

Diabetes Screening Using a Quantitative Urine Glucose Method

*John K. Davidson, M.D., Ph.D., David Reuben, M.D.,
James C. Sternberg, Ph.D., and William T. Ryan, M.S., Atlanta*

SUMMARY

Sensitivity and specificity of three methods (random urine glucose (RUG) > 25 mg. per deciliter; positive Clinitest; and random plasma glucose (RPG) > 140, > 120, and > 100 mg. per deciliter) for detecting the unknown diabetic were compared. In 1,952 screenees, RUG of 96.7 per cent was 3 to 25 mg. per deciliter (normoglycosuria), RUG of 2.0 per cent was 26 to 100 mg. per deciliter (moderate hyperglycosuria), and of 1.3 per cent was > 100 mg. per deciliter (marked hyperglycosuria). Twenty-five randomly selected from each of the first two groups and 18 from the third group had a glucose tolerance test (GTT); seven in the third group had fasting plasma glucose tests > 150 mg. per deciliter. GTTs were evaluated by United States Public Health Service (USPHS), Fajans-Conn (F-C), and summation (S) criteria, and tested screenees divided into nondiabetic (ND) and diabetic (DM). NDs with RUG > 25 mg. per deciliter were false positive screens: renal hyperglycosurics (RHG) if GTT urine glucose \geq 80 mg. per deciliter, nonrenal hyperglycosurics (NRHG) if GTT urine glucose \leq 25 mg. per deciliter. The prevalence of DM was 1.24 per cent

(USPHS), 1.37 per cent (F-C), and 1.45 per cent (S). The prevalence of false positives (USPHS) was 2.04 per cent (1.19 per cent RHG and 0.85 per cent NRHG).

In the normoglycosuria group, 100 per cent who had a GTT were true negatives. In the moderate hyperglycosuria group, 16 per cent (USPHS) were true positives, 84 per cent false positives (44 per cent RHG, 40 per cent NRHG). In the marked hyperglycosuria group, 72 per cent (USPHS) were true positives, 28 per cent false positives (24 per cent RHG and 4 per cent NRHG). By Clinitest, 23 per cent of the DMs (USPHS) were false negatives, and 1.8 per cent in the normoglycosuria group were false positives. Nine per cent of the DMs were false negatives by RPG > 140, and 4.5 per cent were false negatives by RPG > 120.

RUG > 25 mg. per deciliter was as sensitive as the GTT in detecting unknown DMs but was less specific. Random normoglycosuric screenees are unlikely to have diabetes; about 40 per cent of random hyperglycosuric screenees have diabetes. *DIABETES* 27:810-16, August, 1978.

Methods commonly used to determine urine glucose are either insensitive and nonspecific (Clinitest) or sensitive and relatively specific but not quantitative (Clinistix, Keto-diaxix, Tes-Tape).^{1,2} It has been recommended that diabetes screening be done using more sensitive and specific plasma glucose measurements, preferably after a glucose load.³ Unfortunately, such methods involve blood collection; thus, they are invasive, expensive, and slow. For this reason, there appears to be an unmet need for a reliable urine screening technique for diabetes, with the method being glucose specific, sensitive, noninvasive, inexpensive, and rapid.

Two specific enzymatic methods—glucose oxidase^{4,6} and hexokinase⁵—have been developed to measure glucose in blood, plasma, and urine. The original glucose oxidase procedure⁴ was colorimetric and measured hydrogen peroxide formation. Since urine contained substances such as ascorbic acid and uric acid that interfered with measurement of glucose by this technique, it was necessary to pretreat urine to remove them. Fine⁴ reported that pretreated urine collected from normal humans contained 1 to 15 mg. glucose per deciliter; subsequently it was shown that pretreatment of urine resulted in loss of a significant amount of glucose.⁵ A two-step enzymatic method using hexokinase to phosphorylate glucose followed by reduction of triphosphopyridine nucleotide by glucose-6-phosphate dehydrogenase⁵ is interference-free and specific except in the presence of high levels of fructose, but it requires a correction factor for

From the Department of Medicine, Emory University School of Medicine and Medical Service, Grady Memorial Hospital, Atlanta, Georgia 30303.

