Clinitek Auto 2000, and Boehringer Mannheim Urotron—may eliminate many of the avoidable errors commonly encountered.

Nevertheless, I believe that this would be impracticable, expensive, and undesirable. Urine analysis fulfils many of the criteria of the ideal laboratory test, being simple to perform, inexpensive, easy to interpret, quick, applicable in many clinical settings, and able to be carried out in a wide variety of situations. The problems that arise with urine analysis generally occur for explicable reasons. These difficulties are common enough to make current standards unsatisfactory. I urge the adoption of the quality control strategies outlined here with a view to generally improving analytical performance. This can only result in better clinical care.

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Is unselective biochemical urine testing cost effective?

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Forty years ago clinical laboratories could analyse very few biochemical constituents in plasma or serum, and urine testing was widely used as an aid to diagnosis. This testing was usually left to nurses and medical students, who often used out of date or even wrongly prepared reagents and dirty test tubes, with misleading results. Indeed, the validity of the results was so doubtful that in 1962 their diagnostic value was compared to that of palmistry.¹

The development of sensitive plasma or serum assays, which can often detect changes associated with mild or very early disease, should have reduced the need for urine testing. At about the same time, however, it became possible to manufacture reagent strips and tablets; single strips were impregnated with several bands of different reagents and it was soon possible to test for several substances simultaneously, making unselective urine testing deceptively easy but not cheap. Single test strips cost between £1.65 and £6.34/100 (table), whereas the price of the popular multireagent strips varies from £3.20 to £12.00/100 (table); in 1984 this hospital spent about £18 000 on reagent strips and tablets. Collection containers and staff time probably cost at least as much again. Similar conclusions have been reached by other authors.^{2,3}

Because a test is relatively expensive does not necessarily mean that it is not cost effective. Cost effectiveness in medicine cannot be quantified accurately but depends on the speed of obtaining results, the interpretation and clinical use made of them, and, above all, their analytical reliability.

The analytical reliability of urine testing should have improved because commercial strips eliminate the need for test tubes and incorporate standardised reagents. Unfortunately, the clear instructions and warnings issued by manufacturers (for example, Miles Laboratories⁴) about storage and use are often ignored, and multi-

reagent strips are especially liable to be used incorrectly.⁵ Strips may be kept on the wards too long after the bottles have been opened, but rarely are they or their users subjected to the quality control procedures now routine in hospital laboratories.

The interpretation and clinical use of results often depends on the philosophy of the investigator. If testing is used to answer a specific clinical question (for example, is hypoalbuminaemia due to gross proteinuria?) the results are likely to be noted, interpreted correctly, and acted on. If, however, testing is used to screen an unselected population for subclinical disease such as diabetes mellitus in the vague hope that something may turn up the results, in my experience, are more likely to be unreliable, ignored, and, if noted, misinterpreted.

Clinical value of urine testing

The possible clinical value of testing urine varies for each biochemical constituent.

GLUCOSE

Glucose can be detected by routine testing at urinary concentrations of about 5 mmol/l. Glycosuria of this degree occurs either in the usually harmless and relatively common condition of renal glycosuria or if the plasma glucose concentration has exceeded about 11 mmol/l at some time since the last urine specimen was passed (usually due to diabetes mellitus). The diagnosis of renal glycosuria requires proof that the renal threshold for glucose is below 11 mmol/l (198 mg/100 ml).

In a severe diabetic plasma glucose concentrations above 11 mmol/l at all times of day cause thirst and constant glycosuria with polyuria; thirst, polyuria, and other symptoms suggest the need to assay plasma glucose. In such severe disease glycosuria is rarely an unexpected finding. In less severe, often asymptomatic cases plasma concentrations may be high enough to cause glycosuria only after eating; the diagnosis may be missed if reliance is put on screening a random urine specimen, which may have been passed long after a meal. In the least severe cases there may be no

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Commercial urine tests for single and multiple constituents

