A Comparison of Urine and Blood Tests in Diabetes Detection

Henry Packer, M.D., Jean M. Hawkes, M.D., and R. F. Ackerman, M.D., Memphis

Both urine and blood testing procedures have been employed in diabetes detection. Knowledge of the sensitivity and specificity of such tests under conditions of random times in relation to food eaten or after specified periods of time after eating is extremely valuable in providing information regarding the yield of new cases of diabetes which may be expected, and the retest load which may be anticipated under various conditions of testing. A number of evaluations of this type have already been made.[1,2,3]

The newer enzyme tests which measure true glucose in urine have proved as sensitive as older tests which measure total reducing substances, and this is achieved without sacrifice of specificity.[4] These enzyme tests afford the simplest and most rapid method ever devised for testing large numbers of urine specimens within a short time. Nevertheless, the sensitivity and the specificity of such tests, as of any test upon urine, are influenced by the renal threshold for glucose, which when low operates to increase the number of false positive tests (renal glycosuria) encountered, or when high operates to reduce the number of true positive tests, in relation to the true number of diabetics tested.

Testing procedures for blood sugar are not subject to the above limitation, but they are not devoid of other problems. Some commonly employed blood sugar tests (Folin-Wu) measure many reducing substances other than glucose normally present in human plasma although tests are available (Somogyi-Nelson) which, for practical purposes, determine "true" glucose only. Both types of blood tests generally entail more technical manipulation and are more time consuming than urine tests, and for this reason have not been as widely used in routine testing for diabetes. Also, since such tests give quantitative results, a predetermined level must be established for screening purposes, and the results in terms of sensitivity and specificity will obviously depend upon the levels chosen. Although ability to control the screening level possesses many advantages, chosen levels which achieve high sensitivity often pose a problem of low specificity, and vice versa. Urine tests generally do not present such a decision problem, since any degree of positivity, other than trace results for certain tests, such as Benedict's, is usually designated as a positive test.

Some of the major objections to the use of blood sugar determinations in diabetes detection have been overcome by a mechanical laboratory apparatus known as the Hewson Clinitron which uses tablet reagents that are dispensed automatically, and requires only a given amount of either finger-tip or venous blood in 5 ml. of water. This instrument can complete as many tests in an hour as are ordinarily performed by a trained laboratory technician in an eight-hour day. Since the initial cost of this instrument is high, it is adapted mainly to mass testing programs. However, a less expensive instrument, the Glover-Edwards Glucose Test Kit, which employs the same tablet reagents, has recently become available* and may be suitable for small scale or office testing if its performance approaches that already demonstrated for the Clinitron. With either of these instruments testing can be performed at predetermined levels of 130 mg., 160 mg., or 180 mg. of "true" glucose, corresponding to the Somogyi-Nelson method. Once the level for performance of the test has been selected, this method renders reports which are either "positive" or "negative." Information is available regarding sensitivity and specificity achieved at each of these levels under specific circumstances, for example, in relation to time when last food was eaten.[5]

The present study was undertaken to compare the "relative sensitivity" and "relative specificity" of finger-tip blood tests using the Clinitron set to test at 130 mg., with four commonly employed urine tests: Benedict's qualitative test, Tes-Tape,† Clinistix,‡ and the Clinitest.‡ Although a testing level of 160 mg., or 180 mg., can be employed with the Clinitron, as indicated above, we have found that the 130 mg. level produces

From the Division of Preventive Medicine and the Division of Medicine, The University of Tennessee College of Medicine, Memphis, Tennessee.

* E. S. Piver and Sons, Wilmington, North Carolina.

†Eli Lilly and Company, Indianapolis, Indiana.

‡Ames Company, Inc., Elkhart, Indiana.

superior results,[6] and have therefore limited this comparison with urine tests to results achieved with the Clinitron operated at this level.

