RATIONAL TESTING

Interpreting asymptomatic bacteriuria

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School. To suggest a topic for this series, please email us at practice@bmj.com.

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 *(a)* 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. Al-Hasan and colleagues documented an age adjusted incidence rate of 55.3 per 100 000 person years for urinary tract infection complicated by bacteraemia.[4]

When there are other specific indications—Testing for bacteriuria is recommended in pregnant women without symptoms suggesting urinary tract infection[5 6] as 2-7% have clinically significant bacteriuria.[5] 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%.[7] Testing urine for infection is also recommended in the investigation of patients presenting with acute renal failure before major urological procedures.[8 9]

LEARNING POINTS

- Asymptomatic bacteriuria refers to bacteria in the urine at levels often regarded as clinically significant (>100 000 colony forming units per millilitre of urine) in patients with no symptoms suggestive of urinary tract infection. It becomes more common with age
- Testing for and treating asymptomatic bacteriuria is of established value in pregnant women as it reduces the risk of pyelonephritis later in pregnancy by about 75%
- Consider testing for bacteriuria in any patient with clinical features pointing to urinary tract infection (haematuria, dysuria, frequency, urge incontinence, or back pain) or to systemic sepsis without an apparent focus
- If children, non-pregnant adults, or people with diabetes or indwelling urinary catheters lack specific symptoms of urinary tract infection or systemic infection, avoid testing them for and treating bacteriuria
- Testing for bacteriuria in patients with stable stress incontinence is not appropriate as bacteriuria is not associated with stress incontinence in older people
- If you feel obliged to try treating bacteriuria in a patient with non-specific or equivocal symptoms, urine culture can guide selection of the safest and most narrow spectrum agent possible; ensure careful assessment of clinical and microbiological response

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

Features	Likelihood ratio	
	Little et al*[2]	Giesen et al†[3]
Increase in likelihood		
Haematuria	1.72	2
Dysuria	1.3	1.5
Nocturia	1.3	Not reported
Urgency	1.22	Not reported
Frequency	1.10	1.8
Back pain	Not reported	1.6
Costoveterbral angle tenderness	Not reported	1.7
Decrease in likelihood		
Vaginal discharge	0.65	0.3
Vaginal irritation	Not reported	0.2
Vaginal discharge on examination	Not reported	0.7
Absence of dysuria	Not reported	0.5
Absence of back pain	Not reported	0.8

*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.[5] 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.[5 10] 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.[5 9] Although fewer data are available for men, asymptomatic bacteriuria seems to be similarly benign in older men.[5] 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.[11 12]

Although asymptomatic bacteriuria is associated with urge incontinence in older women, it is not significantly associated with stress incontinence, as described by Mrs A.[13] 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).[14] 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.[15] 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).[15]

Women with diabetes

In women of any age, asymptomatic bacteriuria is more common in those with diabetes than in those without.[5 16] 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.[5 14] 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.[17] 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.[18 19]

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 mid-stream 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.[20 21]

GLOSSARY

Bacteriuria

Bacteriuria describes the presence of bacteria in urine. Bacteriuria may result from the presence of bacteria in the urine in the bladder or from contamination of urine during micturition through contact with the normal bacterial flora of the urethra, vagina, or perineum.

Clinically significant bacteriuria

The term clinically significant bacteriuria is used to differentiate laboratory evidence of bacteriuria in the bladder from bacteriuria that probably results from contamination during micturition. Clinically significant bacteriuria is generally accepted as detection of more than 100 000 colony forming units of a single type of bacterium per millilitre of urine. Contamination with normal flora typically results in lower numbers of bacteria per millilitre and/or mixed bacterial species.[5] However, the criterion of more than 100 000 colony forming units per millilitre of urine has limitations, in that numbers as low as 1000 colony forming units per millilitre may be clinically significant in patients with symptoms of urinary tract infection.[2 9]

Asymptomatic bacteriuria

Asymptomatic bacteriuria refers to clinically significant bacteriuria in those without symptoms that point to a urinary tract infection. The term asymptomatic may be unhelpful as it may be taken literally (the patient is without symptoms of any kind).

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.[22 23] 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%.[23]

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.[24] 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 the 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.[25] 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).

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Previous articles in this series

- Postural hypotension (*BMJ* 2011;342:d3128)
- Investigation of diarrhoea in a traveller just returned from India (*BMJ* 2011;342:d2978)
- Investigation of an incidental finding of eosinophilia (*BMJ* 2011;342:d2670)
- Diarrhoea after broad spectrum antimicrobials (*BMJ* 2011;342:d3798)

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10-MINUTE CONSULTATION

Measles, mumps, and rubella vaccination in a child with suspected egg allergy

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This is part of a series of occasional articles on common problems in primary care. The *BMJ* welcomes contributions from GPs.