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background ultraviolet absorbance by urine. Measurements by this method suggested a corrected normal urine glucose range of 0 to 20 mg. per deciliter, and an uncorrected upper limit of normal of 30 mg. per deciliter when it was used for screening purposes.⁵

Development of a polarographic glucose analyzer⁶ made it possible to measure glucose in untreated urine since other substances did not interfere with the reaction. This method is known as the oxygen rate method (ORM) of glucose analysis. Kadish and Sternberg,⁷ using this procedure, indicated that glucose levels in untreated normal urines were 3 to 25 mg. per deciliter.

This study was designed to (1) measure glucose levels by the ORM in randomly collected and undiluted urine samples (RUG) in screening a sizeable population for diabetes mellitus, and (2) compare the sensitivity and specificity of the procedure to that of Clinitest, random plasma glucose, and glucose tolerance test methods of detecting unknown diabetes. Known diabetics were excluded.

MATERIALS AND METHODS

1,952 patients not known to have diabetes were screened by measuring the RUG by the ORM glucose analyzer⁶ and the 2 Drop Clinitest method,⁸ in the Grady Memorial Hospital General Adult Clinic between the hours of 8 a.m. and 4 p.m. Age, sex, race, family history of diabetes, height, weight, and ideal body weight (Hamwi formula) were recorded. Time and amount of prior food intake was not recorded. Patient age range was 16 to 76 years, with race and sex distribution of those screened being 61.7 per cent black female, 23.7 per cent black male, 9.4 per cent white female, and 5.2 per cent white male.

Random venous plasma glucose (RPG), on a sample collected at the same time as the urine sample, was measured by the ORM on 89 randomly selected patients with normoglycosuria (3 to 25 mg. per deciliter) and on 62 of 64 patients with hyperglycosuria (urine glucose > 25 mg. per deciliter). All measurements were done less than 45 minutes after sample collection.

RUG levels were plotted as a continuous variable (figure 1) and patients were divided into three groups for further study: (1) random normoglycosuria (3 to 25 mg. per deciliter),⁷ (2) random moderate hyperglycosuria (26 to 100 mg. per deciliter), and (3) random marked hyperglycosuria (> 100 mg. per deciliter). A diagnosis of diabetes was established in seven individuals in the random marked hyperglycosuria group on the basis of three fasting venous plasma

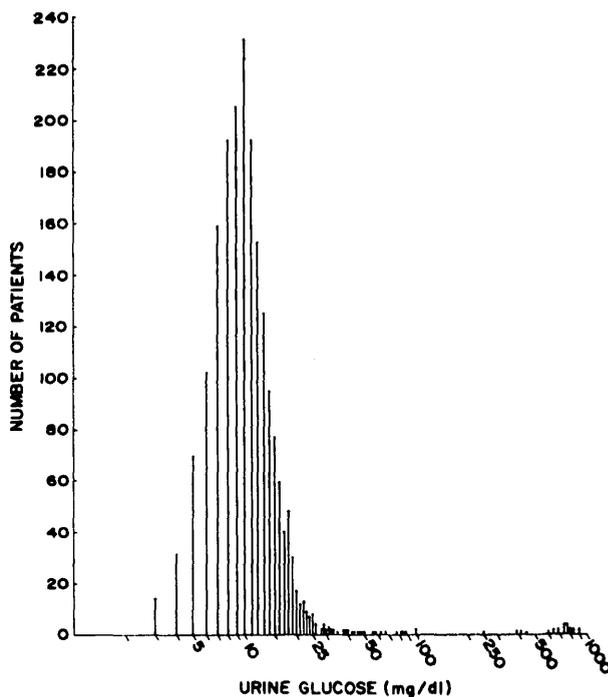


FIG. 1. Distribution of random undiluted urine glucose levels in 1,952 screenees (abscissa: log scale).

glucose levels above 150 mg. per deciliter. The remaining 18 patients in the random marked hyperglycosuria group, 25 randomly selected from 39 in the random moderate hyperglycosuria group, and 25 randomly selected from 1,888 in the random normoglycosuria group were prepared for a six-hour glucose tolerance test (GTT) with 300 gm. of oral carbohydrate for three days before the test.

