RATIONAL TESTING
Interpreting asymptomatic bacteriuria

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Testing for and treating bacteriuria in children and non-pregnant adults without specific symptoms of urinary tract infection or sepsis is of uncertain benefit

Mrs A is a 74 year old woman who saw your locum two days ago with a two to three week history of feeling tired and vaguely unwell. She admitted to “leaking a bit of urine” whenever she coughs or lifts things, but has had this problem for two years. She has not had other urinary tract symptoms and has not had dysuria or frequency in recent years. She was prescribed an antibiotic two or three times in the past year by a doctor in another practice after positive laboratory tests on her urine. Her medical history is otherwise unremarkable and she was not examined. Your locum sent a urine specimen for microscopy and culture as dipstick testing was positive for nitrite (but negative for leucocyte esterase). Mrs A has returned to see you for the results.

What is the next investigation?
Testing urine for evidence of infection

Testing urine for evidence of infection may be appropriate in the following situations.

When clinical features suggest urinary tract infection—A 2002 systematic review concluded that the combination of dysuria and frequency in the absence of vaginal discharge or irritation confirms the diagnosis of urinary tract infection (probability >90%) and (b) dipstick testing cannot lower the post-test probability sufficiently to exclude urinary tract infection if a patient presents with one or more symptoms.1 Urine culture, however, has a value beyond confirming the diagnosis in that it can also direct treatment, on the basis of results of tests for antimicrobial susceptibility. The table summarises the findings of two systematic reviews.

When features of systemic sepsis are present—Testing of urine in patients presenting with clinical features of systemic sepsis (fever, rigors) is useful as the urinary tract is a common source of blood stream infection.

When there are other specific indications—Testing for bacteriuria is recommended in pregnant women without symptoms suggesting urinary tract infection2 as 2-7% have clinically significant bacteriuria.3 A systematic review of 14 studies and 2302 women concluded that treatment of asymptomatic bacteriuria in pregnancy reduces the incidence of pyelonephritis later in pregnancy. The overall incidence of pyelonephritis in pregnant women with asymptomatic bacteriuria is 21%, and treatment leads to a reduction in risk of 75%.4 Testing urine for infection is also recommended in the investigation of patients presenting with acute renal failure before major urological procedures.5 6

Features associated with an increase or decrease in the likelihood of urinary tract infection, according to two systematic reviews

<table>
<thead>
<tr>
<th>Features</th>
<th>Likelihood ratio</th>
<th>Little et al*</th>
<th>Giesen et al†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in likelihood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematuria</td>
<td>1.72</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1.3</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td>Nocturia</td>
<td>1.3</td>
<td>Not reported</td>
<td>1.5</td>
</tr>
<tr>
<td>Urgency</td>
<td>1.2</td>
<td>Not reported</td>
<td>1.6</td>
</tr>
<tr>
<td>Frequency</td>
<td>1.10</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Back pain</td>
<td>Not reported</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>Costovertebral angle tenderness</td>
<td>Not reported</td>
<td>1.7</td>
<td>1.7</td>
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<tr>
<td>Decrease in likelihood</td>
<td></td>
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</tr>
<tr>
<td>Vaginal discharge</td>
<td>0.65</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Vaginal irritation</td>
<td>Not reported</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Vaginal discharge on examination</td>
<td>Not reported</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Absence of dysuria</td>
<td>Not reported</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Absence of back pain</td>
<td>Not reported</td>
<td>0.8</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*16 studies conducted in primary care; 3711 participants.
†Nine studies.
Avoidance of testing

Other than for the groups outlined above, testing for bacteriuria should generally be avoided in patients who do not have specific features suggesting urinary tract infection. The following groups deserve specific mention as they may cause particular concern and useful evidence is available to guide practice.

Older people

Asymptomatic bacteriuria is common in, but not confined to, older people. Asymptomatic bacteriuria is present in about 1% of schoolgirls, rising in frequency with age (to >20% of healthy women aged over 80), and affects about 6-15% of men aged over 75. A prospective cohort study showed that the condition in older people was associated with about double the risk of symptomatic urinary tract infection over two years of follow-up, with similar findings in studies with longer follow-up. Treatment of asymptomatic bacteriuria is not recommended in non-pregnant women of any age because the condition is not associated with adverse long term outcomes and because treatment does not result in durable eradication of bacteriuria or improved clinical outcome. Although fewer data are available for men, asymptomatic bacteriuria seems to be similarly benign in older men. Antimicrobial treatment is associated with increased healthcare costs and avoidable risks, such as the direct adverse effects of antimicrobial agents, disturbance of normal microbial flora leading to mucosal candidiasis and antimicrobial associated diarrhoea, and the promotion of antimicrobial resistance.

Although asymptomatic bacteriuria is associated with urge incontinence in older women, it is not significantly associated with stress incontinence, as described by Mrs A. Thus, although bacteriuria is common in older people, testing for bacteriuria is not recommended in older people who do not have specific clinical evidence of urinary infection. If bacteriuria is detected in patients such as Mrs A, be cautious about accepting it as an explanation for stable stress incontinence or for non-specific symptoms such as tiredness. The clinical decision regarding Mrs A might be more difficult if Mrs A had reported a recent deterioration in stress incontinence as specific studies exploring such a presentation are lacking.

