Boric acid, and some antimicrobial agents such as nitrofurantoin, and gentamicin adversely affect the leucocyte esterase test.

Chemical tests for the presence of blood may be more sensitive than microscopy as a result of the detection of haemoglobin released by haemolysis. The absence of all four infection associated markers (blood, leucocyte esterase, nitrate and protein) had a greater than 98% negative predictive value and a sensitivity and specificity of 98.3% and 19.2% respectively according to one study⁸⁰.

Culture methods

There are several culture methods for the quantification of bacteria in urine. The easiest and most commonly used are the calibrated loop technique, the sterile filter paper strip and multipoint technology⁸⁴⁻⁸⁶. Of these, multipoint methodology using CLED or chromogenic media, are considered to be the most versatile and efficient for

large numbers of specimens. Other methods include use of dipslides, pour plates and roll tubes. These methods are not recommended for routine use in this UK SMI but may be useful in specific circumstances and in accordance with local protocols.

Multipoint inoculation of CLED agar alone may contribute to the under reporting of mixed cultures that are more readily identified using chromogenic agar or a range of identification and susceptibility media. The culture of urine by multipoint methods may be automated, or performed manually using either microtitre trays containing agar or by using 9mm agar plates. Microtitre trays may be read manually or with an automated system where the resulting data are transferred to the laboratory information management system for reporting. Microtitre trays examined manually require background light and some form of magnification to facilitate the recognition of mixed cultures and small colonies.

Chromogenic media contain various substrates which permit presumptive identification of several common species through a change in either colony pigmentation or colour of agar. They perform satisfactorily compared to CLED and have the advantage that mixed cultures are easier to detect. However, chromogenic media from different manufacturers can vary in specificity, and are relatively expensive^{84,87}.

The use of agar plates (rather than microtitre trays) may lead to false negative reporting if antimicrobial substances present in some urines diffuse to neighbouring inocula. When this occurs, repeat culture of the affected inocula is required.

Interpretation of culture

Studies conducted in the 1950s remain the basis for interpreting urine culture results showing that bacterial counts of $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) are indicative of an infection and counts below this usually indicate contamination⁸⁸. The most common organism implicated in UTI in this group is *E. coli*⁵⁶.

In specific patient groups, counts between 10^8 cfu/L (10^5 cfu/mL) and 10^5 cfu/L (10^2 cfu/mL) may be significant^{24,30,31}. A pure isolate with counts between 10^7 and 10^8 cfu/L (10^4 - 10^5 cfu/mL) should be evaluated based on clinical information or confirmed by repeat culture. Overall the confirmation of a UTI requires the demonstration of significant bacteriuria by quantitative culture (defined according to patient group or specimen type). Routine culture methods may not be sensitive enough to detect low bacteria levels (eg $\leq 10^7$ cfu/L / $\leq 10^4$ cfu/mL) and increased sensitivity will be achieved by increasing the inoculum size (see section 4.5.2).

Increased inoculum sizes are also required for persistently symptomatic patients without bacteriuria if the patient has recurrent “sterile pyuria”, or for specimens where lower counts are to be expected, such as SPAs or other surgically obtained urine.

4.7 Other urine investigations

Screening for antimicrobial substances

This may be useful to detect false negative cultures where the inoculum contains an antimicrobial agent which diffuses into the agar and inhibits bacterial growth. Where microtitre trays are used for multipoint culture the highest concentration of antimicrobial is localised to the small area of medium in the microtitre tray. Where agar plates are used for multipoint culture (rather than microtitre trays), both the primary

and neighbouring inocula, may be affected as a result of the diffusion through the medium.

A seeded plate is inoculated after other plates and the absence of growth after incubation indicates the presence of an antimicrobial substance. The procedure is simple if multipoint replicating devices are used (see section 4.5.2) and may reduce further testing of the specimen (eg for fastidious organisms)⁸⁹.

Detection of urinary antigen for *Legionella*

Urinary antigen (UrAg) detection is a convenient and cost effective method of diagnosing Legionnaires' disease⁹⁰. Antigen becomes detectable soon after onset of symptoms and the test may remain positive for several weeks, even after other tests have become negative^{91,92}. The majority of UrAg-positive cases have been found to be a result of infection from *L. pneumophila* serogroup 1⁹³. Equivocal EIA results should be examined by a second person and repeated for serogroup 1⁹⁴.

Note: The UrAG test may not be appropriate in cases of nosocomial or atypical pneumonia.

Where practical, respiratory samples should be obtained from all patients with positive *Legionella* urinary antigen tests, and these (and culture isolates if available) should be sent to the reference laboratory for strain typing.

A sample should be retained at -20°C in the event that re-testing may be required because of legal action (take care to ensure preservation of the chain of evidence)⁹⁵.

Screening for *Salmonella Typhi* and *Salmonella Paratyphi*

S. Typhi and *S. Paratyphi* are present in urine in the early stages of typhoid and paratyphoid fever. Screening urines may be received from suspected cases and/or their contacts for selective enrichment and culture.

Diagnosis of *Schistosoma haematobium* infection

May be undertaken on urine taken at a specific time coinciding with maximum egg excretion, or on the terminal portion of voided urine. Haematuria is the most common presentation of *S. haematobium* infection. Chronic infection can lead to bladder cancer (see [UK SMI B 31 – Investigation of specimens other than blood for parasites](#)).

