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The laboratory diagnosis of urinary tract infection

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Abstract
Urinary tract infection is common, and it is not surprising that urine specimens make up a large proportion of those samples submitted to the routine diagnostic laboratory. Many of these specimens will show no evidence of infection and several methods can be used to screen out negative samples. Those that grow bacteria need to be carefully assessed to quantify the degree of bacteriuria and hence clinical relevance. To influence treatment, a final report should be produced within 24 hours of specimen receipt, with turnaround times continuously monitored. Much work needs to be done to determine the cost effectiveness involved in processing urine specimens and the evidence base for the final report provided.

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Keywords: laboratory diagnosis; urinary tract infection

The aim of the microbiology laboratory in the management of urinary tract infection (UTI) is to reduce morbidity and mortality through accurate and timely diagnosis with appropriate antimicrobial sensitivity testing. Although optimal specimen collection, processing, and interpretation should provide the clinician with a precise answer, no single evaluation method is foolproof and applicable to all patient groups. In practice, laboratories will not be able to approach each specimen individually, and standard operating procedures are generated to cover the processing of most samples, with the aim of detecting the abnormal presence of bacteria and fungi within the urinary tract. The interpretation of results requires an understanding of the limitations of local laboratory protocols and of the clinical context in which the specimen was taken.

Urine specimens make up a large proportion of the samples submitted to a routine diagnostic laboratory. A large laboratory may examine 200–300 urine samples each day. This heavy workload reflects the frequency of UTI both in general practice and in hospital settings. In children, infection is more common in young girls, except in the neonatal age group, where boys predominate. It is estimated that 20% of women develop a UTI during their lifetime; the incidence increases at puberty and remains high throughout adult life, only after the age of 50 years is a similar incidence seen in males. UTI accounts for approximately 23% of all hospital acquired infections. Although the incidence of infection is high, most specimens received will show no evidence of infection and several methods have been developed to screen out negative samples to minimise expense and improve turnaround times. These will also be reviewed.

Most infections at all ages are the result of enteric bacteria, especially Escherichia coli, which colonise the perineum and then ascend the urethra to multiply and infect the bladder, kidney, and adjacent structures. The most common site of infection is the bladder. Haematogenous infection of the urinary tract occurs most notably with Mycobacterium tuberculosis and Salmonella spp, and direct introduction of organisms during instrumentation of the urinary tract is also well recognised. Structural and functional abnormalities result in a wider range of possible infecting organisms.

Urinary tract infection may occur with or without symptoms; the latter is known as covert or asymptomatic bacteriuria. Because urine must pass through the distal urethra and in women over the perineum, it may become contaminated by the normal flora of these regions. Isolation of more than one bacterial strain suggests such contamination, but even when a single strain is isolated, quantitative culture is required to determine whether it indicates true bacteriuria. Kass, in his original studies validating the midstream urine specimen (MSU), showed that 95% of hospitalised patients with acute pyelonephritis had more than 10^5 colony forming units (cfu)/ml of urine, whereas only 6% of asymptomatic patients had this degree of bacteriuria. Subsequent studies have shown that lower bacterial counts can be important; this applies both to men and symptomatic women in whom 30–50% have fewer than 10^5 organisms/ml. These cut off values can be applied to all rapidly growing bacteria but not fungi or fastidious organisms. Patients with frequency dysuria syndrome in whom urine cultures show no appreciable growth should be investigated...
for other agents that cause non-specific urethrit-
sis, such as Chlamydia trachomatis. It should be
noted that above the distal urethra the urinary
tract is normally sterile, and any bacteria
isolated from urine samples taken directly from
the bladder, ureter, or kidney must be viewed
as clinically relevant. The detection of poly-
morphonuclear cells (pyuria) and red blood
cells (haematuria) in urine is useful for the
diagnosis of infection or other renal tract
pathologies.

