

Reproducibility of the Oral Glucose Tolerance Test and the Rice-Meal Test in Mild Diabetics

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SUMMARY

Reproducibility of 100 gm. oral glucose tolerance test and of Sakaguchi's rice-meal test were studied in sixty untreated mild diabetic patients with fasting blood sugar below 140 mg. per 100 ml. (Hagedorn-Jensen method). The tests were performed twice within a one-week interval. There were considerable variations of blood sugar levels in the same individuals between the duplicate tests. Variations were of similar magnitude after glucose or rice-meal and were smaller for the fasting blood sugar. There was no positive relationship between blood sugar levels after loading and their variability. Such a relationship was, however, clearly demonstrated for the fasting blood sugar levels of 360 newly referred diabetics. Average blood sugar levels and standard deviations for each group remained very stable despite individual variability. Implications of the data on evaluation of the results of these oral tests are discussed. *DIABETES* 15:901-04, December, 1966.

The oral glucose tolerance test (GTT) is widely used to establish a diagnosis of diabetes mellitus. Increasing interest in early diabetes and "prediabetes" has led to the development of modifications of the test. Nevertheless, cases with only slight abnormality continue to offer difficulty in interpretation. Often a patient classed as diabetic by the initial test becomes "normal" by another test, and vice versa. Such variations in the results of oral glucose tolerance tests were reported in the literature of 1930's and 1940's,¹⁻⁷ and more recently by Unger⁸ and McDonald et al.⁹ On the other hand, some authors¹⁰⁻¹³ indicate that the GTT is fairly stable. Knowledge of reproducibility of the GTT is important not only in matters of diagnosis but also for evaluation of the clinical courses of mild diabetes, to distinguish spontaneous fluctuations from true improvement or aggravation.

In Japan, besides the glucose tolerance test, a rice-

meal test devised by Sakaguchi¹⁴ has been widely used as a more natural substitute for the GTT. But its reproducibility, in comparison with that of the GTT, has not been studied sufficiently. In the present study either duplicate GTT's or duplicate rice-meal tests were conducted in the same individuals within a one-week interval to test the reproducibility of the procedures.

METHODS

Sixty diabetic patients with FBS concentrations less than 140 mg. per 100 ml. were selected from new untreated patients referred to the Diabetic Clinic in the Third Department of Internal Medicine, University of Tokyo from April to November 1965. Their mean age was forty-eight years (range twenty-four to seventy-two), and thirty-six men and twenty-four women were included. They were halved into two groups, each consisting of thirty patients. Those of the first group received a 100 gm. oral glucose tolerance test, and those of the second group received a rice-meal test described by Sakaguchi.¹⁴ The meal consisted of 270 gm. cooked rice, two eggs and a small amount of vegetables.* After the initial test, the patients were told to continue their daily way of life and adhere to their diets before visit. The second test was carried out three to seven days later.

Capillary blood was taken from a cut on the ear lobe when the patient was fasting, and 30, 60, 90, 120 and 180 min. after ingestion of the glucose or rice diet. The patients remained seated to avoid extra activity during the test. Blood sugar was determined by Hagedorn-Jensen's method.¹⁵ The reproducibility of analyses was investigated by freezing at -20° C. fifty different sera of diabetics with various blood sugar levels. The blood sugar concentrations of each sample were determined

*This test has been widely used in Japan. The test diet contains about 90 gm. carbohydrate, 28 gm. protein and 10 gm. fat. Standard of blood sugar for the abnormality of glucose tolerance by this test is over 150 mg. per 100 ml. at peak, or 130 mg. per 100 ml. at two hours with capillary blood by Hagedorn-Jensen's method.¹⁵

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on two different days, the mean difference of which was 3.1 mg. per 100 ml. Accordingly, differences of blood sugar levels much exceeding this value are judged significant.

For comparison of variabilities of fasting blood sugar levels, data were used also from 360 diabetic patients in whom during the period from April 1962 to November 1965, two fasting blood sugar analyses had been made within one week before initiation of treatment.

RESULTS

(1) *Reproducibility of the oral glucose tolerance test and the rice-meal test.*

Blood sugar values obtained in duplicate glucose or rice-meal tests are shown in figures 1 and 2. In general, there were considerable variations between corresponding blood sugar levels of the first and second tests after loading with both glucose and rice meal. Differences of corresponding blood sugar levels (i.e., blood sugar level of the second test minus that of the first test) ranged from -19 mg. to 18 mg. per 100 ml. at fasting and