Screening for *Chlamydia trachomatis* and *Neisseria gonorrhoea*

May be undertaken on urine specimens from patients with sterile pyuria or as part of investigation for infection with sexually transmitted disease.

5 Technical information/limitations

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (eg sensitivity and specificity) where available, expert opinion and pragmatism, with consideration also being given to available resources. Laboratories should take account of local requirements and undertake additional investigations where appropriate. Prior to use,

laboratories should ensure that all commercial and in-house tests have been validated and are fit for purpose.

Selective media in screening procedures

Selective media which does not support the growth of all circulating strains of organisms may be recommended based on the evidence available. A balance therefore must be sought between available evidence, and available resources required if more than one media plate is used.

Specimen containers^{96,97}

UK SMIs use the term, “CE marked leak proof container,” to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: “The design must allow easy handling and, where necessary, reduce as far as possible contamination of and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes.”

Transport of urine specimens

Rapid transport, culture, or measures to preserve the sample aid reliable laboratory diagnosis. Delays and storage at room temperature allow organisms to multiply, which generate results that do not reflect the true clinical situation. Where delays in processing are unavoidable, refrigeration at 4°C is recommended or the use of a boric acid preservative may be beneficial⁹⁸⁻¹⁰³.

Boric acid preservative at a concentration of 1–2% holds the bacterial population steady for 48–96 hours, and other cellular components remain intact^{98,99}. Toxicity to certain organisms has been reported¹⁰⁰. The toxic effect is delayed and often reflects underfilling of the container^{101,104}.

Boric acid increases the maximum permissible time for transport to the laboratory to up to 96hr¹⁰⁵.

It should be noted that boric acid may be inhibitory to some organisms and may inhibit tests for leucocyte esterase⁹⁹⁻¹⁰¹.

Note: It is essential to follow the manufacturer’s instructions on sample volume in boric acid containers¹⁰⁴.

SI unit nomenclature

Although SI units have been adopted in other UK SMIs, they have been left as optional for urines. Most current literature still refer to the old nomenclature when defining ‘significant bacteriuria’. The following is a list of metric units and their SI equivalents.

$\geq 10^5$ cfu/mL equivalent to $\geq 10^8$ cfu/L

$< 10^5$ cfu/mL equivalent to $< 10^8$ cfu/L

10^4 cfu/mL equivalent to 10^7 cfu/L

$< 10^4$ cfu/mL equivalent to $< 10^7$ cfu/L

10^3 cfu/mL equivalent to 10^6 cfu/L

$<10^3$ cfu/mL equivalent to $<10^6$ cfu/L

10^2 cfu/mL equivalent to 10^5 cfu/L

Validation and verification

Robust validation of the cut offs is required for your local area and should be carried out.

If urine analysers are used as a screening procedure to reduce the number of urine samples set up for culture, then there is a need for a robust validation and the key performance parameter is sensitivity. The cut-off values of the bacterial and WBC counts used to screen out urines can usually be set by individual users using the Sysmex UF-100 demonstrated that they could achieve a high sensitivity (98%) only at the price of reduced specificity (25%) which meant that only 22% of their urines would not be cultured⁷⁰.

Each laboratory should set cut off values to achieve clinically relevant sensitivity and predictive values appropriate for the key local populations (children, pregnant women and patients who are immunocompromised) and under take appropriate validation and verification.

Carry over contamination

Carry-over can be a problem with some automated urine analysers and the potential for this problem should be assessed during the validation and verification of these instruments^{106,107}. There are a number of ways of addressing carry-over concerns such as increasing the number of rinses, but this reduces the throughput; furthermore with one specific analyser even increasing the number of the rinses did not prevent carry-over from specimens with very high bacterial load (10^7 /mL)¹⁰⁸. Other strategies to reduce the carry-over, or its impact, include taking sample aliquots for culture before submitting the specimens for microscopy or culturing all urines before the microscopy is done, weekly disinfection of the probes with methanol, and regular carry-over tests using boric acid tubes^{106,107}.

6 Safety considerations^{96,97,109-123}

6.1 Specimen collection, transport and storage^{96,97,109-112}

Use aseptic technique.

Collect specimens in appropriate CE marked leak proof containers and transport in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

6.2 Specimen processing^{96,97,109-123}

Containment Level 2 unless infection with a Hazard Group 3 organism, for example *Mycobacterium* species, or *Salmonella* Typhi or *Salmonella* Paratyphi A, B and C is suspected.

Where Hazard Group 3 *Mycobacterium* species are suspected, all specimens must be processed in a microbiological safety cabinet under full Containment Level 3 conditions.

Diagnostic work with clinical material that could possibly contain Hazard Group 3 organisms (*Salmonella* Typhi and *Salmonella* Paratyphi A, B & C,) does not normally require full Containment Level 3 containment¹¹⁵ (paragraph 175).

If these Hazard Group 3 organisms are suspected, work should take place at a higher containment level, but full Containment Level 3 may not be required (paragraphs 179-183)¹¹⁵.

If the work to be carried out requires the growth or manipulation of a Hazard Group 3 enteric biological agent then this has to be carried out under full Containment Level 3 conditions¹¹⁵ (paragraph 175).