Each laboratory should aim to have available
a final report with microscopy, culture, and
sensitivity on a substantial number of speci-
mens (for example, >90%) within 24 hours
after the receipt of the specimen, and laborato-
ries should monitor their turnaround times as
part of quality assurance. The ability to screen
out negative specimens as quickly as possible
should also be considered; ideally this is done
at source. The physician can make a clinical
judgement as to whether a negative screen (for
example, by reagent strip testing or bedside
microscopy) is sufficiently accurate to rule out
infection in that individual patient, given the
limitations of the method used.

This broadsheet deals specifically with the
diagnosis of bacterial UTI causing cystitis or
pyelonephritis. It does not address other possible
pathologies.

Collection and transport of specimens

Rigorous care during the collection of urine is
vital to prevent contamination by commensal
flora, especially in female patients and children.
Most samples are MSUs, and patients should
be given clear instructions on discarding the
first part of the stream before collection in an
appropriate sterile container. Female patients
should be instructed to part the labia while
passing urine to avoid contamination. The ini-
tial few milliliters of urine wash away distal
urethral organisms and hence the MSU is rep-
resentative of bladder urine. It requires good
control of micturition and an adequate volume
of urine in the bladder. It may prove difficult
to get such a sample in the elderly or those with
hip joint problems. Early morning samples may
harbour greater bacterial counts but are less
amenable to outpatient clinical practice. How-
ever, they are recommended for the diagnosis
of renal tuberculosis.

Catheter specimens of urine (CSUs) are
often obtained from patients with long term
indwelling catheters. Bacteria are frequently
recovered but only a few are important and
samples should only be taken when signs and
symptoms such as fever, loin pain, or suprapu-
bic pain suggest infection. Urine should be
aspirated directly from the catheter using a
sterile needle and syringe and then placed in a
sterile container. Bacteria multiply in catheter
bags so specimens from this site are unsuitable.
Temporary catheterisation was often used to
diagnose urinary infection in women but
because of the risk of bacteria being introduced
into the bladder this method is no longer
acceptable. Intermittent catheterisation may be
used by patients with neurogenic bladder and
these specimens should be treated as CSUs.

Increasingly, samples are being received
from patients with urological problems, includ-
ing patients with ileal conduits and those who
have undergone bladder reconstruction, and
these can present difficulties with interpre-
tation. Specimens should only be taken if there
are clinical signs of infection (for example,
malaise, pyrexia, or vomiting) and they should
be obtained via careful catheterisation of the
stoma or reconstructed bladder using an asep-
tic technique. The interpretation of the cul-
tures should then be as for any catheter speci-
men.

Suprapubic aspirates (SPAs) were often
obtained from babies and young children and
are still considered the “gold standard” and are
used in difficult cases. Any isolate should be
considered clinically relevant. Obtaining an
SPA involves an invasive procedure; however a
sterile adhesive bag or pad (that is, a sanitary
towel with the appropriate absorption charac-
teristics, lining a nappy) is much simpler but
can still achieve a definitive answer in 50–75%
of cases. After cleansing the perineum, the
baby is maintained in an upright position until
urine is passed into the bag, pad, or alterna-
tively via a clean catch into a container.

Urine samples collected from the ureter (at
cystoscopy) or from the kidney (via a nephros-
tomy) should be treated in the laboratory as a
fluid from a sterile site and all bacterial and
fungal growth viewed as clinically relevant. For
the diagnosis of prostatitis, urine specimens
may be collected after massage of the prostate
via the rectum because this is said to release
any sequestered bacteria or inflammatory cells
from this site.

As can be seen from the above, not all speci-
cmen types are the same and correct interpret-
atation of urine cultures requires accurate data
being clearly present on the request form.

Urine will permit growth of bacteria and if
there is to be a delay in transport (\(\geq 2\) hours)
or in setting up cultures in the laboratory then
it should be stored refrigerated at 4°C; this will
also preserve the white cell count. Boric
acid is often used to retain the bacterial count,
but its antibacterial activity can reduce the
number of organisms present, especially if an
inadequate volume of urine is dispensed into
the container. Hence, rapid transportation/
processing with refrigeration (if necessary)
is the preferred method. A dip slide or dip inocu-
lum is useful in overcoming delays in culturing
urine specimens, but because no microscopy
can be performed on the specimen, it is most
useful for the follow up of patients. It is more
expensive than routine methods.

