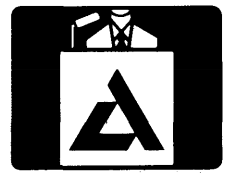
Policy Statement



On Materials for Testing Glucose in the Urine

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Semiquantitative methods for measurement of glucose in the urine are useful for monitoring glucose homeostasis in subjects with diabetes mellitus where quantitative blood and urine glucose measurements are not available. The use of a "plus" scale for glucose measurement is confusing because the same plus values are assigned to different quantities of glucose with different methods. The two-drop Clinitest method is the most quantifiable and readable test for urine sugar, particularly if there is high sugar spill. Therefore, it is the most useful method for monitoring insulin-dependent juvenile diabetes. Its major disadvantages are its potential toxicity, the cumbersome methodology, the cost, and the possibility of interference from other reducing substances. The enzyme "dipstick" methods are most sensitive for detecting the presence of glucose. Among the available "dipstick" methods, Diastix is the most quantifiable and readable. These methods are inhibited by the presence of ketones and a number of other substances. Tes-Tape is the least expensive and, where there are inhibiting substances, the most useful, because it can be read at the liquid front where the glucose reaction is chromatographically separated. Clinistix and Chemstrip are essentially screening methods for the presence of glucose and not useful for quantification. Basing therapy on these and other plus values is irrational and should be discontinued. DIABETES CARE *1*: 64–67, JANUARY–FEBRUARY, 1978.

Urine glucose testing materials are the major tool for monitoring the day-to-day management of diabetes. However, both patients and health care professionals are frequently unaware of the marked variations in different testing materials, in their accuracy and effectiveness. The following report primarily applies to the home methods for urine testing. However, since these are often used within the hospital or clinic setting, at the bedside, or in the laboratory, not only the home testing materials but the commonly used laboratory methods are evaluated. Health care professionals must understand the meaning of various urine-glucose test results if they are to use them in planning the management of the diabetic patient.

PROBLEMS WITH THE "PLUS" SYSTEM:

The common terminology used for urine-glucose test results is a plus system, running from 0 to 4+. However, these "plus" values have been assigned to different concentrations of glucose in the three commonly used home testing methods and some commonly used laboratory methods (table 1). Unfortunately, it is customary in many institutions to base insulin dosage on these pluses without indicating which system is being used. This practice is clearly irrational and detrimental to the achievement of reasonable glucose control. Crude urine tests are not quantitative and, therefore, not appropriate to use in the hospital, where more accurate methods of blood and urine glucose measurement are available.[1–3] There is, however, a role for urine testing when more quantitative methods are not available. Since the values of the "plus" scale vary with different methods, "per cent" glucose spill is a more meaningful method of reporting urine tests. The manufacturers of urine-testing materials are being urged by the American Diabetes Association through the Committee on Materials and Therapeutic Agents to abolish the "plus" terminology and use the "per cent" terminology with a clear indication of the maximum reading (i.e. x per cent *or more*).

QUANTIFIABILITY

A number of studies have been done on the three commonly used home urine-glucose testing methods, Tes-Tape, Diastix, and Clinitest, to see which is more accurate in differentiating the quantity of glucose spilled. Even when the five-drop method is used for Clinitest, studies indicate that it is more quantifiable than the "dipstick" methods.[3–9] Since the "dipstick" methods and five-drop Clinitest have a range only up to 2 per cent, they are obviously less useful than the two-drop Clinitest in quantitating the rather high glucose spill commonly seen in juvenile diabetes mellitus. Therefore, if semiquantitative readings are to be made, two-drop Clinitest is the method of choice.[6–7,9–11]

The Ames multiple-test sticks currently use the Diastix reagent for their sugar reading. Other multiple-test strips are less quantifiable, but Chemstrip is changing their method.

READABILITY

A number of authors point to the difficulty in differentiating within the very narrow range for 1+ to 3+, especially for Tes-Tape, where it is only between 1/10 per cent and ½ per cent.[3,4,6] There is also real difficulty at times in differentiating 3+ from 4+ on Tes-Tape, although this represents a larger difference in amount of sugar.[6,7,12] With both Diastix and the five-drop Clinitest, there has been frequent difficulty in differentiating between 1 and 2 per cent.[4–7,12,13]

FALSE READINGS

When quantitative measurements were compared to the various home methods of testing, both Diastix and Tes-Tape were found to measure too low in the high range and shared a particularly dangerous tendency to be inhibited by the presence of ketones. These deficiencies were seen in as many as 79 per cent of instances with Tes-Tape and 60 per cent with Diastix. Such low readings were seen with only 4 per cent of the five-drop Clinitest. However, Clinitest was shown to measure too low in the low range in 25 per cent of the readings.[4,6] The "pass-through" phenomenon in which the maximal glucose will pass through its color reading and wind up looking falsely low is commonly seen in the five-drop Clinitest, but in the two-drop Clinitest only when glucose was well over 10 per cent.[5,6,10] If there is a question of very high readings, patients can be taught to do one-drop Clinitest and double the percentage read from the two-drop chart to differentiate sugar spills over 5 per cent.[11]

INHIBITION

The "dipstick" methods using glucose oxidase are inhibited by various substances besides ketones, including serotonin, 5-hydroxy-tryptophan, 5-hydroxy-indole acetic acid, and L-dopa, as well as high-dosage salicylates and vitamin C. Proper use of Tes-Tape will allow a correct reading at the liquid front after removal from the urine because the inhibitor is chromatographically separated from the glucose reaction.[14]