To minimize patient discomfort during the course of the test, a no. 19 scalp vein needle was inserted into an antecubital vein and 0.85 per cent saline was infused at a keep-vein-open rate. Plasma glucose was measured fasting, and 100 gm. of glucose as a 25 per cent solution was ingested within five minutes. Plasma glucose was then measured 30, 60, 90, 120, 180, 240, 300, and 360 minutes after the first swallow of glucose. Urine glucose, fasting and during the course of the test, was measured by the ORM and 2 Drop Clinitest methods.

Each of the 68 GTTs was evaluated by United States Public Health Service (USPHS),^{9,10} Fajans-Conn (F-C),¹¹ and summation (S)¹² criteria, and patients were classified as nondiabetic or diabetic. USPHS upper limits of normal were: fasting 130, one hour 195, two hour 140, and three hour 130. One point was assigned for a fasting or three-hour level above 130, and one-half point for a one hour level

above 195 or a two-hour level above 140. Patients with two to three points were classified as diabetic, those with zero to 1½ points as nondiabetic. F-C upper limits of normal were: one hour 185, 1½ hour 165, and two hour 140. Patients with three levels above upper limits were classified as diabetic, and those with zero to two levels above the upper limits were classified as nondiabetic. Upper limit of normal for summed fasting, one-, two-, and three-hour levels was 600, with those above 600 being classified as diabetic and those below being classified as nondiabetic. No age-adjusted criteria were used for interpreting test results.

The 25 patients in each of the three groups were classified as diabetic or nondiabetic (table 1). The false positives (nondiabetics) in each of the two random hyperglucosuria groups were further subdivided into "random renal hyperglucosuria" (urine glucose > 25 mg. per deciliter both at random and ≥ 80 mg. per deciliter during GTT), and "random nonrenal hyperglucosuria" (urine glucose > 25 mg. per deciliter at random but a urine glucose maximum of 25 mg. per deciliter or less during the GTT).

The sensitivity and specificity of 12 different

criteria for detecting patients with unknown diabetes were evaluated (table 2). Sensitivity is defined as positivity in disease and is the percentage of true positives in the diseased (diabetic) population tested, and specificity is defined as negativity in health and is the percentage of true negatives in the healthy (nondiabetic) population tested. The significance of the difference in sensitivity between two tests was determined by a comparison of the number of false negatives observed by each of the two tests in the diseased population, according to the formula described by Galen and Gambino.¹³ Similarly, the significance of the difference in specificity between two tests was determined by the comparison of the number of false positives observed in the healthy population. Probabilities of significance were determined using Student's *t*-test.

RESULTS

ORM-RUG levels on the 1,952 subjects screened were plotted as a continuous variable (figure 1). 1,888 (96.7 per cent) were in the normogluosuria (3 to 25 mg. per deciliter) group, 39 (2.0 per cent) were in the

TABLE 1

Random normogluosuria (3 to 25 mg./dl.)				Random moderate hyperglucosuria (26 to 100 mg./dl.)				Random marked hyperglucosuria (> 100 mg./dl.)						
Pt.	USPHS	F-C	S	Class.	Pt.	USPHS	F-C	S	Class.	Pt.	USPHS	F-C	S	Class.
1	-	-	-	ND	26	-	-	-	RHG	51	-	-	-	RHG
2	-	-	-	ND	27	-	-	-	NRHG	52	+	+	+	DM
3	-	-	-	ND	28	+	+	+	DM	53	+	+	+	DM
4	-	-	-	ND	29	+	+	+	DM	54	+	+	+	DM
5	-	-	-	ND	30	-	-	+	RHG (USPHS, F-C)	55	-	-	-	RHG
6	-	-	-	ND	31	-	-	-	NRHG	56	+	+	+	DM
7	-	-	-	ND	32	-	-	-	RHG	57	-	-	-	NRHG
8	-	-	-	ND	33	+	+	+	DM	58	+	+	+	DM
9	-	-	-	ND	34	-	-	-	NRHG	59	+	+	+	DM
10	-	-	-	ND	35	-	-	-	NRHG	60	+	+	+	DM
11	-	-	-	ND	36	-	-	-	RHG	61	-	-	-	RHG
12	-	-	-	ND	37	-	+	+	RHG (USPHS)	62	-	-	-	RHG
13	-	-	-	ND	38	-	-	-	RHG	63	-	+	+	RHG (USPHS)
14	-	-	-	ND	39	-	-	-	RHG	64	+	+	+	DM
15	-	-	-	ND	40	-	-	-	NRHG	65	+	+	+	DM
16	-	-	-	ND	41	+	+	+	DM	66	-	-	-	RHG
17	-	-	-	ND	42	-	-	-	RHG	67	+	+	+	DM
18	-	-	-	ND	43	-	-	-	NRHG	68	+	+	+	DM
19	-	-	-	ND	44	-	-	-	NRHG	69	+	+	+	DM
20	-	-	-	ND	45	-	-	-	NRHG	70	+	+	+	DM
21	-	-	-	ND	46	-	-	-	NRHG	71	+	+	+	DM
22	-	-	-	ND	47	-	-	-	NRHG	72	+	+	+	DM
23	-	-	-	ND	48	-	-	-	RHG	73	+	+	+	DM
24	-	-	-	ND	49	-	-	-	RHG	74	+	+	+	DM
25	-	-	-	ND	50	-	-	-	RHG	75	+	+	+	DM
Total														
+	0	0	0		+	4	5	6		+	18	19	19	
-	25	25	25		-	21	20	19		-	7	6	6	