Note: *S. Typhi* and *S. Paratyphi* A, B and C cause severe, sometimes fatal, disease; laboratory acquired infections have also been reported. *S. Typhi* vaccination is available. Guidance is given in [Immunisation against Infectious Disease](#) published by UK Health Security Agency.

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet¹¹⁵.

Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

The above guidance should be supplemented with local COSHH and risk assessments.

7 Specimen collection

7.1 Type of specimens

Bag urine, pad urine, catheter urine, prostate massage/secretions, clean catch urine, suprapubic aspirate, cystoscopy urine, ureteric urine, ileal conduit urine, urostomy urine, mid-stream urine, nephrostomy urine

Urine samples are not suitable for the isolation of leptospires due to the presence of other contaminating bacteria and the poor viability of leptospires in urine.

7.2 Optimal time and method of collection¹²⁴

For safety considerations refer to Section 6.

Collect specimens before antimicrobial therapy where possible¹²⁴.

Mid-stream urine (MSU)

MSU is the recommended routine collection method.

The first part of voided urine is discarded and, without interrupting the flow, approximately 10mL is collected into a CE marked leak proof container. The remaining urine is discarded. If boric acid preservative is used, the container is filled up to the mark in a similar manner and the contents mixed well.

Clean-catch urine

A reasonable alternative to MSU.

Periurethral cleaning is recommended. The whole specimen is collected and then an aliquot sent for examination in a CE marked leak proof container.

Suprapubic aspirate (SPA)²⁴

Urine is obtained aseptically, directly from the bladder by aspiration with a needle and syringe. The use of this invasive procedure is usually reserved for clarification of equivocal results from voided urine (eg in infants and small children). Ultrasound guidance should be used to show presence of urine in the bladder before carrying out SPA.

Catheter urine (CSU)

The sample may be obtained either from a transient ('in and out') catheterisation or from an indwelling catheter. In the latter case, the specimen is obtained aseptically from a sample port in the catheter tubing or by aseptic aspiration of the tubing. The specimen should not be obtained from the collection bag.

Bag urine

Used commonly for infants and young children. The sterile bags are taped over the freshly cleaned and dried genitalia, and the collected urine is transferred to a CE marked leak proof container. There are frequent problems of contamination with this method of collection.

Pad urine¹²⁵

An alternative to collecting bag urine from infants and young children. After washing the nappy area thoroughly, a pad is placed inside the nappy. As soon as the pad is wet with urine (but no faecal soiling), push the tip of a syringe into the pad and draw urine into the syringe. Transfer specimen to a CE marked leak proof container. If difficulty is experienced in withdrawing urine, the wet fibres may be inserted into the syringe barrel and the urine squeezed directly into the container with the syringe plunger.

Ileal conduit – urostomy urine

Urine is obtained via a catheter passed aseptically into the stomal opening after removal of the external appliance. Results from this type of specimen may be difficult to interpret.

Cystoscopy urine

Urine is obtained directly from the bladder using a cystoscope.

Ureteric urine

Urine samples are obtained from one or both ureters during cystoscopy via ureteric catheters inserted from the bladder.

Urine samples may also be sent following nephrostomy, other surgical procedures, or bladder washout.

Meares and Stamey localisation culture method for diagnosis of prostatitis²³

The following specimens are collected:

- The initial 5–8mL voided urine (urethral urine)
- MSU (bladder urine)

Investigation of urine

- Expressed prostatic secretions following prostatic massage
- The first 2–3mL voided urine following prostatic massage

Urine for *S. Typhi* and *S. Paratyphi* cultures

Any urine samples from suspected cases or contacts of cases.

Early morning urine

Ideally three entire, first voided, early morning urine specimens are needed for culture for *M. tuberculosis* (see [UK SMI B 40 - Investigation of specimens for Mycobacterium species](#)).

Urine for *S. haematobium* detection

Total urine sample passed into CE marked leak proof container without boric acid preservative is required. Alternatively, a 24hr collection of terminal urine may be examined (see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#)).

Urine for parasites

For investigation of parasites see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#).

7.3 Adequate quantity and appropriate number of specimens¹²⁴

A minimum volume of 1mL for specimens in plain CE marked leak proof container for bacterial pathogens.

Fill to the line marked on containers with boric acid preservative according to manufacturers' instructions.

Numbers and frequency of specimens collected are dependent on clinical condition of patient.

8 Specimen transport and storage^{96,97}

8.1 Optimal transport and storage conditions

For safety considerations refer to Section 6.

Specimens should be transported and processed within 4hr if possible, unless boric acid preservative is used^{102,103}.

If processing is delayed for up to 48hr, refrigeration is essential⁹⁸. Alternatively, the specimen may be collected in a CE marked leak proof container with boric acid preservative^{99-101,126}.

This increases the maximum permissible time for transport to the laboratory to up to 96hr¹⁰⁵.

It should be noted that boric acid may be inhibitory to some organisms and may inhibit tests for leucocyte esterase^{99-101,127}.

Note: It is essential to follow the manufacturer's instructions on sample volume in boric acid containers¹⁰⁴.

9 Specimen processing/procedure^{96,97}

9.1 Test selection

Divide specimen on receipt for appropriate procedures such as investigation for viruses (boric acid samples are unsuitable for viruses) and *C. trachomatis* depending on clinical details.