Initial processing of specimens

A clear specimen of urine is unlikely to grow
bacteria in great numbers but a cloudy
specimen can result from bacteria, crystals, or
leucocytes. Because gross visual examination
cannot always be relied upon, several rapid
screening methods have been developed; these
are best performed at the bedside and accu-
rately detect pyuria or the presence of bacteria.
The laboratory diagnosis of urinary tract infection

Glycosuria, urobilinogen, pyuria, and bacteriuria are the key parameters in the diagnosis of UTI. Strips may be read visually or by machine. A suggested protocol for their use is given in fig 1.

**Protein**
A positive urine test for protein is a poor indicator of infection on its own, with a high rate of false positives and negatives; however, it may indicate several other renal pathologies, including glomerulonephritis and pre-eclampsia.

**Haemoglobin**
Haematuria may also be detected in UTI but can also result from a variety of conditions, including calculi and neoplasia. The strips detect peroxidase activity of haemoglobin and myoglobin, but because ascorbic acid can inhibit peroxidase reactions, false negatives may ensue. Haemolysis may result in negative microscopy.

**Leucocyte esterase**
A chloroacetate stain reacts with the enzyme leucocyte esterase found in primary neutrophil granules. The detection of pyuria by this test is reasonably sensitive (72–97%) and may be more accurate than microscopy because enzyme activity is still retained when white cells have disintegrated. False negatives or reduced reactions occur in the presence of ascorbic acid, boric acid, doxycycline, cefalexin, gentamycin, nitrofurantoin, glycosuria, urobilinogen, or high concentrations of protein; false positives occur with clavulanic acid, imipenem, or contaminated specimens. More recently, strip testing of urinary lactoferrin, a protein found in neutrophil nuclei and granules, has been suggested as an alternative to leucocyte esterase testing.

**Nitrate reductase** (Greiss test)
This enzyme reduces nitrate to nitrite and is present in coliforms but not other bacteria such as *Staphylococcus saprophyticus* and enterococci. The test is best performed on early morning urine and, although specificity is high, sensitivity ranges from 35% to 85%. Combined with the leucocyte esterase test, the sensitivity rises to 70–100% with only a small decrease in specificity.

**OTHER METHODS USED**

**Glucose oxidase**
Glucose is usually present in urine at low concentrations, and bacteria will utilise this energy source; hence, a positive test is indicated by the absence of glucose. The test is quite sensitive but false positives can occur along with false negatives, in patients with diabetes mellitus, or in those patients infected with bacteria that do not metabolise glucose.

**Catalase activity**
Catalase is found in most bacteria that cause UTI (but not streptococci) and in associated somatic cells (leucocytes and erythrocytes). It is measured with a tube based assay (API Uriselect; BioMérieux, Lyon, France) and has been promoted for screening asymptomatic populations. Field trials have given variable results.

**Bioluminescence**
UTI-screen (Coral Biomedical, San Diego, California, USA) is a semiautomated system that measures bacterial ATP. A releasing agent is added along with the firefly enzyme luciferin-luciferase and the sample is incubated at room temperature for 15 minutes, during which time the integrated light output is measured. The specificity of this method at detecting >10³ cfu/ml is 70%, sensitivity 96%, negative predictive value 98%, and positive predictive value 55%. Hence, its principal role is in rapidly screening out negative specimens. False negatives may be seen with candida and enterococcal infection and false positives with gross haematuria.

**Malthus**
The Malthus system (Malthus Ltd, Stoke on Trent, UK) measures conductance between two electrodes immersed in media. Growth is indicated by a change in electrical impedance and has been used for the detection of bacteraemia. Its use in detecting bacteriuria is limited and early evaluations showed that no single medium allows the detection of all bacteria. The system is not suitable if a preservative such as boric acid is used because this alters conductance. If the cut off time is set at 2.5 hours (somewhat longer than most rapid screening methods), 80% of true positives are detected. However, there is a high false positive rate and it has not gained wide acceptance.