ND, nondiabetic; RHG, renal hyperglucosuric; DM, diabetic; NRHG, nonrenal hyperglucosuric; USPHS, U.S. Public Health Service criteria; F-C, Fajans-Conn criteria; S, summation criteria.

TABLE 2

Criterion	n	Sensitivity			Specificity		
		USPHS	F-C	S	USPHS	F-C	S
RUG > 25	75	100	100	100	47	48	50
Clinitest Pos.	75	77*	75*	74*	85*	86*	86*
RPG > 100	73	100	96	96	51	51	51
RPG > 120	73	96	92	92	84*	86*	86*
RPG > 140	73	91	88	88	92*	94*	94*
GTT UG > 400	68	100	95	95	69*	69*	68*
GTT F > 130	68	91	—	84*	100*	—	100*
GTT 1 hr. > 195	68	100	—	83	98*	—	100*
GTT 1 hr. > 185	68	—	100	—	—	98*	—
GTT 1.5 hr. > 165	68	—	100	—	—	94*	—
GTT 2 hr. > 140	68	100	100	100	89*	92*	94*
GTT 3 hr. > 130	68	100	—	100	93*	—	98*

RUG, random urine glucose; RPG, random plasma glucose; GTT, glucose tolerance test; F, fasting; for other abbreviations see table 1.

*p < 0.05; others are not significant.

moderate hyperglucosuria (26 to 100 mg. per deciliter) group, and 25 (1.3 per cent) were in the marked hyperglucosuria (> 100 mg. per deciliter) group. Median RUG was 10 mg. per deciliter.

None of those tested in the normoglycosuria group were diabetic (table 1). Of the 25 tested in the moderate hyperglucosuria group, four (16 per cent) were diabetic by USPHS criteria, five (20 per cent) were diabetic by F-C criteria, and six (24 per cent) were diabetic by summation criteria. Ten (40 per cent) were classified as nonrenal hyperglucosurics. Eleven (44 per cent) were classified as renal hyperglucosurics by USPHS criteria, 10 (40 per cent) by F-C criteria, and nine (36 per cent) by summation criteria. Of the 25 in the marked hyperglucosuria group, seven were diagnosed as diabetic on the basis of three fasting plasma glucose levels above 150 mg. per deciliter. Including these seven individuals, 18 (72 per cent) in this group were diabetic by USPHS criteria, and 19 (76 per cent) were diabetic by both F-C and summation criteria. One (4 per cent) was classified as a nonrenal hyperglucosuric, six (24 per cent) were classified as renal hyperglucosurics by USPHS criteria, and five (20 per cent) by both F-C and summation criteria.