Children

In a prospective community based study bacteriuria was detected in 1.9% of 13 464 schoolgirls and 0.2% of 1595 schoolboys aged (5 to 18 years). There is no evidence that detection and treatment of bacteriuria is of value in infants and children who do not have a clinical presentation that suggests urinary tract infection or systemic sepsis. Moreover, authoritative guidance exists that neither antimicrobial treatment nor follow-up is appropriate in this setting. Therefore it is not appropriate to test children in whom there is no clinical basis for suspecting urinary tract infection. Although most children with urinary tract infection present to primary care with dysuria and frequency it is important also to culture urine in infants and children presenting with fever when no clinical features point to another focus (for example, cough pointing to the respiratory tract).

Women with diabetes

In women of any age, asymptomatic bacteriuria is more common in those with diabetes than in those without. Prospective cohort studies show no difference in outcome, including no difference in the incidence of symptomatic urinary tract infection, between diabetic women with and without asymptomatic bacteriuria at 18 months or at 14 years’ follow-up. Thus, although asymptomatic bacteriuria is more common in women with diabetes, no evidence supports treatment and therefore testing is not appropriate.

People with longstanding urinary catheterisation

Established bacteriuria is almost universal in this group, and defining urinary tract infection in this group is problematic. Consensus guidelines recommend that testing for bacteriuria and antimicrobial treatment of asymptomatic bacteriuria should generally be avoided in patients with indwelling urinary catheters. Expert opinion suggests that treatment should be limited to those with at least one of the following: fever, new costovertebral angle tenderness, new onset delirium, or rigors.

Mrs A presents a difficult management problem. Although she has longstanding urinary tract symptoms (stress incontinence), her current presenting symptoms do not include any specific, new urinary tract features or a specific feature of infection such as fever. Her and her doctor’s views may also be shaped by the fact that she had previously had courses of antibiotics for bacteriuria. The doctor may be concerned that intercurrent urinary tract infection may account for or contribute to her malaise.

What tests for bacteriuria are available?

Tests that may be considered include urine dipstick analysis and microscopy and culture of urine.

In general terms urine dipstick analysis provides immediate results to help decision making and tests for other parameters (for example, glucose, protein, and haemoglobin), which may help in evaluating whether the patient has other medical conditions such as diabetes or glomerulonephritis. However, it does not give a specific microbiological diagnosis or guide selection of targeted antimicrobial treatment, as laboratory microscopy and culture do.

For Mrs A there is no clear indication for testing a urine sample by any method and no need for immediate results to guide treatment. In general, if a doctor decides to test a urine sample in a situation where there is no urgency and a relatively complex history including multiple previous antimicrobial exposures, there are advantages in using the more definitive laboratory result, which will include antimicrobial susceptibility testing if appropriate.

For laboratory tests it is usual to ask patients for a midstream urine sample—on the assumption that the initial urine stream is more likely to be contaminated by bacterial flora from the urethra. However, prospective studies comparing results from mid-stream urine samples with routine urine samples (without reference to timing) show that requesting a urine sample midstream is no better than asking the patient to collect a sample at any stage of micturition.
How to interpret test results

Urine dipstick analysis

Reported positive and negative predictive values of dipstick testing vary considerably between studies, partly owing to differences in the pretest probability in the populations studied. These studies evaluate the performance of dipsticks in patients with symptoms clearly suggestive of urinary tract infection. For example, a recent prospective multicentre study in primary care (including 427 adult female patients from 67 practices with symptoms suggestive of urinary tract infection) found that a positive test result for either nitrite (indicative of bacteriuria) or leucocyte esterase (indicative of pyuria) was associated with an increased probability of urinary tract infection compared with pretest probability. A positive test result both for nitrite and for either leucocyte esterase or red cells had a positive predictive value of 92%, and a negative test for all three parameters had a negative predictive value of 73%. However, the relevance of this study to Mrs A is uncertain. An observational cohort study evaluated 200 patients older than 65 presenting to an emergency department. In one cohort (referred to as asymptomatic) of 100 patients, the patients were afebrile and presented with complaints such as minor trauma or chest pain, so infection was in no way a consideration. The second cohort (referred to as symptomatic) presented with acute confusion, weakness, or fever but without symptoms specifically pointing to urinary tract or other specific source of infection. The findings suggested that test results for nitrite and leucocyte esterase correlate poorly with urine culture results in both groups and are therefore of limited value for patients such as Mrs A.

Laboratory microscopy and culture of urine

A laboratory report of pyuria indicates inflammation of the urinary tract. Some laboratories may perform initial microscopy on all samples and not proceed to culture on most urine samples in which pyuria and/or bacteriuria is not observed on microscopy. This practice helps to manage workload. Evidence from a systematic review indicates that absence of pyuria and bacteriuria on microscopy effectively excludes infection, at least in children. Semiquantitative urine culture to determine the species of bacteria present, estimate their approximate numbers, and perform susceptibility testing if appropriate remains a standard method of evaluation for urinary tract infection.