It should be pointed out that our data do not give information regarding "absolute" sensitivity and specificity performance for these tests. This would have required that every person tested, regardless of whether the screening test was "positive" or "negative," be subjected to definitive procedures either to rule out or rule in a diagnosis of diabetes. This would have made available a more accurate denominator of "true" diabetics for determination of sensitivity, and of "true" nondiabetics for determination of specificity. Strictly speaking, even rates calculated in this manner cannot be considered as "absolute," but would depend upon criteria employed for the diagnosis of diabetes. Since our corresponding denominators were based only upon diabetics discovered as a result of having screened positive to any one of the five tests employed, we are using the terms "relative sensitivity" and "relative specificity" to connote this. We consider that within the limitations described certain useful information has been acquired.

MATERIALS AND METHODS

Persons in this study consisted of 3,309 applicants for employment health cards who applied for examination at the City of Memphis Hospitals outpatient department. These persons were referred by employers, employment agencies, or welfare agencies. Approximately 73 per cent were nonwhite, and 87 per cent of the latter were females. Nonwhite females therefore constituted the largest proportion of the group. Approximately 70 per cent of the total group were between the ages of thirty and fifty years. All but nine of the persons included in the study were over thirty years of age. Additional tests for syphilis, tuberculosis, uterine cancer, and glaucoma were also performed upon these persons.

Finger-tip blood (0.1 cc.) for the Clinitron test was drawn from all persons applying for a health card. The method of operation of the Clinitron and the Wilkerson-Heftman method of blood sugar determination which it employs have been fully described in the literature[1] and will not be detailed here. Suffice to say that the solution in which the blood and reagent tablets are placed remains blue when the preselected level (130 mg. in this study) is not exceeded, and turns colorless when this level is exceeded. The result is therefore read as "positive" or "negative." Reagent tablets required for the Clinitron are available commercially* and the cost of the four tablets required for each test is approximately five cents.

A specimen of urine was also obtained from each person examined. This was tested using Benedict's qualitative test, Clinitest, Tes-Tape, and Clinistix. The first two of these measure total reducing substances in urine, while the latter are enzyme tests which are specific for glucose. "Trace" results with Benedict's solution were ignored. This test was considered negative unless yellow, orange, or red precipitate was seen distinctly at the bottom of the tube after cooling and settling (about five minutes after the end of a five-minute period in the boiling water bath). Clinitest readings were made during the process of boiling as well as fifteen seconds after boiling ceased, in accordance with manufacturer's instructions. Results recorded with Tes-Tape and Clinistix also were in accord with the manufacturers' instructions.

Persons showing a positive test with any of the above blood or urine tests were recalled for a modified glucose tolerance test, in which the fasting blood sugar level and the level two hours after the administration of 100 gm. of glucose were determined. The Folin-Wu method was employed since "true" glucose determinations were not available from our hospital laboratory. Persons showing over 140 mg. on the two-hour blood sugar specimen of the modified glucose tolerance test were referred to the Medicine Clinic for definitive evaluation. However, for the purpose of this study, a diagnosis of diabetes was arbitrarily made, as recommended by Moyer and Womack,[7] when the two-hour specimen exceeded 140 mg. on the modified glucose tolerance test. Definitive evaluation, employing criteria recommended by the American Diabetes Association,[8] confirmed this arbitrary decision in all except four cases whose one-hour blood sugar level was not high enough to satisfy these criteria. The fasting blood sugar level was not considered in our arbitrary evaluation procedure but was useful as a check upon other laboratory reports.

ANALYSIS OF RESULTS

Table 1 indicates the distribution of new cases of diabetes found by all of the tests, by age group. Ninety cases of diabetes (2.7 per cent) were found in the 3,309 persons tested. The highest yield (10.4 per cent) were observed in the sixty- to sixty-nine-year age group.

The percentage with newly discovered diabetes found by each test is indicated in table 2. The percentage

* Eli Lilly and Company.

