Validation of a method for the rapid diagnosis of urinary tract infection suitable for use in general practice

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SUMMARY. A combination of reagent strip testing and examining urine appearance can be used to screen out non-infected cases before urine specimens are sent to the laboratory. A validation of this method was carried out in a microbiology laboratory using 970 specimens received over a three-week period. When the tests for nitrite, blood and protein on N-Multistix reagent strips (Ames) were all negative in a clear urine then the predictive value for the absence of bacteriuria was 98.5%. Positive strip tests in a turbid urine detected 80.1% of infections.

On the basis of these findings it is recommended that general practitioners test the urine samples of all patients with suspected urinary tract infections by this method and only send to the laboratory those specimens with positive findings. Using this method the routine laboratory workload involved in testing urine specimens would be reduced by 40%, instant results would be available in the general practitioner's surgery and the patient would receive immediate and appropriate treatment.

Introduction

THE processing of urine specimens makes up a considerable proportion of the workload of most microbiology laboratories. The cost in terms of the laboratory man hours and finance needed to examine these specimens is high compared with the small percentage of specimens that show a clinically significant bacteriuria, approximately 22% at Taunton Public Health Laboratory. It was decided that a simple inexpensive test procedure was needed that could be carried out as a sideroom test in general practice to select those urine samples that should be sent to the laboratory for further examination. This test would have to predict confidently a high percentage of either positive or negative urine specimens, that is it would have to be both sensitive and selective.

When a patient presents to the general practitioner with a history of urinary tract symptoms the doctor has to decide whether to commence antibiotic therapy. The clinical presentation has been shown to be inaccurate in predicting a bacterial cause of urinary tract infection (unpublished results) and treatment is often started without confirmation by culture on the basis of the symptom history. Other workers have demonstrated that the use of reagent strips with a symptom history screening system at the time of patient attendance can accurately predict the presence of urinary tract infection.[1] We suggest that reagent strip testing is better correlated with urinary tract infections than symptoms and signs.

The presence of nitrite, blood, protein and in some cases leucocyte esterase have been well documented as indicators of urinary tract infection and bacteriuria. All of these tests can be found on commercially available reagent strips. Most reported methods rely on the presence of nitrite, blood or protein in any combination.[2-6] Urine samples should be screened at the initial consultation, so that a decision on treatment can be made on the spot. Accurate performance data must be available so that antibiotic treatment can be confidently withheld after a negative screening test result.

Using a commercially available reagent strip test (N-Multistix SG, Ames) to detect the presence of nitrite, blood and protein, together with the visual appearance of the specimen we have been able to select those specimens meriting further investigation. The validation data presented here should give general practitioners confidence to follow this approach in the surgery.

Method

The Taunton Public Health Laboratory serves a large rural area of 100 miles by 50 miles and specimens are received from general practitioners and 19 hospitals, many specimens reaching the laboratory several hours after collection. Processing takes 24 hours and so the report will reach the sender between 48 and 72 hours after the specimen was taken.

Over a three week period in 1987 1033 mid-stream urine specimens were received by the laboratory. Sixty three samples were excluded from the study either because they were more than 24 hours old and would therefore give unreliable results or were catheter specimens and were therefore likely to be contaminated. Although a small percentage of the specimens were received in plain, sterile universal bottles, most were received in bottles containing 1.8% boric acid which has no effect on the performance of reagent strip tests but inhibits the metabolism of bacteria during transport. All specimens were processed immediately upon receipt at the laboratory.

First, each undiluted, uncentrifuged urine specimen was thoroughly mixed and its visual appearance was recorded as either clear or turbid. Then a calibrated 0.02 ml nichrome wire loop was used to inoculate one half of a cysteine, lactose, electrolyte-deficient plate which was then incubated at 35 °C for 18–24 hours aerobically. A second loopful was examined microscopically for the presence of white cells, erythrocytes, casts and bacteria. Direct sensitivity tests were set up when white cell counts of greater than 50 per mm^3 or bacteria were seen.

The criterion chosen for a clinically significant bacteriuria was a pure or clearly predominant culture of 10^5 organisms per ml of urine or more; 10^4 gram positive organisms per ml or more were considered as significant. Three or more species in similar numbers were regarded as contaminants and a repeat sample

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was requested. Secondary species occurring in counts of 10^4 organisms per ml or less were ignored.

The urine specimen was mixed a second time and an N-Multistix reagent strip was dipped into the sample and read in accordance with the manufacturer's instructions.

Results

Of the 1033 urine samples received nearly two thirds (64.7%) were sent to the laboratory by general practitioners, while the remainder were received from hospitals.

Of the 970 urine specimens examined 191 (19.7%) were shown to have a significant bacteriuria (Table 1). Of the samples with a significant growth 80.1% were both turbid and positive for nitrite, blood or protein. Out of all 970 samples 387 (39.9%) had a clear, visual appearance and negative nitrite, blood and protein results (Table 1). Only six of these samples proved to have a significant bacteriuria (3.1% of those with a significant growth) — five of these specimens were from general practice; three contained 100 or more white blood cells per mm^3 but none contained red blood cells or debris. The remaining 583 specimens examined were positive for one or more of the criteria indicating potential significant bacteriuria, that is they were either turbid or positive for nitrite, blood or protein.