**Electrochemical detection method**
This technique, which determines molecular hydrogen production using a platinum electrode, was first applied to the detection of coliforms in water. In one study, 94% of positive urines (>10⁷ cfu/ml) were detected at four hours, but it should be noted that certain
**Table 1** Common causes of “sterile” pyuria

<table>
<thead>
<tr>
<th>Elements</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female genital tract infection/non-specific urethritis in male patients</td>
<td></td>
</tr>
<tr>
<td>Prostatitis</td>
<td></td>
</tr>
<tr>
<td>Neoplasia of the renal tract</td>
<td></td>
</tr>
<tr>
<td>Renal calculi</td>
<td></td>
</tr>
<tr>
<td>Catheterisation</td>
<td></td>
</tr>
<tr>
<td>Renal tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Fever in children, independent of cause</td>
<td></td>
</tr>
<tr>
<td>Prior antimicrobial chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

- Microorganisms such as staphylococci, streptococci, *Acinetobacter* spp, and *Candida albicans* require longer detection periods.

**Enzyme immunoassay**

An indirect immunoassay has been developed to detect antibodies specific to antigens on bacteria most commonly associated with UTI. Preliminary evaluation found the test to be labour intensive, costly, and to have relatively low sensitivity and specificity (62% and 65%, respectively).

**Microcalorimetry**

Minor changes in temperature as a result of bacterial metabolism can be used to indicate high numbers of bacteria in a urine specimen. No large scale studies of this technique have been published.

**Photometry**

Detects bacterial growth based on changes in light transmission and is more rapid than conventional culture techniques. However, if the interval for detection is prolonged to detect certain pathogens such as *Pseudomonas aeruginosa*, then there is an increase in false positive results. Several automated systems are available.

**Colorimetric filtration**

Urine is passed through a filter that traps cells, Safronin O dye stains these cells which can then be detected visually or using a semiautomated colorimetric system. False positive results caused by cellular elements often occur and sensitivity rates fall dramatically when trying to detect < 104 cfu/ml.

**Turbidimetric screening**

Measuring turbidity using a double beam turbidometer can screen out negative samples. At a 94% sensitivity, 55% of samples are screened negative.

**Methods**

**Microscopy**

- **Detection of pyuria**
  
  A urinary excretion rate of more than $4 \times 10^7$ leucocytes/hour is found in 96% of patients with symptomatic bacteriuria, but in only 10% of patients with covert bacteriuria. This is more readily determined by finding > 10 leucocytes/ml in uncentrifuged urine; in symptomatic infection counts are often much higher than this. However, it should be noted that pyuria only indicates inflammation and does not always mean infection. Table 1 lists the causes of “sterile” pyuria. Pyuria and/or bacteria on microscopy are highly suggestive of UTI and are useful criteria to select specimens for direct sensitivity testing. However, the absence of pyuria does not exclude infection because patients with neutropenia may have an inadequate white cell response to infection. Alkaline urine, such as that encountered with *Proteus* spp infection, results in white cells disintegrating before microscopy being performed. Pyuria is considered by some to be a poor predictor of infection.

- **Detection of haematuria**
  
  Haematuria is commonly seen in acute cystitis but is not diagnostic of that condition. It is rarely seen in other dysuria syndromes but is often seen in non-infective renal disease. Table 2 indicates the importance of other elements seen on urine microscopy.

- **Detection of bacteriuria**
  
  Microscopy of uncentrifuged, unstained urine will detect more than 105 bacteria/ml of urine. Sensitivity increases if the urine is centrifuged and/or Gram stained; this also permits preliminary identification of the pathogenic bacteria. These methods are labour intensive and impractical for routine specimens.