TABLE 1

Distribution of new cases of diabetes by age

Age group	Number tested	New diabetes Number	New diabetes Per cent
Under 30	9	0	0
30-39	1,227	14	1.1
40-49	1,084	26	2.4
50-59	678	24	3.5
60-69	212	22	10.4
70 and over	99	4	4.0
	3,309	90	2.7

found by the Clinitron blood test (2.4 per cent) was twice as high as the highest percentage found by any urine test (1.2 per cent for both Tes-Tape and Clinistix). In this same table, false positive tests are indicated both in relation to the total number of persons tested and to the number who screened positive by each test. Thus, 2.8 per cent of persons tested with the Clinitron blood test screened positive but turned out to be nondiabetic. This represents 52.9 per cent of those screening positive by this method and gives some measure of the retest load which failed to yield new cases of diabetes. Thus, slightly over one half of those screening positive with this test were found to be nondiabetic.

Benedict's test did not achieve a significantly lower retest load (45.5 per cent) of nondiabetics, even though it discovered less than one half as many diabetics (1.1 per cent) as did the Clinitron blood test (2.4 per cent).

Both enzyme tests for urine glucose achieved identical results in per cent new diabetics (1.2 per cent) and per cent false positive of those screening positive (39.4 per cent). Thus, these two tests discovered only half as many new diabetics as did the Clinitron, while the difference in retest load between these tests (39.4 per cent) and that of the Clinitron (52.9 per cent) was not of practical importance in the operation of our program.

TABLE 2

New diabetes and false positive tests in 3,309 persons

	Positive tests	New diabetes Number	New diabetes Per cent	False Positive Number	False Positive Per 100 tested	False Positive Per 100 positive
Clinitron	172	81	2.4	91	2.8	52.9
Benedict's	66	36	1.1	30	0.9	45.5
Tes-Tape	66	40	1.2	26	0.8	39.4
Clinistix	66	40	1.2	26	0.8	39.4
Clinitest	50	34	1.0	16	0.5	32.0

While the lowest discovery percentage of new diabetics of any of the tests was achieved by the Clinitest (1.0 per cent) the retest load (32 per cent) was substantially lower than that for the Clinitron (52.9 per cent).

The term "retest load" as employed above as a measure of specificity refers to the percentage of persons screening positive who were subsequently designated as nondiabetic. Strictly speaking those subsequently designated as diabetic were also subjected to the retesting process and should be included in the "retest load," but the former group appears to us to serve as a more realistic measure of the specificity or lack of specificity of a test.

Table 3 summarizes the relative sensitivity and relative specificity of the tests employed using as a standard of reference the number of new diabetics found by all tests. As noted in the previous data, the Clinitron blood test gave the best performance in relative sensitivity, and the Clinitest urine test, while performing at the lowest relative sensitivity level, gave the highest relative specificity.

TABLE 3

Relative sensitivity and relative specificity percentages for five tests in finding ninety diabetics in 3,309 persons

	Relative Sensitivity per cent	Relative Specificity per cent
Clinitron	90.0	97.2
Benedict's	40.0	99.1
Tes-Tape	44.4	99.2
Clinistix	44.4	99.2
Clinitest	37.8	99.5

Data presented up to this point have been based upon tests performed at random times in relation to eating. Table 4 combines information already presented with reference to per cent of new diabetes and per cent of false positives for each test, with data upon the time the test was performed since last food was eaten. It will be noted that for all of the tests the highest yield of new diabetes occurred when testing was performed between one and two hours after eating. Also, blood specimens examined by the Clinitron method revealed a higher percentage of new diabetes at all time periods in relation to eating than did the other tests. This superiority was most apparent on specimens taken during the period within one hour after eating (3.3 per cent versus 0.9 per cent for the others). The lowest yields of new cases were generally obtained

when testing was done on specimens taken under fasting conditions (including three hours after eating) or less than one hour after eating. The only exception to this was that the per cent of new diabetes found by the Clinitron blood test upon specimens taken within one hour after eating (3.3 per cent) was almost as high as that found between one and two hours after eating (4.0 per cent). Even under fasting conditions the per cent new diabetes found with the Clinitron blood test was as high (1.7 per cent) as the best performance of any of the other tests at any period in relation to eating. The consistently superior performance of the Clinitron blood test in recognizing new diabetes is therefore apparent.