9.2 Appearance

N/A

9.3 Sample preparation

For safety considerations refer to Section 6.2.

9.4 Microscopy or alternative screening methods

9.4.1 Standard

Microtitre tray with an inverted microscope

Mix the urine gently, to avoid foaming.

Using a pipette and disposable tips, dispense known volume (~60µL, see 'Note 2' below) of mixed urine to a numbered well in a flat-bottomed microtitre tray. Make sure that the specimen covers the whole bottom surface area (the use of a template will facilitate matching the specimen and well number).

Allow to settle for a minimum of 5min, but preferably 10–15min, before reading with an inverted microscope.

Scan several fields in each well to check for even distribution of cells and urine.

Count the numbers, or estimate the range, of WBCs and RBCs per representative field and convert to numbers (or range) per litre.

Enumerate and record SECs.

Enumerate and record casts, if present, and state type.

Record if bacteria, yeasts, *Trichomonas vaginalis*, or significant crystals such as cystine are present.

All procedures for enumeration of cells should be carried out according to local protocols.

Note 1: This UK SMI contains a table of multiplicative factors to correct for variability in microtitre tray well size based on varying volumes of urine dispensed, diameter of well and field of vision diameter (refer to Appendix 1)⁶⁵. The number of WBCs counted should be multiplied by the multiplicative factor to take into account all the variables. If the well size, volume of urine dispensed, diameter of well or field of vision diameter are altered, then the multiplicative factor needs to be re-calculated.

Note 2: If the microtitre tray is also to be used for culture by multipoint inoculation, it should be stored at 4°C until culture is performed (unless all specimens in the tray are preserved with boric acid when refrigeration is not necessary).

Note 3: Microscopy should not be performed on screening specimens sent exclusively for the isolation of *S. Typhi* and *S. Paratyphi* for safety reasons.

9.4.2 Alternative methods

See introduction for a discussion on non-culture methods.

Screening by biochemical test strips may be performed in place of microscopy; however, these methods do not detect casts or abnormal cells such as dysmorphic cells.

Automated systems such as those using urine analysers must be validated and used in accordance with manufacturers' instructions.

9.4.3 Supplementary

Microscopy for:

- **dysmorphic RBCs**^{11,12} – Laboratories should consult with local urologists regarding the reporting of dysmorphic RBCs in urine. Fresh specimens (<30min old) are essential
- ***Mycobacterium* species** – (see [UK SMI B 40 - Investigation of specimens for *Mycobacterium* species](#))
- **parasites** – (see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#))

9.5 Culture and investigation

9.5.1 Pre-treatment

Standard

N/A

Supplementary

Mycobacterium species (see [UK SMI B 40 - Investigation of specimens for *Mycobacterium* species](#)) and for parasites (see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#)).

9.5.2 Specimen processing

Choice of culture method is made locally.

Specimens with 'negative' microscopy may be given a screening culture only, whereas those with 'positive' microscopy may include direct susceptibility testing.

Calibrated loop/surface streak method

Mix the urine gently to avoid foaming.

Dip the end of a sterile calibrated loop (eg 1µL, 2µL or 10µL) in the urine to just below the surface and remove vertically, taking care not to carry over any on the shank⁸⁶.

Investigation of urine

Use this to inoculate CLED or chromogenic agar plate and spread according to the number of specimens (see [UK SMI Q 5 - Inoculation of culture media for bacteriology](#)). A maximum of four samples per 9cm plate is recommended for this method with a 1µL or 2µL loop, or two samples if using a 10µL loop.

If a 1µL loop is used, one colony equals 1000 cfu/mL (ie 1×10^6 cfu/L).

SPAs, other surgically obtained urine, and urine samples with expected significant bacteriuria as low as 105 cfu/L (increased inoculum sizes are required)

Inoculate 100µL (0.1mL) of specimen aseptically to a full CLED or chromogenic agar plate.

Spread inoculum over entire surface of plate with a sterile loop or a spreader. Do not use a sterile swab which will absorb much of the inoculum. To isolate individual colonies, spread inoculum with a sterile loop.

No. of cfu/L = No. of cfu on plate $\times 10^4$.

This semi quantitative method is only sensitive for screening down to 10^6 cfu/L if a 5µL or 10µL loop is used (eg 5 or 10 colonies), or 10^7 cfu/L if a 1µL or 2µL loop is used (eg 10 or 20 colonies). (See table below).

Guidance on assessing colony counts (with the exception of filter paper strip method; see Introduction for the clinical interpretation results)

	No. cfu counted using inoculum of:				
Corresponding cfu/L (cfu/mL)	0.3µL	1µL	2µL	5µL	10µL
10^6 cfu/L	-	-	-	5	10
10^7 cfu/L	3	10	20	50	100
10^8 cfu/L	30	100	200	500	1000

Multipoint methods

Using 96 pin head microtitre trays

Prepare microtitre tray and perform microscopy (see Section 4.4).

Label the microtitre tray containing chromogenic or CLED agar medium using the same template as for microscopy (see above Section 4.3.2).

Sterilise the inoculating pins on the multipoint inoculator.

Inoculate the agar microtitre tray with urine (eg 0.3µL, 1µL, 2µL, depending on pin size) from the 60µL aliquots used for microscopy.

Note 1: The tray must be stored at 4°C until full culture is performed (unless all specimens in the tray are preserved with boric acid).