**Table 2** Importance of elements seen on direct microscopy of urine

<table>
<thead>
<tr>
<th>Elements</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells</td>
<td></td>
</tr>
<tr>
<td>White blood cells</td>
<td>Urinary tract infection or inflammation (see causes of sterile pyuria (table 1))</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Urinary tract infection or inflammation</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Acute interstitial nephritis</td>
</tr>
<tr>
<td>Epithelial cells</td>
<td>Contamination of specimen</td>
</tr>
<tr>
<td>casts</td>
<td></td>
</tr>
<tr>
<td>Hyaline</td>
<td>Normal finding in concentrated urine</td>
</tr>
<tr>
<td>Granular</td>
<td>Renal parenchymal disease (non-specific)</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>Glomerulonephritis, vasculitis</td>
</tr>
<tr>
<td>White blood cell</td>
<td>Interstitial nephritis, pyelonephritis</td>
</tr>
<tr>
<td>Epithelial cell</td>
<td>Acute tubular necrosis, interstitial nephritis, glomerulonephritis</td>
</tr>
<tr>
<td>Crystals</td>
<td>Several different types of crystals may develop in the urine including uric acid, calcium phosphate, calcium oxalate, cystine and sulphur. Their evaluation is outside the remit of the diagnostic microbiology laboratory</td>
</tr>
</tbody>
</table>
AUTOMATED MICROSCOPY

The DiaSys R/S 2000 is an automated system for the microscopic examination of urine. It simply draws a sample from a specimen container to an optical slide assembly on the microscope stage. In comparative studies it has a high degree of correlation with standard microscopic examination. Laboratory costs can be reduced by adopting this method.31

An image processing computer (Yellow IRIS; International Remote Imaging Systems, Chatsworth, California, USA) is able to recognise different particle sizes and can be used to analyse stop motion pictures from a video camera on a flow microscope. Several types of cellular elements present in uncentrifuged urine are recognised; however, the application of this technology is limited by cost.32

BACTERIAL CULTURE

The most common cause of urinary tract infection is *E. coli*. In hospital practice, other bacterial species commonly seen include enterobacter, klebsiella, proteus, pseudomonas, enterococci, and staphylococci.33 *Staphylococcus saprophyticus* is a common cause of infection in young sexually active women. The laboratory must also quantify culture results to determine the clinical relevance of an isolate. Table 3 shows a comparison of the organisms isolated in the community with those found in hospital.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Community (%)</th>
<th>Hospital (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>69.4</td>
<td>50.8</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Klebsiella</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Enterobacter</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Enterococcus</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Staphylococcus</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td><em>Others</em></td>
<td>12.1</td>
<td>5.4</td>
</tr>
</tbody>
</table>

IDENTIFICATION OF BACTERIA

Clear protocols for the identification of bacteria and fungi should be in place. In general, it is adequate to report coliforms as such without full identification. *Proteus* spp are urease positive and resistant to nitrofurantoin. *Pseudomonas aeruginosa* is an oxidase positive lactose non-fermenter, resistant to most first line antibiotics. If clinical details suggest that a

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non-lactose fermenting coliform may be a Salmonella spp and the urease and oxidase tests are negative then slide agglutinations with “O” and “H” antisera should be performed from cultures on blood (or other non-selective) agar plates. Any positive results should be followed up with biochemical confirmation. If typhoid fever is suspected, 5–10 ml of uncentrifuged urine should be inoculated into double strength selenite, incubated overnight at 37°C in air, then subcultured on to deoxycholate citrate agar, which in turn is incubated overnight at 37°C in air. Any suspect isolate should be dealt with in containment level 3 accommodation.

One advantage of using blood agar alongside CLED is that Gram positive bacteria are more easily characterised. If uncertainty exists, a catalase test will distinguish streptococci (negative) from staphylococci (positive). Staphylococcus aureus is DNase, slide, and tube coagulase positive. Staphylococcus saprophyticus can be identified by its resistance to novobiocin and this makes a useful distinction from other coagulase negative staphylococci, which are usually only important in specific situations such as instrumented or catheterised patients. If the appearance of the colony is typical of Enterococcus faecalis report the organism as such; if uncertain, perform a bile aesculin test. β-Haemolytic streptococci can be readily identified by Lancefield group testing.

