Standardization of the Oral Glucose Tolerance Test

Criticisms and Suggestions Invited

Curtis L. Meinert, Ph.D., Chairman, Committee on Statistics, American Diabetes Association

Publication of "Standardization of the Oral Glucose Tolerance Test" by the Committee on Statistics of the American Diabetes Association (DIABETES *18*:299-310, 1969) appears to have been successful in stimulating the production of much needed further data and an increased awareness of the importance of full disclosure with study reports. The originating Committee recognized that initial standards would require some arbitrary recommendations and consequently need periodic revision. Prior to a current review, the Committee invites readers, both here and abroad, to provide constructive criticism and suggest changes in the Committee's 1968 recommendations which are reproduced here in their summary form:

I. Preparatory Phase

A. Diet: Intake of at least 150 gm. of carbohydrate per day for three days preceding test, if the patient has been on a normal diet previously.

B. Acute Illness: Delay of at least two weeks after period of acute illness before performing test.

C. Medication: Discontinuance of drugs proven or believed to influence the GTT, including hormones, oral contraceptive drugs and hypoglycemic agents, for at least three days prior to test.

D. Fasting Period: No intake of any food value for at least eight and not more than sixteen hours preceding the test.

E. Miscellaneous Restrictions: Avoidance of coffee, smoking and unusual physical exercise for at least eight hours prior to the test.

F. Postponement of Test: Omission of test in event of unexpected illness (fever, gastritis, etc.), or if there has been ingestion of food within eight hours.

II. Testing Phase

A. Time: Conduct test between 7 a.m. and 12 noon, i.e., take fasting specimen between 7 a.m. and 9 a.m.

B. Glucose Load: Administer in dose of 40 gm. per square meter of body surface diluted to a volume of 300 ml. and consumed within five minutes after obtaining fasting blood specimen.

C. Specimen Timing: Draw antecubital venous blood specimen at fasting. Note time zero when the patient starts drinking the glucose. Draw additional blood specimens exactly 60, 120, and 180 minutes after time zero (30, 90, and 150 minute specimens may be obtained for additional definition of the GTT curve).

D. Patient Behavior: Have patient avoid physical exertion, emotional stress, and stimulants (tobacco, alcohol, coffee, tea).

III. Processing of Specimen

A. Type of Sample: Plasma or serum are preferable to whole blood. Separation by centrifugation should be performed within thirty minutes.

B. Preservation of Sample: Freezing or addition of sodium EDTA (1 mg. per ml. of blood) and sodium fluoride (2 mg. per ml. of blood) are required if chemical determination is not performed on the same day the specimen was drawn. Thymol must not be present during the color development phase of the chemical test.

C. Chemical Method: The glucose oxidase (not usable if sodium fluoride is present). Nelson-Somogyi and AutoAnalyzer (Hoffman's ferricyanide) methods are all acceptable. The importance of primary standards and reference sample determinations with every run is stressed.

IV. Interpretation of Test Results

A. Reporting: Wherever possible, all four plasma glucose levels should be reported (i.e., fasting, 1, 2 and 3 hour levels).

B. Diagnosis: Individual or grouped data should be classified into "diabetic" and "nondiabetic" according to *each* of the following criteria and reported accordingly:

1) The Wilkerson Point Method (adjusted for plasma glucose and 40 gm./m² glucose load)

Time		mg. per 100 ml.		Points
Fasting	—	130 or more	=	1
1 hour	—	195 or more	=	½
2 hour	—	140 or more	=	½
3 hour	—	130 or more	=	1

Two points or more indicate diabetes.

2) The Fajans-Conn Criteria (adjusted for plasma glucose and 40 gm./m² glucose load)

1 hour 185 or more, 1½ hour 165 or more and 2 hour 140 or more = diabetes.

The test should be reported even if the 1½ hour determination is omitted.

3) Summation of Fasting, 1, 2, and 3 hour plasma glucose levels. If the sum is 600 or more, a diagnosis of diabetes is made.

4) Other methods at the author's discretion.

Criticisms or suggestions should be confined to items supported by a cited source of data. Support for diagnostic criteria should ideally document the morbidity and mortality risks related to initially asymptomatic, uncomplicated diabetes identified by the test. The Committee, in recognizing the complexities involved and the paucity of valid data, issues this invitation in order to ensure that existing data might not be overlooked and that emerging data be brought to its attention.

Please address communications to Curtis L. Meinert, Ph.D., Chairman, Committee on Statistics, American Diabetes Association, 18 East 48th Street, New York, New York 10017.