	Cost per 100 (£)*	Glucose	Reducing substances	Ketones	pH	Protein	Blood	Bilirubin	Urobilinogen	SG	Ascorbate
<i>Single constituents</i>											
Clinistix (Ames)	3.10	+									
Diastix (Ames)	2.68	+									
Diabur-test 5000 (MCP)	2.52	+									
Glucose (Camlab)	3.50	+									
Clinitest (Ames)	2.58		+								
Acetest (Ames)	1.65			+							
Ketostix (Ames)	2.82			+							
Ketur Test (BCL)	2.44			+							
Keton (Camlab)	3.50			+							
Albustix (Ames)	3.84					+					
Albun Test (BCL)	3.34					+					
Hemastix (Ames)	6.34						+				
Sangur Test (BCL)	6.32						+				
Ictotest (Ames)	5.43							+			
Urobilistix (Ames)	6.24								+		
<i>Multiple constituents</i>											
Bilugen (BCL)	7.60							+			
Urbi (Camlab)	8.00							+	+		
Protein 2 (Camlab)	3.50				+	+		+	+		
Ketodiastix (Ames)	3.20	+		+							
Keto-Diabur (BCL)	4.32	+		+							
Uristix (Ames)	4.62	+				+					
Glucose 2 (Camlab)	3.50	+									+
Glucose 3 (Camlab)	5.00	+		+							+
BM Test 3 (BCL)	3.86	+			+	+					
Combi 3 (Camlab)	5.00	+			+	+					
BM Test 4† (BCL)	4.52	+			+	+					
Combi 4† (Camlab)	7.50	+			+	+	+				
BM Test 5L (BCL)	6.20	+		+	+	+	+				
Combi 5 (Camlab)	8.00	+		+	+	+	+				+
Hema-Combistix (Ames)	6.34	+		+	+	+	+				
Labstix (Ames)	7.04	+		+	+	+	+				
N-Labstix† (Ames)	7.88	+		+	+	+	+				
Bili-Labstix (Ames)	7.94	+		+	+	+	+	+			
Combi 7† (Camlab)	10.00	+		+	+	+	+				
BM Test 7 (BCL)	7.19	+		+	+	+	+	+	+		+
Multistix SG (Ames)	8.19	+		+	+	+	+	+	+	+	
BM Test 8† (BCL)	8.30	+		+	+	+	+	+	+		+
Combi 9† (Camlab)	12.00	+		+	+	+	+	+	+		+

*Catalogue prices (February 1985).

†Also contains a test for nitrite for microbiological tests.

glycosuria, even after eating, and the negative results obtained may lull the doctor into a false sense of security.

Thus unselective urine testing is a very crude method of screening for diabetes and, especially if performed on random specimens, is likely to have a low yield and miss all but the most severe and often clinically obvious cases. The assay of plasma glucose is the only reliable way of confirming or excluding diabetes mellitus. Such testing is certainly a waste of money unless positive results are acted on; in a study of 182 patients undergoing unselective screening 28 patients had glycosuria but clinicians ignored the finding in a third of these.² Any patient found to have glycosuria must be further investigated.

REDUCING SUBSTANCES

Many urinary metabolites associated with inborn errors of metabolism are reducing substances. It is important to remember that negative results in very ill infants do not exclude such disease since the metabolite may not be excreted at the time of testing; for instance, cases of galactosaemia without galactosuria have been reported.⁶ Unselective screening for reducing substances is not indicated in adults.

KETONES

A case could be made for the unselective screening of the urine of newborn infants for ketones since some inborn errors of metabolism are associated with ketonuria. Results of screening tests with reagent strips should not be relied on to exclude such disease; if suspected, the presence or absence of ketonuria must be confirmed by the laboratory.

Unless associated with obvious symptoms, slight ketonuria in adults is most commonly due to fasting. The finding of ketonuria may suggest the need for a parenteral energy supply in pregnant women who are vomiting or undergoing prolonged labour. The need for testing will be indicated by the clinical picture in the patient with diabetic ketonuria, who is usually very ill. Unselective

screening for ketonuria in adults is unlikely to yield useful clinical information.

PROTEIN AND BLOOD

A weakly positive test for urinary protein in a symptomless woman is often due to contamination of the urine from the perineum. Menstruation must always be excluded as a cause of apparent haematuria and proteinuria. Slight proteinuria is a non-specific finding of no diagnostic importance that may be found in most pyrexial illnesses and in congestive heart failure. Gross proteinuria is rarely an unexpected finding; it may occur in pre-eclampsia or in the nephrotic syndrome, which is often suggested by the clinical picture or the finding of hypoalbuminaemia.

The urine must be examined by microscopy and microbiological methods if urinary infection is suspected; this is much more useful than testing for protein. Microscopy for casts is also more useful in detecting suspected chronic renal disease, but in such cases plasma urea or creatinine assays must always be performed. There is no need to test for obvious blood. Usually, the clinical indications will suggest the need to test for the occult haematuria that may be found in patients with acute glomerulonephritis or with stones.

Screening for haematuria to detect an unsuspected neoplasm of the urinary tract may be justified if care is taken in testing and the results noted. Nevertheless, in the study referred to earlier,² of 182 patients in whom unselective urine testing was carried out, the clinicians ignored the finding of proteinuria in 23 out of 37, and of haematuria in 29 out of 49 patients, possibly because the cause was known to be artefactual (an unclean specimen or contamination with menstrual blood). In most of the remaining cases the diagnosis was already clear. In only two patients (one with proteinuria and one with haematuria) did the information lead to a reassessment of the diagnosis. Although these findings suggest that unselective screening for urinary protein and blood is usually clinically unrewarding, the value might have been greater if more results had been acted on; perhaps even such a small yield is worth the extra cost, although doubt has been expressed about the clinical importance of the unexpected finding of trace proteinuria.⁷

BILIRUBIN AND UROBILINOGEN

Results of plasma assays to detect liver disease are more useful than those of urine testing. Bilirubinuria reflects an increase in the plasma concentration of conjugated bilirubin, and urine testing helps to determine if established jaundice is predominantly due to an increase in this fraction. Plasma transaminase assays detect acute hepatitis at an early stage. Testing for urinary bilirubin in a non-icteric patient is of doubtful value.