Problems of testing and treatment

In clinical practice it can be difficult to decide whether to test for and treat bacteriuria in an individual patient with non-specific symptoms. Difficulties may be compounded, as with Mrs A, by a background of stress incontinence, which may tend to focus attention on the urinary tract even though the available evidence does not suggest an association between this symptom and urinary tract infection. If testing and a trial of treatment of bacteriuria are considered in a non-pregnant patient with symptoms that are not clearly related to urinary tract infection, we suggest that laboratory microscopy and culture are the most likely tests to be useful. If bacteriuria is present it may be appropriate—particularly in women—to determine with a repeat culture whether bacteriuria is persistent. If a decision to treat it is made it is appropriate to use the results of the culture and susceptibility tests wherever possible to guide the selection of a safe and narrow spectrum agent (such as nitrofurantoin or trimethoprim). It is then important to explain the uncertainty of benefit to the patient and critically assess the clinical and microbiological response to treatment. Our experience is that once a patient with bacteriuria has an established conviction that they live with repeated or chronic urinary tract infection it can be difficult to persuade them otherwise. This can distract the patient and doctor from dealing with other important concerns and tends to result in repeated courses of antimicrobial agents or prolonged prophylactic antimicrobial treatment, as well as perhaps resulting in unnecessary specialist referral and investigation.

Outcome

Culture of Mrs A’s urine as requested by your locum showed ≥100 000 colony forming units per millilitre of Escherichia coli resistant to ampicillin, cefuroxime, co-amoxiclav, trimethoprim, and ciprofloxacin but susceptible to nitrofurantoin. On review, Mrs A’s tiredness and malaise have improved. You explained that the urine sample contained bacteria but that bacteria can be found in the urine of about one in every five women of her age and that this is not a problem for most people. You explained that antibiotics often fail to eradicate the unwanted bacteria in the urine but that they can kill “good” bacteria and so can cause thrush (candida) and diarrhoea. You advised that you would like to hold off the antibiotics while checking out her problem with leaking urine. Mrs A agreed to this plan.

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Patient consent not required (patient anonymised, dead, or hypothetical).
A mother presents with her 12 month old son requesting testing for an egg allergy before the measles, mumps, and rubella (MMR) vaccination; his older sister has a severe egg allergy.

What you should cover

Understanding of allergy can vary notably between patients and healthcare professionals. Explore the mother’s concerns surrounding MMR vaccination, focusing on egg allergy in particular.

Egg allergy usually presents with rapid onset of angioedema, urticaria, or gastrointestinal symptoms. Most reactions are mild with no evidence of respiratory or cardiovascular involvement. Severe reactions can involve the upper airways (for example, hoarse cry, change in voice, stridor) or lower airways (cough, wheeze, breathlessness); pallor and floppiness can also occur.

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A mother presents with her 12 month old son requesting testing for an egg allergy before the measles, mumps, and rubella (MMR) vaccination; his older sister has a severe egg allergy.
What you should do

Discuss the likelihood of a food allergy. Differentiate between intolerance (non-immunological reaction) and allergy (IgE-mediated in most cases). Explain that allergic reactions involve the immune system and can be triggered by exposure to even small amounts of egg or products that contain egg. Explain that screening for an egg allergy without suspected previous clinical reaction is unhelpful because false positives are common. In particular, if egg or products that contain egg (except baked eggs—for example, in cakes) are tolerated there is no indication for allergy testing (see box). If there is a clinical suspicion of an egg allergy, request a test for egg-specific IgE or refer for a specialist assessment.

Explain the risks of measles, mumps, and rubella to the child’s mother. Although these diseases are usually mild, delaying or withholding the vaccination puts the child at risk of potentially serious illness.

Discuss the MMR vaccine and reassure the mother that risks, even in children with severe egg allergy, are very low. Ensure that other fears about the MMR vaccination, such as the unfounded bad publicity about MMR and autism, are discussed. Although the vaccine is cultured in fibroblasts derived from chick embryos, the amount of egg protein in the vaccine is negligible and is most unlikely to trigger a reaction. The British Society for Allergy and Clinical Immunology and the National Institute of Allergy and Infectious Diseases recommend that all children with an egg allergy, no matter how severe, should still have their MMR vaccine as per the usual immunisation schedule.1 Appropriate resuscitative facilities should always be available when any vaccinations are given, irrespective of egg allergic status.

Vaccination should be delayed if the child is unwell or severely immunocompromised. Children who have had previous serious reactions to any vaccine should be vaccinated under hospital supervision.

Ensure all concerns are addressed and arrange for the child to receive the MMR vaccination. If egg allergy is confirmed, take a comprehensive assessment for other allergic problems (such as coexistent cow’s milk, nut, or peanut allergy), advise on avoidance measures (dietician input can be invaluable), and issue antihistamines and, if necessary, adrenaline autoinjectors to manage accidental exposure. Refer patients with a history of life-threatening reactions for a specialist assessment.3 Explain that long-term prognosis is good, with spontaneous resolution in most cases.1

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