Note 2: To prevent the inoculated agar in the microtitre trays from drying out in the incubator overnight, place the microtitre trays either in a moist box or stack carefully with a lid on the top tray.

Note 3: This method is only sensitive for screening down to 10^7 cfu/L. A larger inoculum may be required in selected patient groups or specimens when greater sensitivity is needed.

Using agar plates

Multipoint inoculation of no more than 20 specimens per 9cm plate is recommended.

Prepare inoculum in sterile cupules, arranged according to the configuration of the inoculation head.

Label CLED/chromogenic agar plate to correspond to inoculation configuration.

Sterilise the inoculating pins on the multipoint inoculator.

Dip inoculating pins into inoculum.

Inoculate CLED/chromogenic agar plate.

Note: Detection of antimicrobial substances must be undertaken if a multipoint culture method is used with agar plates, rather than microtitre trays, as diffusion of antimicrobial substances from some urine samples may affect neighbouring inocula and give false negative results (see section below: 'Detection of antimicrobial substances'). Any sample thought to be affected in this way should be retested.

Filter paper method⁸⁵

Dip the commercially prepared sterile filter paper strip in the urine up to the mark indicated.

Remove excess urine by touching the edge of the strip against the side of the specimen container. Allow the remaining urine to absorb into the strip before inoculating a CLED or chromogenic agar plate.

Bend the inoculated end of the strip and press flat against the agar for a few seconds.

Several specimens may be inoculated onto one CLED agar plate in this technique, although this is less effective than plating to chromogenic agar, as mixed cultures are easier to detect⁸⁴.

Note: This method is only sensitive for screening down to 10^7 cfu/L. A larger inoculum will be required in selected patient groups or for specimens where lower counts are expected.

Guidance on assessing colony count using the filter paper strip method

No. cfu counted*		Corresponding cfu/L (cfu/mL)
Gram negative bacilli	Cocci	
0–5	0–8	10^7 ($\leq 10^4$)
5–25	8–30	10^7 – 10^8 (10^4 – 10^5)
25	30	10^8 (10^5)

*Refer to individual manufacturer's instructions.

Automated methods

Semi-automated systems such as urine analysers must be validated and used in accordance with manufacturers' instructions.

9.5.3 Other screening methods

Enteric fever screen

Enteric salmonellae may be recovered from urine following pre-enrichment in mannitol selenite, which can be prepared by carefully adding an equal volume of urine to mannitol selenite broth (see section: Safety Considerations).

Detection of antimicrobial substances⁸⁹

This method is performed most easily using multipoint systems, but inoculation of urine is possible with a sterile loop or pipette and disposable tips.

Surface seed plates or microtitre tray containing a defined susceptibility testing agar with a broth culture or spore suspension of *Bacillus subtilis* (NCTC 10400) diluted to give a semi-confluent growth. *B. subtilis* is the preferred organism as it is susceptible to a wider range of antimicrobials than either *E. coli* or *S. aureus*.

Dry before use.

Inoculate plate or microtitre wells with urine as described earlier, ensuring that the seeded plate is inoculated last to prevent contamination of other media with *B. subtilis*.

9.5.4 Culture media, conditions and organisms⁸⁴

Clinical details/ conditions	Standard media	Incubation			Cultures read	Target organism(s)
		Temp. °C	Atmos.	Time		
UTI Screening in pregnancy for asymptomatic bacteriuria by culture	CLED agar or Chromogenic agar	35–37	Air	16–24hr	≥16hr	Enterobacteriaceae Enterococci Lancefield Group B streptococci Pseudomonads <i>S. saprophyticus</i> Other coagulase-negative staphylococci <i>S. aureus</i>
Enteric fever screen*	Mannitol selenite broth subcultured to: XLD	35–37	Air	16–24hr	N/A	S. Typhi
		35–37	Air	16–24hr	≥16hr	S. Paratyphi
For these situations, add the following:						
Clinical details/ conditions	Supplementary media	Incubation			Cultures read	Target organism(s)
		Temp. °C	Atmos.	Time		
Urine of patients in Intensive Care, Special Care Baby Units, Burns Units and	Sabouraud agar	35–37	Air	40–48hr	≥40hr	Fungi

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any from a Transplant Unit or if yeast have been seen in microscopy						
Multipoint culture using agar plates	Susceptibility testing agar seeded with <i>B.subtilis</i> (NCTC 10400)	35–37	Air	16–24hr	≥16hr	Antimicrobial substances
Optional media		Incubation			Cultures read	Target organism(s)
		Temp. °C	Atmos.	Time		
If sterile pyuria and no antimicrobials detected	Fastidious anaerobe agar	35–37	anaerobic	40–48hr	≥40hr	Anaerobes Streptococci
	Chocolate agar	35–37	5-10% CO ₂	40–48hr	≥40hr	Fastidious organisms
Susceptibility testing agar seeded with <i>B.subtilis</i> (NCTC 10400) (optional for all except multipoint agar plates)		35–37	Air	16–24hr	≥16hr	Antimicrobial substances
Other organisms for consideration – <i>C. trachomatis</i> , MRSA, <i>Mycobacterium</i> species, parasites and viruses (see relevant UK SMI).						
* These samples are rarely received by the laboratory.						