Urinary urobilinogen excretion is so variable in normal subjects that it is of no diagnostic value as a test for liver disease. In vivo haemolysis that is so gross as to cause unequivocally high urobilinogen excretion is likely to be suspected on clinical and haematological grounds.

URINARY pH

Urinary pH is very variable in normal subjects. Measurement is indicated, under strictly controlled conditions and with a knowledge of the blood findings, only to diagnose renal tubular acidosis, and in such cases a pH electrode should be used; unselective screening is not indicated.

"SPECIFIC GRAVITY"

The SG strip introduced by Ames in 1981⁸ measures ionic strength and not specific gravity or osmolality. Important unionised urinary constituents such as urea and glucose do not react with the reagent, but if the strip is used under experimental conditions there is usually a good correlation with equally carefully performed specific gravity measurements.⁹

Renal tubular cells can concentrate urine only when vasopressin secretion is stimulated and then only if they are capable of responding to the hormone. Even if the cells are capable of responding the urine will be dilute if vasopressin is not being secreted. Urinary "specific gravity," whether measured to test for renal disease or for diabetes insipidus, can be interpreted only if there is plasma hyperosmolality or gross volume depletion; these are the physiological stimuli for hormone secretion and hence for formation of a concentrated urine. The finding of a dilute urine in a well hydrated patient neither confirms nor excludes renal damage since this is an appropriate response in a normal subject. In the differential diagnosis of dilutional hyponatraemia the finding of an inappropriately concentrated urine despite plasma hypo-osmolality and normovolaemia suggests inappropriate secretion of antidiuretic hormone (vasopressin). Renal concentrating or diluting ability can thus be assessed, preferably by measuring urinary osmolality in the laboratory, only under defined clinical and biochemical conditions; unselective screening is not only useless but the results are very often misinterpreted.

Multireagent strips

Manufacturers have now adjusted the price of multireagent strips so that it is cheaper to perform several tests simultaneously than separately. This is often false economy because testing for a single constituent is even cheaper, and it is unnecessary to screen unselectively for all of them. I have suggested that bedside testing for urinary pH, "specific gravity," and urobilinogen is not of clinical value and that testing for bilirubin is valuable only if jaundice is present; despite this, a pH indicator is included in many strips, the reagent for bilirubin in two, and strips incorporating multiple test reagents—including those for pH, bilirubin, urobilinogen, and "specific gravity"—are the most commonly used and expensive. Buying such strips is almost certainly a waste of money.

Unselective screening for glucose on a postprandial specimen of urine, and perhaps for protein and blood, might be considered to be of clinical value; if so, it is cheaper to use Hemacombistix (Ames) than to test for each of these constituents individually. Nevertheless, the evidence that many apparently positive results are ignored

should lead to careful consideration of the value of even such limited unselective screening.

Quality assurance

Urine testing must be subjected to quality assurance procedures as stringent as those for any laboratory test. Incorrect results may be more dangerous than none. If a test is clinically indicated it is important that the answer is correct. To ensure this, five recommendations must be adhered to. Firstly, strips and tablets must be stored as directed by the manufacturers and discarded by the expiry date. Secondly, preferably regular checks should be made by the laboratory, using standard solutions on sample strips from wards and clinics, to ensure that they are likely to yield valid results if used correctly, and that outdated and wrongly stored batches are discarded. Thirdly, the risk of contamination from the perineum and by menstrual blood in women should be minimised by careful collection procedures. Fourthly, only freshly passed urine specimens should be tested. Finally, the instructions for use, including careful timing of the readings, must be followed to minimise the chance of false positive and negative results. The operator should occasionally test a quality control specimen, preferably one that is indistinguishable to the naked eye from a patient's specimen.

Conclusion

Carefully performed, selective biochemical urine testing that aims to answer specific clinical questions can be useful and cost effective. Unselective testing is a waste of resources and, as often practised, frequently yields misleading results that are ignored or misinterpreted.

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What treatment is advised for a man in his 60s with dermatomyositis?

This patient may well have an underlying malignancy, and this should be looked for and treated if found. Sometimes the dermatomyositis will then improve. Otherwise systemic steroids remain the first line of treatment, but those which may themselves cause myopathy, such as triamcinolone, are best avoided. Bed rest is important during the active phases of the disease. Starting doses of prednisolone will vary from 50 to 100 mg a day and should be determined by the severity of the muscle disease, the most serious component of the condition, and not by the activity of the skin eruption, which often responds poorly. Similarly, the speed with which dosage drops to maintenance levels will depend on clinical assessments of muscle strength and serial estimations of serum muscle enzyme activities such as creatine phosphokinase. Maintenance treatment, often within the range of 5 to 15 mg prednisolone a day, may be needed long term. If after a few weeks the response has been poor add azathioprine or methotrexate to the regimen. The skin lesions may respond incompletely to the systemic treatment and poorly to topical corticosteroids. Sunscreens, the avoidance of sunlight, and emollients may be of limited value, but some degree of residual skin disease may have to be accepted.—J A SAVIN, consultant dermatologist, Edinburgh.