Of the 22 diabetics diagnosed by USPHS criteria, 14 were black females, four were black males, two were white females, and two were white males. Two additional black males (for a total of six) were diabetic by F-C criteria, and three additional black males (for a total of seven) were diabetic by summation criteria. The group prevalence of diabetes by USPHS criteria was 1.13 per cent, by F-C criteria was 1.23 per cent, and by summation criteria was 1.28 per cent. The prevalence of diabetes in black females was 1.16 per cent; in black males was 0.86 per cent by USPHS, 1.30 per cent by F-C, and 1.51 per cent by summa-

tion criteria; in white females was 1.08 per cent; and in white males was 2.0 per cent. Thus, there was no significant difference in the prevalence of diagnosed diabetes in the four subgroups by race and sex.

Eighty-two per cent of the diabetics and 57 per cent of the nondiabetics were over 40 years of age, 36 per cent of the diabetics and 32 per cent of the nondiabetics had a family history of diabetes, and 71 per cent of the diabetics and 38 per cent of the nondiabetics were greater than 120 per cent of ideal body weight. One of the diagnosed diabetics had a combination of no family history, was less than 40 years of age, and was less than 120 per cent of ideal body weight. Age-adjusted criteria¹⁴ were evaluated and influenced the diagnosis of diabetes in only one individual (patient no. 63, table 1). This individual was a black male, 69 years of age, who had a fasting level of 115, one hour 193, 1½ hour 184, two hour 148, and three hour 168. Without age adjustment, he had 1½ points USPHS (nondiabetic), three levels above upper limit F-C (diabetic), and 624 summation (diabetic). By adding 1 mg. per deciliter for each year of age above 50 years to the one-, 1½-, two-, and three-hour levels, he retains one point USPHS but becomes nondiabetic by both F-C and summation criteria.

The Clinitest method missed five of the diabetics by USPHS criteria (where RUGs were 29, 39, 44, 47, and 103), six by F-C criteria (where RUGs were 29, 39, 39, 44, 47, and 103), and seven by summation criteria (where RUGs were 26, 29, 39, 39, 44, 47, and 103). Thirty-four (1.8 per cent) of the 1,888 in the 3 to 25 mg. per deciliter RUG group were false positives by Clinitest. GTT fasting > 130 missed three of the diabetics by USPHS criteria and six by summation criteria. RPG > 140 missed two of the diabetics by USPHS criteria and three by both F-C

and summation criteria; RPG > 120 missed one of the diabetics by USPHS criteria, and two by both F-C and summation criteria; RPG > 100 missed none by USPHS criteria, but missed one by both F-C and summation criteria. Of the 75 individuals tested (table 1), RUG > 25, GTT urine glucose > 400, GTT 1 hour > 195, 1½ hour > 165, 2 hour > 140, and 3 hour > 130 missed no diabetics.

The sensitivity of the RUG > 25 is significantly greater than that of the Clinitest method (table 2), but is not significantly different from RPG at any level tested or from any time interval during the GTT. The specificity of the RUG > 25 is significantly less than the Clinitest method, RPG > 140 and > 120, and during the GTT at all time intervals, but is not different from the RPG > 100.

The most important aspect of these statistical comparisons is that the RUG > 25 missed no diabetics and was equal in sensitivity to the GTT in its ability to detect the unknown diabetic. On the other hand, Clinitest missed one fourth of the diabetics (all in the RUG range 26 to 103), and fasting plasma glucose during GTT and RPG at all evaluated levels missed some of them.

The means and ranges of urine glucose levels at random, fasting, and during the GTT for hyperglucosuric diabetics, normogluosuric nondiabetics, and renal and nonrenal hyperglucosuric nondiabetics are summarized in table 3. The seven diabetics diagnosed by three fasting plasma glucose levels above 150 had marked fasting hyperglucosuria, but five of the 15 diagnosed (USPHS criteria) during glucose tolerance testing had fasting normogluosuria (4, 8, 12, 20, 22). During the GTT, urine glucose in these 15 individuals ranged from 429 to 7,400. RUG in the diabetics ranged from 29 to 5,780. Mean fasting urine glucose levels in all groups of nondiabetics was 11, with a range of 4 to 24 for 52 of the 53 nondiabetics and a fasting level of 30 for the other.