The higher per cent of false positive tests obtained with the Clinitron blood test has already been noted, and is also evident in table 4 at all hourly time periods in relation to eating. However, the difference indicated between the per cent false positive of those screening positive with the Clinitron blood test and similar figures for the other tests was not considered to be of practical importance in our program except possibly for the difference observed between the Clinitron blood test and Clinitest urine test on fasting specimens. Clinitest showed the lowest per cent false positive tests (18.8 per cent of those positive) upon fasting specimens while still comparing favorably with the other tests with respect to the per cent of new diabetes found (0.9 per cent). Under many circumstances the Clinitest urine test would be the test of choice upon fasting specimens, especially where retest load is an important consideration.

DISCUSSION

Among the 3,309 persons in our study, 2.7 per cent were found to have previously unrecognized diabetes. Obviously one cannot generalize from a rate such as this regarding similar rates which might be encountered in other groups, whose characteristics may be different in important respects. The importance of adjusting rates for such factors as age is evident from our observation that persons in the sixty- to sixty-nine-year age group of our study showed a new diabetes rate almost ten times as high as that observed in the thirty- to thirty-nine-year age group. Also, the fact that 73 per cent of our study group were nonwhite and that 87 per cent of the latter group were females undoubtedly influenced our detection rate for new diabetes, since national mortality figures indicate a generally higher mortality rate for diabetes in nonwhites than in whites, and in nonwhite females than in nonwhite males. Another factor which may contribute to the detection rate of unrecognized diabetes in a group is the frequency with which its members undergo general physical examinations, either periodic or during episodes of illness, which may uncover subclinical diabetes. In a mathematical sense, the yield of previously unrecognized diabetes in any group from a detection program is therefore a function of many variables.

We have employed "relative sensitivity" and "relative specificity" rates in comparing the five diabetes detection tests of our study. Such rates have certain limitations, since they are based upon the total number of cases of new diabetes discovered by the simultaneous use of these tests, rather than being based upon the number discovered had it been possible to perform definitive diagnostic tests for diabetes upon all persons tested regardless of the result of the screening test. Nevertheless, these rates have provided us with useful information regarding the relative ability of the five tests under consideration to identify new cases of diabetes, and regarding the relative retesting load required

TABLE 4

Per cent new diabetes and per cent false positives in relation to last meal

	Time since eating							
	Fasting		Under 1 hour		1-2 hours		2-3 hours	
	Per cent new diabetes	Per cent* false positive	Per cent new diabetes	Per cent* false positive	Per cent new diabetes	Per cent* false positive	Per cent new diabetes	Per cent* false positive
Clinitron	1.7	53.7	3.3	57.7	4.0	44.0	2.1	59.5
Benedict's	0.9	23.5	0.9	75.0	1.4	44.4	1.3	47.4
Tes-Tape	0.9	33.3	0.9	50.0	1.7	33.3	1.4	47.6
Clinistix	0.9	30.0	0.9	50.0	1.7	36.8	1.4	47.6
Clinitest	0.9	18.8	0.9	57.1	1.3	25.0	1.1	40.0

*of those screening positive.

to achieve the performance observed for each test.

We have chosen to use as a measure of the retest load the per cent of persons screening positive by the test who were ultimately designated as nondiabetic upon further evaluation by other procedures. This has been considered by us as the "per cent false positive of those screening positive" category and is dependent in part upon the prevalence of diabetes in the population tested. We consider the size of this group to be of critical importance in any detection program for several reasons. The anxiety, as well as the expense incurred by a positive screening test does not generally appear to be compensated for by relief that the disease suspected is actually not present. Even when retesting is performed as part of the screening process at no expense to the patient, a negative final report is often received with mixed feelings. This is a problem inherent in all detection programs, since false positive screening results are an inevitable consequence of efforts to secure a maximum of true positive determinations.