INTERFERENCE

False-positives can occur with the enzymatic glucose oxidase methods from peroxide detergents in the vessel used to catch the urine. Clinitest is a copper-reduction method and so is affected by reducing substances such as other sugars; salicylates in large doses, including PAS; high-dose antibiotics, such as penicillin, cephalosporins, streptomycin, isoniazid, and nalidixic acid; barbiturates, chloral hydrate, L-dopa, and probenecid.[14,15]

EASE OF USE

Clinitest is clearly more difficult to use, requiring droppers, tablets, test tubes, and the collection of the urine in a cup. However, it has been our experience that some children find Clinitest "more fun." An advantage is that timing is not as critical unless there is a "pass-through" phenomenon. However, the most accurate reading is at 15 seconds after color change. The enzymatic "dipstick" methods are much easier to use. These do require rather critical timing, which patients may ignore.[13]

TOXICITY

Another disadvantage of the Clinitest is the corrosive toxicity of the tablets, particularly if there are small children or disoriented adults in the household.

COST

At the current time the cost varies from 3.5¢ to 7.29¢ per test (table 2). Clinitest entails an additional initial expenditure for the test tube, dropper, and kit.

LABORATORY SCREENING METHODS

Since Ames has changed to Diastix reagent on their multiple-test urinalysis dipsticks, they are more quantitative than the Bio-Dynamics strips. However, this company is planning to change its glucose strip. In a study by Dyerberg et al. comparing Ames Clinistix (formerly the basis for Ames multiple-test sticks) and the Mannheim Boeringer s-Glukotest (distributed in this country as Chemstrip), five different factors were studied that might present difficulties in interpretation. They studied (1) urine factor, (2) technician factor, (3) environmental factor (location, light, heat), (4) batch factor (13 different batches of material were studied), and (5) time factor (the order in which the tests were done). Variance analysis was significant for different urines and standard amounts of glucose put in different urines ($p < 0.0005$). There was also significant variance in laboratory technicians ($p < 0.0005$). Environment, batch, and time were not sig-

TABLE 1
Relationship of plus system to grams per cent glucose

Glucose grams %:	0	1/20	1/10	1/4	1/2	3/4	1	2	3	5
Clinitest two-drop	Neg			Tr	1/2%		1%	2%	3%	5%
Clinitest five-drop	Neg			Tr	+	++	+++	++++		
Diastix*	Neg		Tr	+	++		+++	++++		
Tes-Tape	Neg		+	++	+++			++++		
Benedict's	Neg			+			++		+++	++++
Chemstrip	Neg	+		++			+++			
Clinistix	Neg		Small	Medium		Large				

* Diastix is now incorporated into all Ames multiple-test sticks.

TABLE 2
Cost of urine-testing methods
(Based on manufacturer's recommended retail price in September, 1977)

Trade name	Cost per test (cents)
Clinitest*	7.29
Clinistix	4.60
Diastix	4.36
Tes-Tape	3.55
Ketodiastix	8.72
Ketostix	6.88
Acetest	5.94

* Plus initial $1.92 investment for kit.

nificant factors. Both of these methods are primarily for qualitative rather than quantitative measurements of glucose for urine-screening tests in hospital and clinic laboratories. The findings of the study were that in 169 testings Clinistix had 24 doubtful cases, four false positives, and seven false negatives, whereas these were not problems with the Chemstrip method. These authors also came to the conclusion that basing therapy on these nonquantitative methods was a dangerous practice.[16]

CONCLUSIONS

1. The "plus" system is confusing and ought to be replaced by percentages for all methods so that people can better understand what they are measuring. The use of "plus" values as a basis for therapy within hospitals is particularly inappropriate and should be abandoned.

2. "Dipstick" methods for home use (e.g., Diastix, Tes-Tape) are mainly useful in stable diabetes, in which sugar spill is rare, to identify the presence of sugar rather than actually attempting to quantitate it. Qualitative "dipstick" methods (e.g., Chemstrip, Clinistix) can be useful for large-scale screening, such as during routine urinalysis in clinics and hospitals, but should not be considered quantitative.

3. The two-drop Clinitest method is the most quantitative and easiest to read, although the most cumbersome and expensive to use. It should be considered the method of choice for labile juvenile diabetes, preferably with instructions to the family concerning urine-volume assessments, so that true amounts of glucose spill can be estimated. The prescriber should warn the family of the toxicity of the tablets.

4. When a "dipstick" method is used for convenience in labile diabetes, Diastix is the more readable and quantifiable. When ketones are present, urines should be checked by Clinitest because of the inhibitory effect of ketones on the glucose oxidase enzyme reaction for urine glucose.

5. When medical inhibitors of the glucose oxidase reactions (e.g., L-dopa or high-dosage aspirin) must be used, proper use of Tes-Tape as a chromatographic record can give a reasonably correct reading.

At the June, 1977, meeting of the American Diabetes Association, the Committee on Materials and Therapeutic Agents made the following three recommendations, which were approved by the Board of Directors:

1. It is recommended that manufacturers of urine-testing devices be encouraged to change those scales using "plus" values to "per cent" readings for quantitating urine glucose, since the "plus" scales indicate different glucose concentrations with different methods.

2. It is recommended that the two-drop Clinitest method of urine testing be indicated as the method of choice in labile juvenile diabetes.

3. It is recommended that "dipstick" methods be considered useful in qualitative assessment in stable diabetes.

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