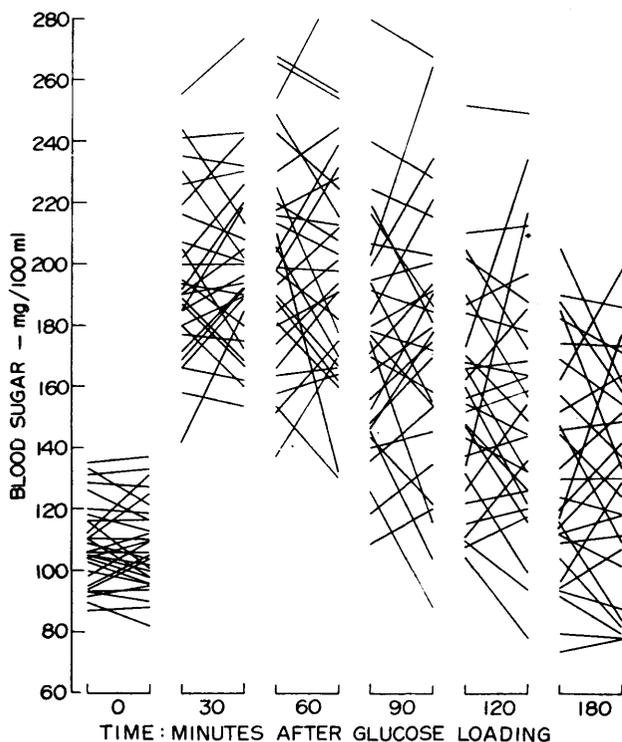


FIG. 1. Reproducibility of 100 gm. oral glucose tolerance tests in thirty mild diabetics. The test was repeated on the same individual within one week. The left end of each line represents the result of the first test and the right end represents that of the second test of the same subject.

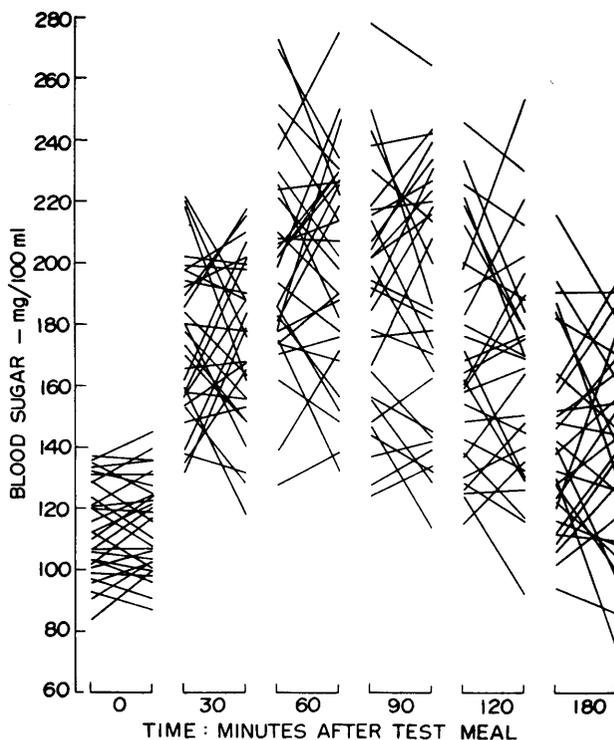


FIG. 2. Reproducibility of Sakaguchi's rice-meal test in thirty mild diabetic patients. The test was repeated twice on the same individual within one week. The left end of each line represents the result of the first test and the right end represents that of the second test of the same subject.

from -78 to 84 mg. per 100 ml. at 1, 2 and 3 hr. after glucose or meal. Standard deviations of the blood sugar differences were similar in both tests and approximately ± 15 mg. per 100 ml. at fasting and ± 25 to ± 50 mg. per 100 ml. after loading (table 1). In view of the variability of individual cases, it is noteworthy that the mean blood sugar curves of each group were in close agreement between the first and the second tests, the difference being in the range of the errors of blood sugar determinations (table 1).

(2) *The variability of fasting blood sugar of diabetic patients.*

The two successive fasting blood sugar levels of freshly referred diabetic patients determined within a one-week interval are shown in figure 3. The variation appears wider for those cases who had higher concentrations. This is in contrast to the variation of blood sugar levels of similar height after both types of tolerance tests. Herein the variability is nearly the same independent of blood sugar levels (figure 4).

