A study of microscopical and chemical tests for the rapid diagnosis of urinary tract infections in general practice

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SUMMARY. Aids to the rapid diagnosis of urinary tract infection were assessed by the examination of 325 consecutive urine samples taken in the normal course of work in a general practice. Of these samples 103 produced a pure growth of at least 10^5 organisms per ml. The appearance and smell of each sample was noted and it was then tested by simple low-power microscopy of a drop of urine and by a dipstick which measured leucocyte esterase and nitrite, together with protein, blood and pH. In addition, pus cell counts per mm^3 were performed on 272 of the samples using a cytometer chamber. This method is too time-consuming for routine use in the surgery. Neither a cloudy appearance nor haematuria were sufficiently specific to be of much use in the diagnosis of urinary tract infection. In the prediction of a 'positive' culture the sensitivity and specificity of the other tests were as follows: drop method microscopy 95% and 76%, respectively; cytometer count 95% and 81%; leucocyte-esterase estimation 89% and 68%; and nitrite 57% and 96%. These figures may underestimate the true values of the tests in the diagnosis of urinary tract infection because infection may be present in some cases producing growths of less than 10^5 organisms per ml. It is concluded that the most useful aid to the diagnosis of urinary tract infection is low-power microscopy of a drop of urine.

Introduction

THE rapid diagnosis or exclusion of urinary tract infection is valuable both to the general practitioner and to the hospital physician. Several aids to the diagnosis of urinary tract infection are available. This study was designed to determine the most useful method for general practice. Two different methods of microscopy were examined and compared with chemical tests for leucocyte-esterase as a measure of pyuria and for nitrite as a measure of bacteriuria. The diagnostic value of the appearance and smell of the urine and of tests for haematuria, proteinuria and urine pH were also examined.

Method

During the 15 month period January 1988 to March 1989 all patients in one rural practice with relevant symptoms were requested to provide a urine sample, preferably a mid-stream specimen, in a universal container. The urine samples were examined by microscopy and dipstick chemistry and the results compared with those obtained by microscopy and culture in the microbiology laboratory at Scarborough General Hospital. The appearance and smell of the samples were noted before testing.

Testing techniques in the practice

Drop method microscopy. A drop of urine was transferred to a slide and examined without a cover slip. The number of leucocytes per low-power field were counted using a Beck microscope with an x6 eyepiece (total magnification x75; diameter of field 2.1 mm). The upper limit of normal is 18 leucocytes per low-power field with this level of magnification.

Cytometer count. The number of leucocytes per mm^3 was counted using the same magnification and a modified Fuchs-Rosenthal haemocytometer (square size 0.06 mm^2, depth 0.2 mm). This procedure is time-consuming and could only be carried out for 85% of the samples. The upper limit of normal is 20 leucocytes per mm^3.

Dipstick tests. The stick used was the Nephur-test plus leuco (Mannheim Boehringer). This stick detects nitrite by the Greiss test and pyuria by leucocyte-esterase estimation (leucotest). Positive leucotests are graded one to three. In addition the stick measures pH and detects glucose, protein and blood in the urine. The nitrite test was read after 60 seconds and the other tests after 120 seconds.

Hospital tests

Transfer of samples to the hospital takes at least two hours. Specimens not reaching the laboratory on the day of collection were preserved in boric acid. In the laboratory the urine was examined by the inverted microscope technique which gives a count of the number of leucocytes per high-power field. The upper limit of normal is four leucocytes per field. Bacterial culture was performed by standard techniques. Colony counts of less than 10^5 per ml were not reported.

Results

Of the total of 325 consecutive urine samples examined, 103 gave a pure growth of 10^5 or more organisms per ml ('culture positive' samples). A further 16 samples produced a heavy mixed growth. These samples were repeated and the original results excluded from the study. The remaining 206 samples were reported as having no significant growth ('culture negative' samples). The main organisms grown from the culture positive cases were *Escherichia coli* (72%), *Proteus mirabilis* (9%), *Streptococcus spp.* (7%) and *Staphylococcus spp.* (5%.)

The clinical indications for taking the samples are shown in Table 1 together with the number in each group that were culture positive. The results for patients with frequency and dysuria and with clinical pyelitis were as expected. The number of positive results from patients in other categories demonstrates the value of urinalysis in such cases. Post-treatment samples were usually taken on the seventh day of treatment. The presence of an antibiotic makes the culture result difficult to interpret. For this reason post-treatment samples and those from patients on prophylactic antibiotic treatment were excluded from the assessment of the diagnostic tests. Since pregnancy itself is a known cause

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Table 1. The clinical indications for testing urine samples and the number with positive bacterial culture.