Our comparison of blood and urine tests in diabetes detection revealed that the Clinitron blood test, when employed at the 130 mg. level, showed the highest relative sensitivity (90.0) of the tests under consideration. This rate was over twice as high as that of any of the other tests. While the retest load of false positive tests (52.9 per cent of those screening positive) was somewhat higher for this test than for the other tests, this difference is not of practical importance in our program excepting possibly in comparison to the Clinitest. There can be little question that the Clinitron blood test proved superior to the other tests employed, by virtue of greater relative sensitivity, and a relative specificity that was not markedly inferior to that of the other tests, except for Clinitest. The performance of the Clinitest in this respect is of interest, and under conditions where considerations of retest load may supersede those of enhanced sensitivity, the Clinitest may serve as a very acceptable detection test.

When the performance of the tests under study was examined in relation to time when food was eaten, it was of interest to note that even under fasting conditions the per cent new diabetes found with the Clinitron blood test was as high (1.7 per cent) as the best performance of any of the other tests at any period in relation to eating. The latter includes the period one to two hours after eating, when all tests achieved their best performance in this respect. At all of the hourly time periods in relation to eating, the Clinitron blood test was superior to the other tests in the discovery of new cases of diabetes. Concomitantly, the per cent false positive with the Clinitron blood test was also higher at each of these periods, although the differences observed are not of practical importance in our program except possibly in comparison with the Clinitest urine test on fasting specimens.

It is evident that under the conditions of our study, a blood testing procedure for determining whether or not a level of 130 mg. of glucose was exceeded proved to be the procedure of choice in the detection of previously unrecognized diabetes. Under circumstances where a low retest load upon fasting specimens is desirable, the Clinitest urine test would appear to be the test of choice.

It should be pointed out that in this study all tests were compared at maximum or close to maximum sensitivity. Different results would have been obtained had a level of 180 mg. been employed with the Clinitron.

SUMMARY

1. A comparison was made of the relative sensitivity and specificity of the Clinitron ("true" glucose) blood test, using the 130 mg. level, with four urine tests, Benedict's qualitative test, Tes-Tape, Clinistix, and Clinitest.

2. The Clinitron blood test showed the highest relative sensitivity, uncovering over twice as many new cases of diabetes as any of the urine tests.

3. While the retest load of false positive tests with the Clinitron blood test (53 per cent of those screening positive) was somewhat higher than for the urine tests, this difference was not considered to be of practical importance in our program, except possibly in comparison to the performance of Clinitest.

4. Even under fasting conditions, which are recognized as far from ideal for diabetes detection procedures, the per cent new diabetes found by the Clinitron blood test was equal to the best performance of any of the urine tests at any period in relation to eating.

5. Under the conditions of our study, blood testing at the 130 mg. level proved to be the diabetes detection method of choice when testing is done at random times in relation to eating.

6. Under circumstances where a low retest load upon fasting specimens is desired, the Clinitest urine test appears to be the test of choice.

SUMMARIO IN INTERLINGUA

Un Comparation de Tests de Urina e de Sanguine in le Detection de Diabete

1. Esseva interprendite un studio pro comparar le sensibilitate e le specificitate relative del test sanguinee a Clinitron ("ver" glucosa) al nivello de 130 mg con

illos de quatro tests urinari, i.e., le test qualitative de Benedict, le test a Tes-Tape, le test a Clinistix, e le test a Clinitest.

2. Le test sanguinee a Clinitron monstrava le plus alte sensibilitate relative. Illo detegeva plus que duo vices le numero de nove casos de diabete detegite per ulle del quatro tests de urina.

3. Durante que le requirimento de retestage in consequentia de false positivitate esseva plus alte in le caso del test sanguinee a Clinitron que in le tests de urina (53 pro cento del positivitates initial a Clinitron esseva false), iste differentia non esseva reguardate como un factor de importantia practic in nostre programma, excepte possibilemente in comparation con le comportamento de Clinitest.