TABLE 1

Means and standard deviations of blood sugar levels and of differences between corresponding blood sugar values (the value of the second test minus that of the first test) in duplicate 100 gm. oral glucose tolerance tests and Sakaguchi's rice-meal tests

(a) 100 gm. oral glucose tolerance test			
Time after glucose (min.)	Blood sugar (mg./100 ml.)		Blood sugar difference second-first (mg./100 ml.)
	First test	Second test	
0	106.7±11.66	108.3±13.81	1.6±11.47
30	196.6±27.25	199.4±27.71	2.8±19.96
60	206.1±38.93	207.9±51.40	1.8±32.32
90	176.4±38.05	176.6±42.88	0.2±28.10
120	170.8±57.75	170.2±57.69	-0.6±32.88
180	142.2±43.47	134.2±42.88	-8.0±40.44

(b) Sakaguchi's rice-meal test			
Time after glucose (min.)	Blood sugar (mg./100 ml.)		Blood sugar difference second-first (mg./100 ml.)
	First test	Second test	
0	115.1±15.30	116.3±15.28	1.2± 9.71
30	174.8±25.57	175.0±27.77	0.2±30.67
60	201.9±37.03	200.9±35.70	-1.0±36.92
90	189.7±38.51	187.3±40.46	-2.4±27.26
120	173.7±36.73	167.7±38.92	-6.0±29.60
180	145.1±30.49	142.8±32.53	-2.3±31.40

DISCUSSION

The oral glucose tolerance test is of special importance for the diagnosis of mild diabetes for it may be the sole means of detection. The present data, obtained from mild diabetics, reveal that neither the oral glucose tolerance or the rice-meal test gives satisfactorily reproducible results. The subjects who showed very similar responses to duplicate tests were few. Variations were of approximately the same magnitude for both the glucose tolerance test and the rice-meal test.

The lack of good reproducibility in oral glucose tolerance test was reported in early literature soon after the introduction of blood sugar determination as a routine test in clinical medicine.^{1-5,10-12} More recently Unger,⁸ conducting duplicate two-hour glucose tolerance tests in forty-nine apparently normal subjects, demonstrated fairly wide variations in two-hour blood sugar in about half of the subjects. A large scale study of repeated oral glucose tolerance tests in 443 prisoners was recently reported also by McDonald et al.⁹ In this study, six tests repeated on the same individuals revealed considerable variations over a one-year period.

The results of glucose tolerance tests may be affected by many factors, among which are the amount and composition of the diet, particularly the amount of carbo-

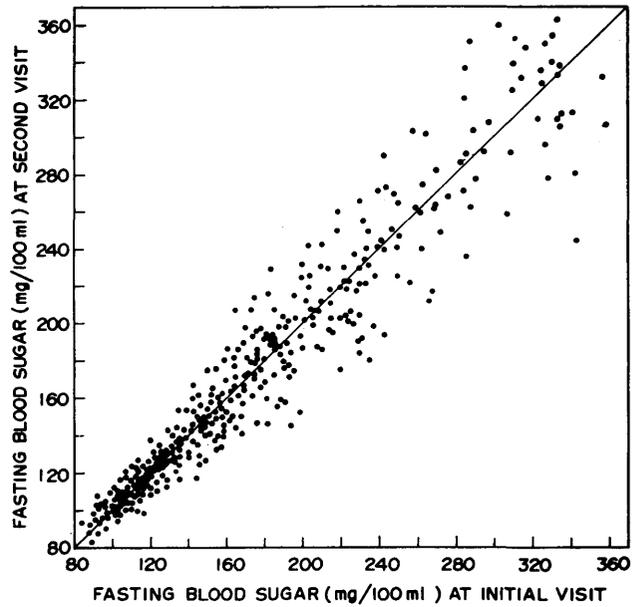


FIG. 3. Variability of fasting blood sugar levels of diabetics determined repeatedly within one-week interval.

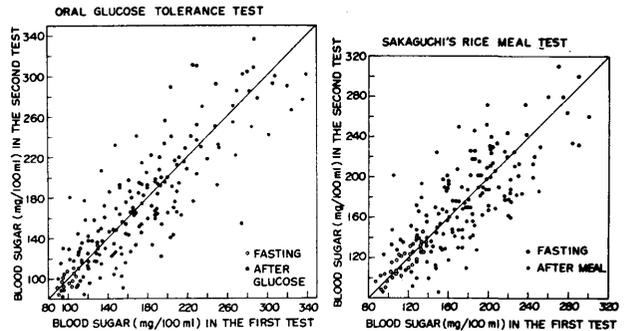


FIG. 4. Comparison of corresponding blood sugar levels in duplicate 100 gm. oral glucose tolerance tests or duplicate Sakaguchi's rice-meal tests.

Blood sugar values of different time points after loading are pooled.

hydrate, the time of fasting period, and certainly other unmeasured physiological and psychic factors which could influence the gastrointestinal motility, intestinal absorption, and various phases of blood sugar regulation. In the present study, the two tests were performed within one week, in hopes to minimize the differences in metabolic states. As the patients were ambulatory, their diet was not strictly controlled.

In view of the Japanese dietary habit and from individual questioning, it is unlikely that the carbohydrate content of their diets was lower than 250 gm., or altered between the two tests. It has been reported that

variations in glucose tolerance tests were not eliminated even in hospitalized patients who were upon standard diet.^{3,5,6} Nausea occurs frequently after ingestion of 100 gm. glucose, and might bring about variations in results, but the variations were similar in the rice-meal test which was tolerated very well.