Clinical indication[a]	Number of samples	Number (%) with positive culture[b]
Frequency and dysuria[c]	67	51 (*76*)
Clinical pyelitis	11	10 (*91*)
Other urinary symptoms	42	5 (*12*)
Past history of UTI	34	10 (*29*)
Abdominal or back pain	65	10 (*15*)
Systemic illness	38	12 (*32*)
Pregnancy screen[d]	15	0 (*0*)
Post-antibiotic treatment	27	1 (*4*)
Receiving prophylactic antibiotics	17	2 (*12*)
Others	9	2 (*22*)
Total	325	103 (*32*)

UTI = urinary tract infection. [a]Samples from patients with more than one indication are listed according to their most important symptom. [b]A pure growth of at least 10^5 organisms per ml. [c]Includes only patients with both symptoms. [d]Pregnant patients who also had relevant symptoms are listed according to their symptoms.

of pyuria, samples from pregnant patients were excluded from the assessment of those tests which use pyuria as the criterion of infection. In addition, samples with heavy proteinuria or containing boric acid were excluded from the leucotest because they interfere with this test.

Table 2 gives the results of the assessment of the various diagnostic aids studied. The sensitivity and specificity of each test in the prediction of a positive culture are shown together with the predictive values of positive and negative test results. A cloudy appearance was present in 85% of samples which became culture positive (sensitivity of the test = 85%) but only 60% of culture negative samples had a clear appearance (specificity = 60%). Culture was positive in 61% of cloudy samples (predictive value of positive test = 61%) and 86% of clear samples were culture negative (predictive value of negative test = 86%). Thus, although a cloudy appearance detected 85% of all culture positive samples its usefulness was limited by its relatively poor specificity. Strong smell was present too infrequently to be of use on its own. Both types of microscopy had a sensitivity of 95% and a predictive value of a negative test of 96%; the more accurate cytometer cell count had a higher specificity (81%) than the drop method (76%). The leucocyte-esterase test showed 89% sensitivity but only 68% specificity; the nitrite test was highly specific (96%) but had a sensitivity of only 57%. Used together these two tests achieved a sensitivity of 91% but with a specificity of only 66%.

The other chemical tests on the dipstick were less useful. Neither an atypical pH nor the presence of protein had any value in the prediction of a positive culture. Blood was present in 77% of the culture positive samples, but only 55% of samples containing blood were culture positive.

Using four cells per high power field as the upper limit of normal the inverted microscope cell counts performed in the microbiology laboratory achieved a sensitivity of 89% and a specificity of 92% in spite of a variable transit time of samples to the laboratory.

Many of the false positive practice microscopy results were due to samples giving cell counts not far above the upper limits of normal. In practice it is useful to consider such specimens as borderline. By adopting borderline ranges of 19–40 leucocytes per low-power field (includes 15% of all samples) and of 21–30 leucoctyes per mm^3 (10% of samples), the percentages of false positive results are reduced to 14% and 12%, respectively. Similarly, designating leucotest result grade one (10% of samples) as borderline reduces the percentage of false positive results to 30%.

None of the 15 routine pregnancy screening samples were culture positive. Pyuria in these samples was very variable (5–180 leucocytes per mm^3). In seven samples the leucocyte count was more than 20 per mm^3, the upper limit of normal for samples from non-pregnant patients. A further 14 pregnant patients had symptoms of possible urinary tract infection. Samples from two of these were culture positive. Both had pyuria in excess of 20 leucocytes per mm^3. No sample from a pregnant patient without pyuria was culture positive.

For 27 patients samples were taken within 24 hours of completion of a seven-day course of antibiotic treatment. The mean

Table 2. The results of the assessment of tests for urinary tract infections.

Test	Results	No. of samples	No. of samples culture positive	Sensitivity (%)	Specificity (%)	Predictive value of positive test (%)	Predictive value of negative test (%)
Appearance	Clear	96	15	*85*	*60*	*61*	*84*
	Cloudy	141	86				
Smell	None	237	79	*22*	*96*	*76*	*67*
	Strong	29	22				
Microscopy							
Drop method (leucocytes per low-power field)	0–18	111	5	*95*	*76*	*74*	*95*
	>18	126	93				
Cytometer count (leucocytes per mm^3)	0–20	93	4	*95*	*81*	*77*	*96*
	>20	91	70				
Dipstick							
Pyuria (leucotest)	Negative	102	10	*89*	*68*	*66*	*90*
	Positive	127	84				
Nitrite	Negative	202	43	*57*	*96*	*89*	*79*
	Positive	64	57				
Pyuria + nitrite	Both negative	99	8	*91*	*67*	*66*	*92*
	Either or both positive	130	86				
Blood	Negative	126	24	*76*	*62*	*55*	*81*
	Positive	140	77				

Samples from 59 patients having just completed antibiotic treatment or on prophylactic treatment are excluded from all tests, 29 samples from pregnant patients are excluded from tests which assess pyuria and nine samples with heavy proteinuria or containing boric acid are excluded from the leucotest (one sample from a pregnant patient also contained boric acid).

leucocyte count in these samples was 52 per mm^3. In only 10 samples was the leucocyte count within normal limits.