Other isolates are identified using standard laboratory techniques, all multiply antibiotic resistant organisms need to be fully identified. Fungi need only be identified if there is evidence to suggest that the isolate is clinically relevant. Because cut off values vary from author to author, we recommend that repeat sampling is performed to determine that there is persistent funguria (catheters should be changed). Candida albicans is germ tube positive and usually sensitive to fluconazole, itraconazole, and amphotericin. Sensitivity testing and the identification of other candida and fungal species are only necessary in selected patients, such as those who are severely immunocompromised.

The detection of antimicrobial substances is not routinely recommended but should be incorporated in the multipoint set to exclude false negative culture results. The detection of antibody coated bacteria in urine is not recommended in the routine diagnostic laboratory but may be useful to distinguish between upper and lower urinary tract infection in selected patients.

**SENSITIVITY TESTING**

The choice of agents to test will depend upon local antibiotic policies and resistance patterns. In general, the primary agents tested target coliforms and enterococci, and second line sensitivities need only to be performed if less common bacteria or resistant isolates are encountered. The suggested first line agents include amoxicillin, trimethoprim, cefalexin (or other oral cephalosporins), nitrofurantoin, co-amoxiclav, and ciprofloxacin. Urine is used as the primary inoculum when there is evidence of infection (pyuria and/or bacteriuria) so as to permit rapid reporting. This method may be more representative than picking individual colonies for subculture, particularly given the heterogenous nature of urinary tract infection. The degree of pyuria that triggers the performance of direct sensitivity testing should be decided locally depending on the patient group examined. It is suggested that all urines that show bacteria on microscopy and those with pyuria > 100 white cells/mm³ should be tested. Recent recommendations for disc content and zone size interpretation have been published by the British Society for Antimicrobial Chemotherapy.

Each sensitivity report is tailored to guide clinicians to the most appropriate agents and it is often necessary to suppress antibiotics if the isolate is not deemed to be clinically relevant. Suppressing antibiotic sensitivities on the results of positive specimens may be a particularly useful way of educating users that treatment of a positive catheter urine is not normally warranted. In addition, the presence or absence of pyuria may be used to decide which sensitivities are reported. However because the definition of UTI is based on bacterial counts and not on the presence or absence of pyuria, performing sensitivities should be related to the number of bacteria present and the relevant clinical situation. Specific agents may be unsuitable in particular situations—for example, the reporting of intravenous antibiotics to general practitioners—and certain antibiotics are relatively contraindicated in pregnancy. If sensitivity testing is not performed (for example, on mixed cultures) then culture plates should be kept for five days so that further testing may be performed if necessary.

**Interpretation and reporting of culture results**

The interpretation of culture results can be considered as more of an art than a science. A urine culture result depends on so many variables, such as appropriate collection, transport, and the limits of the methods of detection. The reliability of single positive urine culture in diagnosing UTI is only 80%, rising to 90% if a repeat culture shows identical results. Traditionally, > 10⁵ bacteria/ml of urine showing a single isolate is taken to indicate bacteriuria and distinguishes infection from contamination in asymptomatic patients. This degree of bacteriuria is usually used in surveillance and epidemiological studies to allow standardisation of data. Mixed culture with a predominant organism should also be considered as clinically relevant, although the possibility of contamination exists. Counts as low as 10³/ml in symptomatic women are relevant when enterobacteriaceae are grown, but this is not necessarily the case with other microorganisms. A count of 10⁷/ml is viewed as the lower limit of clinical relevance in symptomatic men. Therefore, pure culture of even a low count of bacteria should always be considered as potentially important and sensitivity
Table 4  Common causes of falsely low bacterial counts in urine specimens