9.6 Identification

Refer to individual UK SMIs for organism identification.

9.6.1 Minimum level of identification in the laboratory

Note: All work on *S. Typhi* and *S. Paratyphi* must be performed in a microbiological safety cabinet under Containment Level 3 conditions.

Anaerobes	"anaerobes" level UK SMI ID 14 - Identification of anaerobic cocci UK SMI ID 8 - Identification of Clostridium species UK SMI ID 25 - Identification of anaerobic gram negative rods
β-haemolytic streptococci	Lancefield group level
Enterobacteriaceae (except <i>Salmonella</i> species)	"coliform" level
Enterococci	genus level
Pseudomonads	"pseudomonads" level
S. saprophyticus	species level

Other coagulase negative staphylococci	"coagulase negative" level
S. aureus	species level
S. Typhi/Paratyphi	species level
Yeasts	"yeasts" level
Mycobacterium	UK SMI B 40 - Investigation of specimens for Mycobacterium species
Parasites	UK SMI B 31 - Investigation of specimens other than blood for parasites
Fungi (in urines from patients species level in Intensive Care, Special Care Baby Units, Burns Units and any from Transplant Units)	species level

Organisms may be further identified if this is clinically or epidemiologically indicated.

9.7 Antimicrobial susceptibility testing

Refer to [British Society for Antimicrobial Chemotherapy \(BSAC\)](#), [EUCAST](#) and/or [CSLI](#) guidelines or manufacturer's validation for proprietary methods.

This UK SMI recommends selective and restrictive reporting of susceptibilities to antimicrobials. Any deviation must be subject to consultation that should include local antimicrobial stewardship groups.

9.7.1 Antimicrobial Susceptibility Testing and Reporting Table

It is recommended that the antimicrobials in bold in the table below are reported. Those antimicrobials not in bold may be reported based on local decisions.

For more information on Detection of Bacteria with Carbapenem-Hydrolysing β -lactamases (Carbapenemases) refer to [UK SMI B 60 - Detection of bacteria with carbapenem-hydrolysing \$\beta\$ -lactamases \(carbapenemases\)](#).

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Bacteria	Examples of agents to be included within primary test panel (recommended agents to be reported are in bold depending on clinical presentation)	Examples of agents to be considered for supplementary testing (recommended agents to be reported are in bold depending on clinical presentation)	Notes
Enterobacteriaceae	Ampicillin (or Amoxicillin) Cefpodoxime ¹ Nitrofurantoin ² Trimethoprim	Amikacin Cefalexin Cefotaxime (or Ceftriaxone) Ceftazidime Ciprofloxacin (or Norfloxacin) Co-amoxiclav ³ Ertapenem Fosfomycin Gentamicin Mecillinam Meropenem (or Imipenem) Piperacillin/Tazobactam Temocillin Aztreonam	1. Cefpodoxime resistant organisms should be tested for the presence of ESBLs and screened for reduced susceptibility to carbapenems. 2. Nitrofurantoin for uncomplicated UTI only 3. Co-amoxiclav resistant organisms should be tested at a local level for sensitivity to an indicator carbapenem.
<i>P. aeruginosa</i> and <i>Acinetobacter spp.</i>	Ceftazidime (for <i>P.aeruginosa</i> only) Ciprofloxacin Gentamicin Meropenem (or Imipenem) Piperacillin/Tazobactam ⁴	Amikacin Colistin	4. Tazobactam should not be rested or reported for <i>Acinetobacter spp.</i>
<i>S. saprophyticus</i>	Cefoxitin ⁵ (or Oxacillin) Nitrofurantoin (uncomplicated UTI only) Trimethoprim	Ciprofloxacin (or Norfloxacin) Gentamicin Penicillin Vancomycin	5. Report as Flucloxacillin
<i>S. aureus</i> and other coagulase negative Staphylococci	Cefoxitin ⁵ (or Oxacillin) gentamicin Tetracycline ⁶ Trimethoprim Nitrofurantoin	Clindamycin Daptomycin Fusidic acid Linezolid Mupirocin Penicillin Rifampicin Teicoplanin Vancomycin	5. Report as Flucloxacillin 6. Suppress report in children and pregnant women
Group B Beta-Haemolytic Streptococci	Nitrofurantoin ² Penicillin Trimethoprim	Clindimycin	2. Nitrofurantoin for uncomplicated UTI only may be useful in interpretation
<i>Enterococcus spp.</i>	Ampicillin (or Amoxicillin) Nitrofurantoin ²	Teicoplanin Vancomycin	2. Nitrofurantoin for uncomplicated UTI only

10 Referral to reference laboratories

For information on the tests offered, turnaround times, transport procedure and the other requirements of the reference laboratory [click here for user manuals and request forms](#).

Organisms with unusual or unexpected resistance, or associated with a laboratory or clinical problem, or anomaly that requires elucidation should be sent to the appropriate reference laboratory.

Contact appropriate devolved national reference laboratory for information on the tests available, turnaround times, transport procedure and any other requirements for sample submission:

[England](#)

[Wales](#)

[Scotland](#)

[Northern Ireland](#)

11 Reporting procedure

11.1 Microscopy

11.1.1 Microscopy

Report on the actual numbers, or range of WBCs and RBCs per litre or per mL according to local protocol.