Although the fasting blood sugar concentration tended to be more labile at higher levels, no positive relationship was noted between the blood sugar levels after glucose or diet and their variations. McDonald et al.⁹ reported greater variation at higher blood sugar level, but in their study all the blood sugar data were pooled regardless of whether samples were obtained in the fasting state or after glucose. Their group with lower blood sugar probably included more fasting blood sugar values which are more stable than values after glucose loading. Furthermore, they were dealing with an apparently normal population.

The variability of the oral glucose tolerance test has important implications. First, a single test may not be sufficient to establish the diagnosis of mild diabetes. The same individual might be diagnosed differently upon repeated tests carried out on different occasions. Second, caution is necessary in evaluating the effects of treatment on glucose tolerance. Unless the changes in blood sugar are sufficiently large, it may be difficult to decide whether or not there is improvement. The follow-up of a group selected by a detection program as "borderline" diabetics, also needs cautious interpretation. In the second test performed after an interval, some subjects may become "true diabetic" and some may become "normal," but these apparent changes may be at least in part due to simple fluctuations. For instance, O'Sullivan and Hurwitz¹⁶ have reported recently that spontaneous improvements in glucose tolerance test occur frequently in early diabetics. Some of these improvements, however, may not reflect true remissions but may be fluctuations.

Despite the difficulty in evaluating individual results, it is noteworthy that the mean values and the standard deviations of blood sugar levels of each group were extremely stable between duplicate tests. This is in agreement with the data of McDonald et al.⁹ In the conduction of mass-scale detection programs, single tests may be fairly reliable with respect to certain group characteristics such as the prevalence of diabetes, the mean values of blood sugar levels of

a given group, etc. Recognition of spontaneous fluctuations in glucose tolerance or rice-meal tests should not lessen the need, however, for establishment of proper diagnostic criteria. Instead, it should serve to help in interpretation of the results of the tests.

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REFERENCES

- ¹ Hale-White, R., and Payne, W. W.: Dextrose tolerance curve in health. *Quart. J. Med.* 19:393, 1926.
- ² Lennox, W. G., and Bellinger, M.: Blood sugar. Comparison of blood sugar curve following ingestion and intravenous injection of glucose. *Arch. Intern. Med.* 40:182, 1927.
- ³ Nielson, O. J.: On oscillations of blood sugar values within brief periods, and the blood sugar curves on uniform ingestion of glucose. *Biochem. J.* 22:1490, 1928.
- ⁴ Glassberg, B. Y.: The diagnostic value of the sugar tolerance curve in endocrinopathies. *Arch. Intern. Med.* 49:984, 1930.
- ⁵ Soisalo, P.: On the blood sugar curve in healthy persons. *Acta Med. Scand. Suppl.* 34:184, 1930.
- ⁶ Freeman, H., Looney, J. M., and Hoskins, R. G.: Spontaneous variability of oral glucose tolerance. *J. Clin. Endocr.* 2:431, 1942.
- ⁷ Horvath, S. M., Wisotsky, R., and Corwin, W.: The oral glucose tolerance test in old men. *J. Geront.* 2:25, 1947.
- ⁸ Unger, R. H.: The standard two-hour oral glucose tolerance test in the diagnosis of diabetes mellitus in subjects without fasting hyperglycemia. *Ann. Intern. Med.* 47:1138, 1957.
- ⁹ McDonald, G. W., Fisher, G. F., and Burnham, C.: Reproducibility of the oral glucose tolerance test. *Diabetes* 14:473, 1965.
- ¹⁰ Horsters, H.: Über die individuelle Konstanz der Blutzuckercurven beim Menschen. *Z. Ges. Exp. Med.* 83:72, 1932.
- ¹¹ John, H. J.: Glucose tolerance studies in children and in adolescents. *Endocrinology* 18:75, 1934.
- ¹² John, H. J.: Repeated glucose tolerance test in children. *J. Pediat.* 14:737, 1939.
- ¹³ Goto, Y.: Significance of the two-dose glucose tolerance test. Criticism of the Staub-Effect. *Metabolism* 4:323, 1955.
- ¹⁴ Sakaguchi, K.: *Treatment of Diabetes Mellitus (Japanese)*, 2nd Ed., Tokyo, Tohodo, 1926, p. 35-36.
- ¹⁵ Hagedorn, H. C., and Jensen, B. N.: Zur Mikrobestimmung des Blutzuckers mittels Ferricyanid. *Biochem. Z.* 135:46, 1923.
- ¹⁶ O'Sullivan, J. B., and Hurwitz, D.: Spontaneous remissions in early diabetes mellitus. *Arch. Intern. Med.* 117:769, 1966.