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonisation without infection</td>
</tr>
<tr>
<td>Dilutional through excessive rehydration</td>
</tr>
<tr>
<td>Acidification or alkalinisation of urine</td>
</tr>
<tr>
<td>Urinary frequency</td>
</tr>
<tr>
<td>Concurrent use of a systemic antimicrobial agent and/or other growth inhibitor</td>
</tr>
<tr>
<td>Use of a topical cleansing agent with antimicrobial activity during specimen collection</td>
</tr>
<tr>
<td>Haematogenous infection of the urinary tract</td>
</tr>
<tr>
<td>Obstruction of the renal tract distal to the site of infection</td>
</tr>
<tr>
<td>Infection with a fastidious or slow growing organism</td>
</tr>
</tbody>
</table>

testing performed if there are appropriate clinical details. Table 4 lists the causes of low bacterial counts in urine specimens. These recommended cut off values are taken from carefully conducted studies and in routine diagnostic work specimen collection, storage, and transportation may be suboptimal. Each laboratory should define which groups of patients or wards or departments warrant additional work or consideration of low bacterial counts so that appropriate sensitivity testing and reporting can occur. In general, repeat culture should be requested before treatment is started in any patient in whom the diagnosis of UTI is doubtful, or if contamination is suspected. When doubt exists about a culture result, the comment “Please repeat if clinically indicated” may be added to the standard comment. Table 5 indicates a possible schedule for reporting specimens. Bacterial counts or the presence or absence of pyuria cannot be used to localise the specimen. Bacterial counts or the presence of skin flora should only be sent when these conditions are suspected clinically. These patients may have polymicrobial bacteriuria and should not be dismissed, especially if repeat cultures from correctly taken specimens are positive.

However, for most CSUs sensitivity testing on several isolates is unnecessary provided culture plates are available for five days in case symptomatic infection develops. Exposure to antibiotics in hospital favours alteration of regional flora and the acquisition of resistant strains which, as a consequence of cross infection, may result in outbreaks. To avoid unnecessary treatment with antibiotics, suppressing results of antibiotic sensitivity is recommended with an appropriate comment such as “catheter associated bacteriuria does not require treatment unless there are clinical signs of infection” and if appropriate add “sensitivities available on request”.

SPECIMENS FROM CHILDREN
These may be from a pad specimen or a urine bag and therefore contamination can readily occur. Negative cultures or a slight growth may be diagnostically useful. However, positive cultures should be confirmed by a repeat specimen, more than 10^2 cfu/ml is taken as relevant, especially if there is a single isolate. Further investigation using a DMSA ("99mTc-dimercaptosuccinic acid) scan or ultrasound is warranted in children under 5 years to exclude urinary tract abnormalities that might be amenable to surgery. Routine screening of urine in infants or children is not recommended, although if renal abnormalities are suspected, including those infants who have been exposed to cocaine in utero, then screening should be performed.

URINARY TRACT INFECTION IN PREGNANCY
Asymptomatic bacteriuria occurs in 2–10% of pregnant women. In the absence of specific treatment it tends to persist and in one third of those affected progresses to cause acute pyelonephritis. Infection may be complicated by low birth weight and prematurity, pre-eclampsia, maternal anaemia, amnionitis, and intrauterine death. The treatment of asymptomatic bacteriuria is thought to reduce these risks. The optimal method for screening is urine culture, which should be repeated to exclude contamination. Reagent strip testing only is less effective in identifying those patients who will develop pyelonephritis, but it does offer considerable cost savings. In the future, other rapid methods described above may be useful screening tests to complement urine culture.

Symptomatic urinary tract infection during pregnancy usually presents in the second
Unlike asymptomatic bacteriuria it has a low relapse rate after treatment and progression to pyelonephritis is uncommon. Because pregnancy itself may result in frequency and nocturia it may be difficult to distinguish symptomatic from asymptomatic bacteriuria.

Several antibiotics used to treat urinary tract infection should be avoided during pregnancy. These include aminoglycosides, quinolones, tetracyclines, and trimethoprim (first trimester). Laboratory reporting of sensitivity data should reflect this.