Table 2 shows the level of agreement between detection of significant bacteriuria and nitrite detection and specimen appearance, with a breakdown of the particular organisms isolated. As would be expected from the predominance of specimens from general practice, coliforms proved to be the most common isolate (73.2% of significant growths) followed by proteus species (8.5%), faecal streptococci (5.6%) and staphylococci (5.2%). Only 58.3% of the coliforms proved to be nitrite positive; however, 77.8% of proteus species were positive as would be expected and 21.9% of the staphylococci and streptococci were positive.

The sensitivity, specificity and predictive values are shown in Table 3. The sensitivity increases from 54.5% when using the nitrite test alone through 89.2% for nitrite and appearance together to 96.9% when using nitrite, blood, protein and appearance, whereas the specificity decreases from 99.5% to 48.9%. The predictive value for a negative test increases as more parameters are considered, while the reverse trend is observed for the predictive value for a positive test.

Discussion

With the present problem of constantly increasing laboratory workloads, there is a real need to economize on the time spent performing unnecessary testing. Two-thirds of all urine specimens sent to the laboratory in this study come from general practice and consequently the age and condition of many of these specimens are open to question; only 20% of all the specimens received were subsequently confirmed as being significantly bacteriuric.

This study has shown that using the simple expedients of reagent strip testing and looking at the urine specimen, only 3% of infected specimens may be missed, a failure rate which is no worse than that for most laboratory culture methods. Forty per cent of all specimens were clear and strip negative for nitrite, blood and protein and if these were eliminated by sideroom testing they would represent a major saving in work for the laboratory.

Possible causes of false-negative nitrite results include excessive sample age, insufficient bladder incubation and the presence of non-nitrate-reducing organisms. There are no known causes of false-positive nitrite reactions and the few urine samples with a positive nitrite result but negative culture were probably missed by the culture method used. Ten per cent of the samples were non-infected and strip negative but turbid. This is probably the result of age or the presence of phosphates.

This study has shown that the nitrite test alone will detect over half of random bacteriuric urine samples; the addition of the specimen appearance increased the sensitivity to 89%, although reducing the specificity and using the combination of strip tests for nitrite, blood and protein raised the sensitivity still

Table 1. Comparison of strip results, appearance and culture results.

Appearance/strip result[a]	No. (%) of specimens (n = 970): Significant growth	No. (%) of specimens (n = 970): Non-significant growth	% of samples with significant growth (n = 191)
Clear/negative	6 *(0.6)*	381 *(39.3)*	*3.1*
Clear/positive	23 *(2.4)*	174 *(17.9)*	*12.0*
Turbid/negative	9 *(0.9)*	93 *(9.6)*	*4.7*
Turbid/positive	153 *(15.8)*	131 *(13.5)*	*80.1*

[a] Negative = nitrite, blood and protein all negative; positive = one or more of nitrite, blood or protein positive.

Table 2. Level of agreement between detection of organisms and nitrite detection and specimen appearance.

Culture result (organisms ml^{-1})	Clear: Negative nitrite	Clear: Positive nitrite	Turbid: Negative nitrite	Turbid: Positive nitrite	Total
10^5 coliform	14	6	34	75	129
10^5 faecal streptococcus	1	0	5	4	10
10^5 haemophilus	0	0	1	0	1
10^5 proteus	1	2	3	12	18
10^5 pseudomonas	0	0	0	4	4
10^5 staphylococcus	0	0	7	3	10
10^5 streptococcus	1	0	6	0	7
10^4–10^5 coliform	3	0	6	0	9
10^4–10^5 streptococcus	0	0	1	0	1
MG 10^5 coliform	1	1	2	4	8
MG 10^5 faecal streptococcus	0	0	1	0	1
MG 10^5 pseudomonas	0	0	2	0	2
Non-significant growth	550	1	216	3	770
Total	571	10	284	105	970

Number of specimens appearing: Clear / Turbid.

MG = mixed growth with significant growth of organism indicated. NB: In this table 10^4 – 10^5 coliform is considered significant.

Table 3. Performance of strip tests and appearance in detecting the presence or absence of significant growth.

Test	Sensitivity (%)	Specificity (%)	Predictive value for positive test (%)	Predictive value for negative test (%)
Nitrite alone	*54.5*	*99.5*	*96.7*	*88.8*
Nitrite + appearance	*89.2*	*71.5*	*46.3*	*96.0*
Nitrite, blood, protein + appearance	*96.9*	*48.9*	*31.7*	*98.4*

further to 97%, again at the expense of specificity. The most important feature, however, is the exceedingly high predictive value (98%) when the urine sample is both strip-negative and clear. This means that such a combination can be used with confidence by the general practitioner to predict non-infection and the patient can receive prompt advice.

The cost to the general practitioner of the reagent strip test is approximately 15p; much less than the costs of processing the specimen in the laboratory. The method is therefore cost effective with the advantages that a negative urine sample is rapidly identified, unnecessary drug treatment is avoided and there are consequent cost savings.

Having validated this approach, we recommend that general practitioners adopt this testing procedure and only send specimens that are strip-positive or turbid to the laboratory. The general practitioner would have instant results, the patient would receive immediate and appropriate treatment and the drug bill of the National Health Service would be reduced. We are now recommending such an approach in our district.

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