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.[1 2] Dislike of or refusal to eat eggs do not necessarily indicate an allergy, but may do so.

Ask about previous investigations for food allergy, including any tests done by complimentary or alternative medicine practitioners.

Egg allergy is common in infancy with a prevalence of 1-2% in children aged 2.5 years.[1] The risk is increased in those with a family history of food allergy, although not necessarily to the same food. Ask about other conditions such as eczema or viral induced wheeze, which increase the possibility of an egg allergy.[2]

Ask about any other vaccinations that the child has had and whether any problems occurred. Previous severe reaction to vaccination is a predictor of future reactions but is usually caused by vaccine constituents other than egg, such as gelatine or neomycin.[3]

USEFUL READING

For patients

NHS choices. MMR (www.nhs.uk/Conditions/MMR/Pages/Introduction.aspx)

Allergy UK. Information about allergies for patients (www.allergyuk.org)

For healthcare professionals

Department of Health. Green book: immunisation against infectious disease (www.dh.gov.uk/greenbook)

Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-sponsored expert panel report. *J Allergy Clin Immunol* 2010;126:1105-18

EXAMPLES OF RAW OR PARTLY COOKED PRODUCTS THAT CONTAIN EGG

- Ice cream
- Lemon curd
- Mayonnaise
- Pancakes
- Pizza
- Quiche
- Yorkshire pudding

bmj.com Previous articles in this series
- Osgood-Schlatter disease (*BMJ* 2011;343:d4534)
- Otitis media with effusion ("glue ear") (*BMJ* 2011;343:d3770)
- Sexual dysfunction in cardiovascular disease (*BMJ* 2011;343:d4437)
- The watery eye (*BMJ* 2011;343:d4029)

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.[4] Explain that long-term prognosis is good, with spontaneous resolution in most cases.[1]

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4 National Institute for Health and Clinical Excellence. NICE clinical guideline 116: food allergy in children and young people. 2011. www.nice.org.uk/guidence/CG116

CORRECTIONS AND CLARIFICATIONS

Diagnosis and management of premenstrual disorders
In the "Psychotropic drugs" section of this clinical review by Shaughn O'Brien and colleagues (*BMJ* 2011;342:d2994, print publication 11 June, pp 1297-1303) the authors state that selective serotonin reuptake inhibitors have not been shown to be teratogenic. This is wrong; they have been. The reference quoted in support of the authors' erroneous statement actually reads: "Paroxetine has been associated with significant risks of major malformation, particularly cardiac defects, when used during pregnancy."

We should publish the cost of each piece of research
We introduced a couple of errors when editing this recent Personal View by Penny Hawe (*BMJ* 2011;342:d4026, print publication 2 July, p 45). The final sentence in the fourth paragraph should end, "…this allows the perpetuation of myths about what an appropriate allocation for research is" [not "what an appropriate allocation for evaluation of research is"]. And the first sentence in the final paragraph should start, "It's just my guess that 10% of the total funds for a programme or policy reserved for evaluation [not "reserved to evaluate research"] is not enough."

Obituary: John Harold Wallis
In this obituary by Michael Wallis (*BMJ* 2011;342:d3876, print publication 25 June, p 1422) we should have said that John Harold Wallis was in partnership for 33 years, not three years as published. We apologise for this error, which we did not pick up when the obituary was retyped for processing.

Use of medical titles by non-doctors can mislead patients
We failed to send a proof to the authors for this Personal View (*BMJ* 2011;343:d4241, print publication, 23 July, p 209) and did not inform the authors of our policy that such articles shoud have only one author or of the changes to authorship that we made. Tahwinder Upile, who was originally acknowledged at the end of the article, meets the criteria for authorship in addition to Waseem Jerjes, and both should be listed as authors. The version on bmj.com has been corrected to reflect this.

The management of tennis elbow
Figure 1 in this clinical review by John Orchard and Alex Kountouris (*BMJ* 2011;342:d2687, print publication 28 May, pp 1199-202) shows the right forearm bones and muscles, not the left, as stated in the legend.

Norway's new principles for primary prevention of cardiovascular disease: age differentiated risk thresholds
A problem during the initial processing of this article resulted in the deletion of the first digit in each item of a bulleted list, leading to an overenthusiastic interpretation of Norway's recommendations for preventive drug treatment in this article by Ole Frithjof Norheim and colleagues (*BMJ* 2011;343:d3626, print publication 16 July, pp 132-5). The correct age groups for drug treatment are:
40-49 years: if 10 year risk of cardiovascular death is ≥1%
50-59 years: if 10 year risk of cardiovascular death is ≥5%
60-69 years: if 10 year risk of cardiovascular death is ≥10%.