ABSTRACTS

Ammon, H. P. T.; and Steinke, J. (Joslin Res. Lab. in Dept. of Med., Harvard Med. Sch. and Peter Bent Brigham Hosp., and Joslin Diabetes Foundation, 170 Pilgrim Road, Boston, Mass.): EFFECT OF 6-AMINONICOTINAMIDE ON INSULIN RELEASE AND C-14 GLUCOSE OXIDATION BY ISOLATED PANCREATIC RAT ISLETS. DIFFERENCE BETWEEN GLUCOSE, TOLBUTAMIDE AND AMINOPHYLLINE. Endocrinology *91*:33-38, July 1972.

Isolated pancreatic islets from rats were demonstrated to release significant amounts of insulin into incubating media in response to glucose but not to tolbutamide or aminophylline unless glucose were present in which case they potentiated the insulin-releasing effect of glucose. Islets obtained from animals pretreated with 6-aminonicotinamide (6-AN) released less insulin in response to glucose and were found to incorporate less C-1 carbon into $14\text{-}CO_2$. The latter finding implies interference with adequate functioning of the pentose phosphate shunt. The addition of tolbutamide did not restimulate oxidation but did continue to promote release of large amounts of insulin. The effect of aminophylline on insulin release was blunted in the 6-AN treated animals and it did not improve glucose oxidation. It was concluded that glucose requires oxidation at C-1 to induce insulin release. Tolbutamide potentiates the action of glucose and will do so even when C-1 oxidation is depressed by 6-AN pretreatment. Similar to glucose, the insulin releasing action of aminophylline is reduced if glucose C-1 oxidation is impaired. It appears that tolbutamide can substitute for a malfunctioning pentose phosphate shunt in the insulin releasing system. C.R.S.

Bengtsson, Kristina; Karlberg, Bengt; and Lindgren, Soren (Dept. of Intern. Med. Regional Hosp., Linkoping, Sweden): LACTIC ACIDOSIS IN PHENFORMIN-TREATED DIABETICS. Acta Med. Scand. *191*:203-08, March 1972.

This is a report of the author's experience with lactic acidosis in a large diabetic population. All the patients were taking phenformin (100 mg. or less) in addition to other drugs for their diabetes. Most of the patients had prodromal symptoms of drowsiness, anorexia and nausea with an inadequate fluid and food intake prior to the episode of lactic acidosis. All but one of the patients had an elevated creatinine value on admission to the hospital and several of them had an abnormal liver function test. The initial blood pH of the group ranged from 6.8 to 7.3. Seven of the patients were hypoglycemic at the time of admission. Although large amounts of bicarbonate were used in most of the patients, one patient was treated with glucose and insulin and bicarbonate with a favorable response. There were seven deaths for a mortality rate of 33 per cent. Two of the patients had a myocardial infarct at postmortem but there was no obvious cause of death in the remaining five patients. H.G.M.

Bottger, Ingolf; Schlein, Edward M.; Faloona, Gerald R.; Knochel, James P.; and Unger, Roger H. (Dept. of Intern. Med., The Univ. of Texas, (Southwestern) Med. Sch. at Dallas, and V.A. Hosp., Dallas, Tex.): THE EFFECT OF EXERCISE ON GLUCAGON SECRETION. J. Clin. Endocrinol. Metab. *35*:117-25, July 1972.

The effect of intensive physical exercise upon plasma levels of pancreatic glucagon was investigated in dogs and in man. In seven dogs, treadmill exercise until collapse was invariably associated with a rise in plasma glucagon, which at the time of collapse averaged 426 pg./ml. (S.E.M. ± 71), more than four times the baseline average of 111 pg./ml. (S.E.M. ± 26) ($P < 0.005$). Glucose rose in parallel from 88 mg./100 ml. prior to exercise (S.E.M. ± 2) to a peak of 105 mg./100 ml. (S.E.M. ± 4) at collapse ($P < 0.01$). Hypoglycemia did not occur in any dog. Insulin remained unchanged but rose briefly soon after collapse. In four human volunteers exercised to exhaustion on a stationary bicycle, glucagon rose from 68 pg./ml. (S.E.M. ± 17) to 116 pg./ml. (S.E.M. ± 114) ten minutes after the exhaustion point ($P < 0.02$), and again glucose rose in parallel from a pre-exercise value of 93 mg./100 ml. (S.E.M. ± 3) to 124 mg./100 ml. (S.E.M. ± 8) during recovery. Insulin also rose during recovery.

When dogs were exercised to collapse during a 15 mg./kg./min. intravenous glucose infusion begun one hour before the start of exercise, glucagon, which had been suppressed by the hyperglycemia to 57 pg./ml. (S.E.M. ± 22) before exercise, rose to a peak of only 160 pg./ml. (S.E.M. ± 49) ($P < 0.02$) at the time of collapse, significantly less than