OTHER PATIENT GROUPS
Asymptomatic bacteriuria in the elderly is not associated with an increased mortality rate or with morbidity, such as hypertension or renal dysfunction. UTI may present atypically—for example, as falls, immobilisation, or confusion—and although urine culture should be considered as part of any geriatric assessment, routine screening is not recommended. Incidental detection of bacteriuria in men warrants further investigation, in particular for prostate or bladder outflow infections. Infection is more common in diabetic women, but not in diabetic men or school age diabetics, and routine screening in the absence of symptoms is not recommended. Urinary tract infection is seen more frequently after renal transplantation: it occurs in up to 79% of patients and is often asymptomatic. It can result in graft dysfunction, so routine screening, as part of a regular review, is recommended. All isolates need to be carefully evaluated and repeat cultures requested as appropriate. Screening for UTI is also recommended in patients who require urological procedures, including extra-corporeal shock wave lithotripsy. Many of these patients may have ureteric stents in place that also predispose to infection.

Human immunodeficiency virus infection, particularly when CD4 counts are below 200 cells/mm³, appears to be associated with an increased risk of bacteriuria. Other immunosuppressed patients (for example, transplant patients, patients on chemotherapy, or high dose corticosteroids) also have an increased risk of UTI.

CANDIDURIA
The kidney is involved in 90% of patients with disseminated candida infection and candiduria is an early indicator of systemic candidosis. However, Candida spp may colonise the perineum and urethral meatus resulting in contamination of urine during collection. Treatment is started on the basis of other risk factors for disseminated infection. Clinically relevant candiduria in other situations is more difficult to define and, in the absence of a recognised clear cut off in colony count that distinguishes between contamination and infection, repeated isolation of candida is a useful guide in deciding on further evaluation. Risk factors for funguria include urinary tract abnormalities, diabetes mellitus, antibiotic treatment, and immunosuppression. Chronically catheterised patients may develop asymptomatic candiduria and, in this situation, the catheter should be changed whenever possible. Some authors recommend alkalisation of the urine but consideration should also be given to systemic fluconazole or amphotericin bladder washouts or irrigation. Sometimes, cystoscopy will provide visual proof or histological evidence of candida infection, thereby avoiding the need for repeat sampling. Urethral candidiasis occurs as an extension of candida vaginitis in women and in men as a result of sexual contact.46

Quality issues
Laboratories should seek Clinical Pathology Accreditation (CPA (UK) Ltd) or other appropriate accreditation for all clinical microbiology work. Inherent in this is the performance of internal audit, internal quality assessment, participation in the National External Quality Assurance Scheme (NEQAS), and involvement in internal quality assessment of near patient testing facilities. Involvement in the “Q” probes and Q Track system of the College of American Pathologists allows comparative audit with other laboratories. Q probes specific to the diagnosis of UTI include studies on transport, handling of urine samples, and urine culture contamination.10 11 In addition, The Clinical Benchmarking Company (UK) has looked at specific UTI projects with a view to improving cost effectiveness.48 Evidence based practice for the reporting of urine culture results is still unfortunately lacking.

Conclusion
Because the sensitivities of uropathogens are relatively predictable, uncomplicated cystitis is often treated with empirical short course antibiotics without urine culture. If, however, antimicrobial prescribing is to focus on the treatment only of true bacterial infections, as has been recommended in the recent National Health Service Executive guidance,49 then urine culture should be performed. The first step in controlling the workload of the diagnostic laboratory is to have clear and appropriate guidelines for sending urine cultures from symptomatic and asymptomatic patients, both in general practice and in hospitals, and to be certain that bedside screening tests are applied as appropriate. Specimens should be collected and transported in a correct manner, so that contamination and bacterial overgrowth are minimised. The use of automation will allow large numbers of specimens to be processed with reduced technical input, but results are not as well standardised as they are for quantitative culture, which permits the detection of low numbers of bacteria, mixed samples, and sensitivity results. Thus, urine culture will remain the “gold standard” until these issues can be dealt with.

The laboratory diagnosis of urinary tract infection


Further reading


ACP Best Practice No 167: The laboratory diagnosis of urinary tract infection

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