4. Mesmo sub conditiones de jejunation (que recognoscitemente non representa un base ideal pro manovras de detection in diabete), le procentage del nove casos de diabete detegite per le test sanguinee a Clinitron esseva equal al melior resultatos obtenite per ulle del quatro tests de urina a non importa qual periodo de tempore in relation al ingestion de alimentos.

5. Sub le conditiones de nostre studio, le test sanguinee al nivello de 130 mg esseva le methodo de election in le detection de diabete quando le momento del test es sin fixe relation temporal al ingestion de alimentos.

6. In situationes in que un basse requirimento de retestage in specimens jejun es desirabile, le test de urina a Clinitest pare esser le test de election.

ACKNOWLEDGMENT

Acknowledgment is expressed to Mr. Robert M. Thorner, of the Chronic Disease Program, and Miss Nina V. Fisher, of the Atlanta Regional Office, United States Public Health Service, Department of Health, Education, and Welfare, for their assistance in the analysis of statistical data.

This project was aided in part by grants received from the Chronic Disease Program and from the Shelby County Tuberculosis and Health Association.

REFERENCES

[1] Diabetes Program Guide: U. S. Department of Health, Education, and Welfare, Chronic Disease Program. Supt. of Documents, Washington, D. C. Public Health Service Publication No. 506 (revised 1960).

[2] Kurlander, A. B., Iskrant, A. P., and Kent, M. C.: Screening tests for diabetes. A study of sensitivity and specificity. Diabetes *3*:213-19, May-June, 1954.

[3] Wilkerson, H. L. C., Cohen, A. S., and Kenadjian, B. G.: Screening for diabetes. Journal of Chronic Diseases *4*:464-76, October, 1955.

[4] Packer, Henry, and Ackerman, R. F.: A comparison of Benedict's and the glucose oxidase tests for the mass detection of diabetes. Diabetes 7:312-15, July-August, 1958.

[5] Haunz, E. A., and Weisberg, Jerry: A multi-interval blood glucose method utilizing the Clinitron. Diabetes *5*:297-302, 1956.

[6] Packer, Henry, Ackerman, R. F., and Hawkes, J. M.: Screening for diabetes with the Clinitron. Public Health Reports *4*:1020-24, November, 1960.

[7] Moyer, J. A., and Womack, C. R.: Glucose tolerance: 1. A comparison of 4 types of diagnostic tests in 103 control subjects and 26 patients with diabetes. Am. J. M. Sc. *219*:161-73, 1950.

[8] Diabetes Guide Book for the Physician. New York, American Diabetes Association. 2nd Edition, page 13.

On Teaching Diabetes

Correlation Clinics

Correlation clinics can be effective aids to medical teaching, but all too frequently these are held without adequate preparation. The clinician may spend two thirds of the hour presenting detailed clinical observations that mean little to the freshman medical student. The basic scientist follows, often simply repeating material that he has presented to the students previously. A correlation clinic given for freshmen in medical school should not be a predigested, capsule version of clinical medicine, even though the medical students are eager to hear a case history and to learn about treatment. They will have plenty of opportunity to do this in later years. Rather a correlation clinic should emphasize the way in which a given patient illustrates a particular aspect of anatomy, biochemistry, physiology, or endocrinology. I believe that to do a really adequate job the person preparing a correlation clinic should spend many hours in preparation, as much as ten to twenty hours for each correlation clinic. The participating clinician should know exactly what is being taught in the basic science departments, and he should seek out clinical material that will emphasize and illuminate the subject matter of the week. All too frequently, however, the most recently appointed instructor or even an intern or resident is asked to select the material, half an hour before the conference begins, and as a consequence the resulting clinic provides little correlation.

By Arnold Lazarow, M.D., in
Teaching and Research in Diabetes,
Charles C Thomas, Springfield,
Illinois, p. 47, 1960.