Report on the presence of bacteria, epithelial cells, casts, yeasts and *T. vaginalis*.

Report on supplementary microscopy for dysmorphic RBCs, (see [UK SMI B 40 - Investigation of specimens for Mycobacterium species](#)) and parasites

(see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#)).

11.1.2 Chemical and semi-automated screening methods

Report the results obtained together with a quantitative interpretation if applicable.

The following comments may be added:

“Culture not indicated – bacterial count below significant threshold”.

“If symptoms persist or recur please submit a further sample indicating culture required”.

11.1.3 Microscopy or chemical screening reporting time

All results should be issued to the requesting clinician as soon as they become available, unless specific alternative arrangements have been made with the requestors.

Urgent results should be telephoned or transmitted electronically in accordance with local policies.

11.1.4 Urine for antigen testing

Positives

Legionella pneumophila urine antigen positive

Comment – Provisional positive for *Legionella pneumophila* serogroup 1 antigen in urine. Please send a respiratory sample for Legionella culture. Specimen has been referred to the Reference laboratory for confirmatory testing.

Negatives

Legionella pneumophila serogroup 1 urine antigen not detected

11.2 Culture

Report bacterial growth in either metric or SI units, according to local protocol (see section: Technical Information/Limitations at end of Introduction).

Including comments where appropriate (refer to Appendix 3) or

Report no significant growth or

Report absence of growth.

Report presence of antimicrobial substances, if detected.

Report results of supplementary investigations.

11.2.1 Culture reporting time

Interim or preliminary results should be issued on detection of potentially clinically significant isolates as soon as growth is detected, unless specific alternative arrangements have been made with the requestors.

Urgent results should be telephoned or transmitted electronically in accordance with local policies.

Final written or computer generated reports should follow preliminary and verbal reports as soon as possible.

Supplementary investigations: *Mycobacterium* species (see [UK SMI B 40 - Investigation of specimens for Mycobacterium species](#)) and parasites

(see [UK SMI B 31 - Investigation of specimens other than blood for parasites](#)).

11.3 Antimicrobial susceptibility testing

Report susceptibilities as clinically indicated. Prudent use of antimicrobials according to local and national protocols is recommended.

Refer to table 9.7.1. The table includes guidance on some of the of agents that should be tested on the bacterial isolates listed. The table also includes additional agents that can be considered for inclusion in test panels in specific clinical scenarios.

Any deviation from the guidance should be subject to local consultation and risk assessment.

Generally, all non-intrinsic resistant results should be reported as this is good practice and informs the user.

12 Notification to UKHSA^{128,129}, or equivalent in the devolved administrations¹³⁰⁻¹³³

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify UK Health Security Agency (UKHSA) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local UKHSA Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to UKHSA. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to UKHSA and many UKHSA Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCIs) and Creutzfeldt–Jakob disease (CJD) under 'Notification Duties of Registered Medical Practitioners': it is not noted under 'Notification Duties of Diagnostic Laboratories'.

<https://www.gov.uk/government/organisations/public-health-england/about/our-governance#health-protection-regulations-2010>

Other arrangements exist in [Scotland](#)^{130,131}, [Wales](#)¹³² and [Northern Ireland](#)¹³³.

13 Public health responsibilities of diagnostic laboratories

Diagnostic laboratories have public health responsibility as part of their duties. Amongst these are additional local testing, or referral to further characterise the organism as required, primarily for public health purposes e.g. routine cryptosporidium detection; serotyping or microbial subtyping; and a duty to refer appropriate specimens and isolates of public health importance to a reference laboratory.

Diagnostic laboratory outputs inform public health intervention, and surveillance data is required to develop policy and guidance forming an essential component of healthcare. It is recognised that additional testing and referral of samples may entail some costs that has to be borne by the laboratory but in certain jurisdictions these costs are covered centrally.

Diagnostic laboratories should be mindful of the impact of laboratory investigations on public health and consider requests from the reference laboratories for specimen referral or enhanced information.

Appendix 1: Multiplicative factors based on varying volumes of urine dispensed, diameter of well & field of vision (Fov) diameter⁶⁵

Volume of urine dispensed (µL)	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80
Diameter of well (mm)	8	8	8	8	8	8	7	7	7	7	7	7	7	6	6	6	6	6
FOV diameter (mm)	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50
Multiplicative Factor	0.8	1.0	1.3	1.6	2.2	3.2	0.6	0.8	1.0	1.3	1.7	2.5	0.5	0.6	0.7	0.9	1.3	1.8
Multiplicative Factor (rounded)	1	1	1	2	2	3	1	1	1	1	2	2	0.005	1	1	1	1	2
Volume of urine dispensed (µL)	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70
Diameter of well (mm)	8	8	8	8	8	8	7	7	7	7	7	7	7	6	6	6	6	6
FOV diameter (mm)	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50
Multiplicative Factor	0.9	1.1	1.4	1.9	2.5	3.7	0.7	0.9	1.1	1.4	1.9	2.8	0.5	0.6	0.8	1.0	1.4	2.1
Multiplicative Factor (rounded)	1	1	1	2	3	4	1	1	1	1	2	3	1	1	1	1	1	2
Volume of urine dispensed (µL)	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
Diameter of well (mm)	8	8	8	8	8	8	7	7	7	7	7	7	7	6	6	6	6	6
FOV diameter (mm)	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50	1.00	0.90	0.80	0.70	0.60	0.50
Multiplicative Factor	1.1	1.3	1.7	2.2	3.0	4.3	0.8	1.0	1.3	1.7	2.3	3.3	0.6	0.7	0.9	1.2	1.7	2.4
Multiplicative Factor (rounded)	1	1	2	2	3	4	1	1	1	2	2	3	1	1	1	1	2	2