This individual had the highest level of all renal hyperglucosurics during GTT, 3,150, thus suggesting that he had the lowest renal threshold for glucose of all tested nondiabetic individuals. The 11 random nonrenal hyperglucosurics, 10 of whom were males, had a mean random level of 44 (range 26 to 125) and a mean level of 16 (range 5 to 25) during the GTT. The 25 normogluosurics had a mean random level of 14 (range 8 to 22), and a mean level of 35 (range 5 to 196) during the GTT. Eighteen ranged from 5 to 24 during GTT with the other seven being 26, 58, 61, 62, 77, 172, and 196. The 17 random renal hyperglucosurics during GTT had a mean level of 872 (range 34 to 3,150), with 10 ranging from 313 to 3,150; one was not tested, and the other six were 34, 80, 118, 120, 187, and 225.

DISCUSSION

The results of this study suggest that screening sensitivity of the ORM-RUG > 25 mg. per deciliter is similar to that of contemporary GTT methods in detecting the unknown diabetic. The ORM method is chemically specific for glucose, is quantitative, and is free of interference by other substances in urine. In contrast, the Clinitest method gave a negative reaction at all urine glucose levels below 124 mg. per deciliter, except for 34 false positives (1.8 per cent) in 1,888 subjects in the RUG 3 to 25 mg. per deciliter group. At 124 mg. per deciliter, Clinitest gave a trace (0.25 per cent) reaction, and in the 414 to 601 mg. per deciliter range, it gave a 1+ (0.5 per cent) reaction. This confirms previous reports concerning the insensitivity and nonspecificity of the Clinitest method.^{1,2}

It became apparent during the course of the study that false positive subjects (nondiabetics with RUG > 25 mg. per deciliter) fell into two distinct groups: (1) those with RUG > 25 mg. per deciliter and GTT

TABLE 3
Mean and range of urine glucose levels (mg./dl.) random, fasting, and during glucose tolerance test in diabetics, nondiabetic normogluosurics, and nondiabetic renal and nonrenal hyperglucosurics

	Random urine glucose		Fasting urine glucose		Maximum urine glucose (GTT)	
	Mean	Range	Mean	Range	Mean	Range
Diabetes diagnosed by three fasting plasma glucose levels > 150 mg./dl. (7)			3,380	1,860-5,780		
Diabetes diagnosed by GTT (USPHS) (15)	518	29-5,780	902	4-9,160	3,543	429-7,400
Nondiabetic normogluosurics (25)	14	8-22	11	5-19	35	5-196
Nondiabetic renal hyperglucosurics (17)	144	26-743	11	4-30	872	34-3,150*
Nondiabetic nonrenal hyperglucosurics (11)	44	26-124	10	5-16	16	5-25

*One not tested.

urine glucose \leq 25 mg. per deciliter, and (2) those with RUG $>$ 25 mg. per deciliter and GTT urine glucose $>$ 25 mg. per deciliter. Those in the former group were classified as random nonrenal hyperglucosurics. Since 10 of 11 were males and since semen contains glucose,¹⁵ the hypothesis that transient semenuria was responsible is being investigated. Those in the latter group were classified as random renal hyperglucosurics. Ninety-six per cent of these individuals had GTT urine glucose levels \geq 80 mg. per deciliter. Of those who were classified as random normoglusurics (3 to 25 mg. per deciliter), 92 per cent had a GTT urine glucose \leq 80 mg. per deciliter. Thus, there was some overlap in GTT urine glucose levels in random renal hyperglucosurics and random normoglusurics, no doubt in part reflecting individual differences in the renal threshold for glucose. The lowest RUG in an individual diagnosed as diabetic by any criteria was 26 mg. per deciliter (patient no. 30, table 1). This individual had 658 summation (diabetic), 1½ points USPHS (nondiabetic), and two levels above normal F-C (nondiabetic). The lowest RUG in any individual diagnosed diabetic by all three sets of criteria was 29 mg. per deciliter (patient no. 28, table 1). Thus, this study appears to confirm the fact that an appropriate cut-off point in diabetes screening is a RUG of 25 mg. per deciliter as the upper limit of normal.⁷ A more extensive study with more follow-up GTTs will be needed to determine how frequently those in the RUG 3 to 25 mg. per deciliter group have a high renal threshold for glucose which prevents diabetes detection by the RUG method. None were detected in this study.