Discussion

The study of tests for urinary tract infection is made difficult by the lack of an absolute standard against which to judge them. Since 1956 colony counts of 10^5 per ml have been considered to indicate infection,[1] but it is now believed lower counts may indicate infection.[2-4] Since, as is commonly the case, the local microbiology laboratory in this study only reports growths of 10^5 per ml or more, this had to be used as the criterion of infection. It is to be expected that the effect of this will have been to produce some apparently false positive tests in cases where infection was present but not reported.

This study suggests that the appearance of the urine is of limited value. Although the urine was cloudy in 85% of culture positive samples only 61% of cloudy urine samples were culture positive. Almost certainly examination of the urine immediately after it is passed is necessary if its appearance is to be useful in diagnosis. The presence of a strong smell was too infrequent to be of much value. Haematuria was even less sensitive to urinary tract infection than was cloudiness and only 55% of samples with haematuria were culture positive; neither proteinuria nor an atypical pH had any diagnostic value.

Simple microscopy of the urine is recommended in textbooks for the diagnosis of urinary tract infection.[4] However, a recent study from Devon and Cornwall found that less than a third of general practices had a microscope;[5] this instrument also appears to be rare on the modern hospital ward. A previous study in general practice,[6] involving a practice technician and centrifuged urine samples, showed the value of urine microscopy. The drop method of low-power microscopy described here is easy to learn and takes less than half a minute to perform — less time than it takes to complete a microbiology request form. In this study the method 'missed' only five cases from 98 culture positive specimens. Four of these five samples were from infants, two of whom had balanitis and a third a rectovesical fistula. The other infant and one adult did have urinary tract infections and both came back the next day with heavy pyuria and were then treated. The results suggest that it is not normally necessary to send to the laboratory specimens without significant pyuria as determined by simple low-power microscopy. However, the specificity of the method and the predictive value of a positive test are not so good at 76% and 74%, respectively. This partly reflects the fact that there are other causes of pyuria than infection and that some bacteria are not detectable by normal culture methods; but there is no doubt that there is a borderline range of pyuria within which the test should be considered equivocal and the specimen should be sent for culture and the patient treated on clinical grounds. About 15% of samples fell within this range in the present study. Using this borderline range reduced the proportion of false positive results to less than 15%. As described above it is probable that some of these represent false negative cultures, rather than false positive pyuria tests.

The cytometer count method of microscopy measures the actual number of pus cells per mm^3 and thus is a more accurate test of pyuria than low-power microscopy of a drop of urine. However, in this study it proved only slightly better than the latter in the diagnosis of urinary tract infection. The method is technically more difficult and takes more time than the drop method and for routine use these disadvantages outweigh any slight advantage in accuracy.

Neither method of microscopy can be used for the positive diagnosis of urinary tract infection in pregnancy or immediately after a course of antibiotic treatment as then pyuria is often present in the absence of infection. However, in this study none of the samples from pregnant patients without pyuria were found to be culture positive. It is doubtful whether it is necessary to culture the urine from such cases.

Reports of the accuracy of the leucocyte-esterase test vary widely.[7-9] In the present study the test had a sensitivity of 89% in the prediction of a positive culture compared with 95% for microscopy. Its specificity (68%) and the predictive value of a positive test (66%) were considerably less than those of microscopy, partly because its lowest positive reading straddles the division between normal and abnormal degrees of pyuria.

The nitrite test depends on the conversion of nitrates into nitrites by bacteria in the bladder. It requires an incubation period of several hours in the bladder and so is best performed using an early morning urine sample. Unfortunately some organisms, especially gram-positive ones, do not convert nitrates into nitrites. Because of this the nitrite test has a poor sensitivity in the diagnosis of urinary tract infection (57% in the present study). However, a high specificity (96%) was found. These results are typical of previous reports.[8-10] Higher sensitivities can be achieved by ensuring bladder incubation for at least four hours in every case.[11] Previous evaluations of the predictive value of combining leucocyte-esterase and nitrite tests have produced conflicting results,[9,11,13] but the present study, using the Nephur-test plus leuco stick, finds these tests to be of value. A positive nitrite test is a strong indication of infection; and infection is unusual with a negative leucotest. Although not as reliable as simple microscopy the combined tests do provide a useful aid to the rapid diagnosis of urinary tract infection for those who do not have access to a microscope; in addition the dipstick can be used by the bedside during home visits.

The results of this study suggest that the most useful aid to the rapid diagnosis or exclusion of urinary tract infection in the general practitioner's surgery is simple low-power microscopy of a drop of urine.

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