Appendix 2: Multiplicative factor equation⁶⁵

Multiplicative Factor for Appendix 1

$$\text{Multiplicative factor} = \frac{1}{\text{Volume observed (V}_o\text{)}}$$

$$V_o = \pi(\text{FOVr})^2 \times \text{fd}$$

$$\text{Fluid depth (fd)} = \frac{\text{Volume dispensed}}{\pi(\text{Radius of the well})^2}$$

Where:

π — Known as Pi whose constant value is known as 3.14

FOVr - The radius of the Field of Vision (in , calculated by dividing the diameter of the FOV which is calculated as FOV number (marked on eyepiece) divided by the objective magnification or by direct measurement with a micrometre.

Appendix 3: Guidance for the interpretation of urine culture

Note: This table is intended for guidance only - supplementation with local reporting policies may be necessary.

Growth cfu/L	No. isolates	Specimen type	Clinical details/microscopy influencing report*	Laboratory interpretation	Susceptibility testing recommended	Comments to consider
$\geq 10^8$	1	Any	None	Probable UTI	Yes	If old specimen or no pyuria consider repeat to confirm Consider SPA or CCU if bag specimen
	2	Each org $\geq 10^8$ or $\geq 10^8$ and $\geq 10^7$	MSU, CCU, SCU, BAG	Possible UTI – colonisation, faulty collection or transport	Yes	Consider repeat to confirm
			CSU, (IL)	Indwelling catheter Neurogenic bladder	No – Consider keeping plates $\leq 5d$ in case patient becomes septic	Consider discuss if patient systemically unwell and therapy required
	2	1 organism predominant at $\geq 10^8$ or 10^7	Any	None	Possible UTI – ?colonisation, faulty collection or transport	Yes, predominant organism If old specimen or no pyuria consider repeat to confirm Consider SPA or CCU if bag specimen
	≥ 3	Mixed growth - none predominant	Any	None	Faulty collection or transport	No Heavy mixed growth – probable contamination. Consider repeat if symptomatic
$10^7 - 10^8$	1	Any	WBC present Symptomatic	Possible UTI – patient evaluation necessary	Yes	Consider repeat to confirm
	2	1 predominant at $\geq 10^7$	Any	WBC present Symptomatic Children	Probable UTI with predominant species 2nd isolate probable contamination	Yes, predominant organism but suppress results Consider repeat or SPA/CCU Sensitivities are available if required
		1 at $< 10^7$ or 10^8 but not predominant		None	Probable contamination	No Mixed growth – probable contamination
	≥ 3	1 organism predominant at $\geq 10^7$	Any	WBC present Symptomatic	Possible UTI with predominant species. Others probable contamination	No – keep plates $\leq 5d$ if catheter specimen in case patient becomes septic Mixed growth – consider repeat if symptomatic
		Any combination	CSU	Indwelling catheter Neurogenic bladder	Colonisation	No – keep plates $\leq 5d$ in case patient becomes septic Please discuss if therapy indicated

Appendix 3 (continued): Guidance for the interpretation of urine culture

Note: This table is intended for guidance only – supplementation with local reporting policies may be necessary.

Growth cfu/L	No. isolates		Specimen type	Clinical details/micros copy influencing report	Laboratory interpretation	Susceptibility testing recommended	Comments to consider
10 ⁶ – 10 ⁷	1		MSU, CCU, CSU, IL	Symptomatic female Prostatitis WBC present	Possible UTI – clinical evaluation necessary	Yes	Consider repeat to confirm
	2	Each org ≥10 ⁶ - including possible pathogen, eg <i>E. coli</i> or <i>S. saprophyticus</i>	Any		Possible UTI – clinical evaluation necessary	Yes	Consider repeat to confirm
10 ⁵ – 10 ⁸	1		SPA, CYS, (SCU)	None	Probable UTI	Yes	
	2	Each ≥ 10 ⁶		WBC present	Probable UTI – patient evaluation necessary	Yes	
	≥3	1 organism predominant at ≥ 10 ⁶		WBC present	Probable UTI – patient evaluation necessary	Yes, predominant organism	Mixed growth: Consider repeat to confirm
No growth		ie: < 10 ⁶ if 1 µL loop used < 10 ⁵ if 10 µL loop used	Any	None or asymptomatic	No UTI		
				Symptomatic Marked/persistent pyuria	<ul style="list-style-type: none">• Patient on antibiotics?• Consider <i>Chlamydia</i>, AFB etc• Fastidious organism?• Consider bacteriuria < 10⁵ cfu/L		As appropriate
MSU – Midstream specimen; CCU – clean catch; SPA – Suprapubic aspirate; IL– Ileal conduit; CSU – Catheter; SCU – Single, intermittent catheter (“in and out”); CYS – Cystoscopy * - see Introduction for interpretation of culture results							

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An explanation of the reference assessment used is available in the [scientific information section on the UK SMI website](#).

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