Assuming that the prevalence of diabetes, renal hyperglucosuria, and nonrenal hyperglucosuria was the same in the nontested 14 individuals as in the tested 25 individuals in the RUG 26 to 100 mg. per deciliter group, the corrected overall prevalence of diabetes becomes 1.24 per cent (USPHS), 1.37 per cent (F-C), and 1.45 per cent (summation) and the overall prevalence of renal hyperglucosuria becomes 1.19 per cent, and of nonrenal hyperglucosuria becomes 0.85 per cent. In the ongoing mass-screening program of the Diabetes Association of Greater Cleveland, using a 75 gm. carbohydrate load, capillary blood, and an upper limit of normal 1 hour of 190 and 2 hour of 140, the prevalence of positive subjects was 1.8 per cent.¹⁶ Although the Cleveland study and this study are not comparable for a variety of reasons, the overall prevalence of confirmed diabetes in the two studies was not remarkably different.

Since laboratory tests play a critical role in providing essential feedback to the physician in detecting the unknown diabetic, it is not surprising that the reference test for establishing the diagnosis of diabetes is, and will continue to be, the oral glucose tolerance test in the properly prepared individual. It is more sensitive and specific than either semiquantitative urine tests or fasting or random blood samples. Unfortunately, the reproducibility of the GTT leaves a good deal to be desired, with factors such as age, diet, activity, and various medications, and acute and chronic illnesses having a significant effect on the results; the meaning of a moderately abnormal or borderline test on the subsequent development of the diabetic syndrome is debatable; and whether a patient is classified as diabetic or nondiabetic depends on which of several sets of criteria are used.^{9-12,17,18} In this study, for instance, 22 were diabetic by USPHS criteria, 24 were diabetic by F-C criteria, and 25 were diabetic by summation criteria.

When quantitative tests are used, positivity and negativity may be varied by changing the cut-off point for the upper limit of normal. With a lower cut-off point, there is higher sensitivity but lower specificity, and with a higher cut-off point, there is lower sensitivity but higher specificity. In recent years, because of limited retesting facilities and resources and the desire to keep false positives at a reasonable level, there has been a tendency to make the cut-off point higher by adding 1 mg. per deciliter for each year of age beyond 50 years,¹⁴ and to selectively screen high risk groups^{17,18} (age over 40 years, obese, and family history of diabetes). In this study, limiting screening to groups with one, two, or even all three of the risk factors would have missed some diabetics. Applying age-adjusted criteria changed the outcome in only one individual. He was nondiabetic by USPHS criteria and diabetic by F-C and summation criteria, but became nondiabetic by F-C and summation criteria when age-adjusted criteria were applied.

The availability of a noninvasive, inexpensive, quantitative, glucose-specific, sensitive method such as the ORM-RUG $>$ 25 mg. per deciliter makes it possible to improve diabetes screening strategy. Thus, screening in the physician's office and/or hospital at appropriate intervals with a follow-up GTT when indicated can detect most unknown diabetics early,¹⁹ with definitive diagnosis being accomplished in one week, and with education, treatment, and follow-up being carried out efficiently, and at minimum cost.²⁰

The availability of the ORM-RUG > 25 mg. per deciliter also makes it possible to identify individuals with renal thresholds for glucose that are only moderately lower than normal. The diagnosis of renal glucosuria has been restricted to those who have an extremely low renal threshold for glucose and who have persistent, including fasting, glucosuria as measured by semiquantitative methods.²¹ The prevalence of renal glucosuria so defined in the Joslin Clinic series was 0.17 per cent; no such individuals were identified in this study. Inconstant, not including fasting, glucosuria was designated in the Joslin Clinic series as unclassified glucosuria.²¹ The highest fasting urine glucose level encountered during this study was 30 mg. per deciliter, but during GTT, 15 of 16 random renal hyperglucosurics who were tested had urine glucose levels \geq 80 mg. per deciliter. Additional studies are needed to define a more precise upper limit of normal for the urine glucose level during GTT. At present, the upper limit of normal that is being used is 80 mg. per deciliter, with all RUGs > 25 mg. per deciliter who are not diabetic and who have GTT urine glucose > 80 mg. per deciliter being classified as renal hyperglucosurics. The adjusted prevalence of random renal hyperglucosuria as defined in this study was 1.19 per cent.

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