The Effect of Prior Carbohydrate Intake on the Oral Glucose Tolerance Test

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Although starvation can produce decreased tolerance to glucose, sometimes called "hunger" diabetes, clinicians differ regarding the extent and necessity of dietary preparation of the patient before an oral glucose tolerance test for diabetes. Some advocate at least three days' preparation with a minimal daily carbohydrate intake of 300 gm.; others recommend a daily intake of 200 gm., while many feel that no preparation is necessary to obtain a valid test in the apparently well-nourished individual.

In 1940, Conn[1] attempted to quantitate the phenomenon of decreased glucose tolerance following restricted diets, by placing a group of nine volunteers on special diets prior to glucose tolerance testing. First, the group was given a high carbohydrate diet for three days consisting of 300 gm. of carbohydrate in a daily diet of 3000 calories. Glucose tolerance tests followed and showed normal glucose tolerance curves for all subjects. Next, the daily diet was restricted to 20 gm. of carbohydrate, 1600 calories for five days. Repeat glucose tolerance tests showed a marked decrease in glucose tolerance with three undernourished subjects having the greater abnormalities. On the basis of his study, Conn suggested that an inadequate carbohydrate diet before testing might result in false-positive reactions for diabetes, while a prior intake of 300 gm. of carbohydrate in a daily diet of 3000 calories would preclude such reactions. However, Conn did not determine what level of carbohydrate intake was necessary to restore to normalcy the glucose tolerance that had been impaired deliberately by the restricted 20 gm. carbohydrate 1600-calorie diet.

We therefore undertook a study of the problem to determine whether glucose tolerance of healthy individuals, if impaired by drastically restricted carbohydrate intake, could be restored to normalcy by as little as 150 gm. of carbohydrate intake. Since the standard dietary preparation (300 gm. of carbohydrate) often imposes hardship on such patients as pregnant women, elderly persons, and those already on other special diets, more pertinent was the question whether interpretation of glucose tolerance curves, after 150 gm. of carbohydrate intake, would be valid and would not result in a false diagnosis of diabetes or "possible" diabetes.

PROCEDURE

The study sample consisted of nine healthy male subjects aged twenty-two to thirty-seven years volunteering from a Catholic missionary order and nine healthy female subjects aged twenty-three to fifty-three years volunteering from a Massachusetts state institution.

The usual dietary pattern of each participant was obtained by a nutritionist through interview. The men averaged 311 gm. carbohydrate, 74 gm. protein, 2417 calories, and the women averaged 207 gm. carbohydrate, 66 gm. protein and 2001 calories. No subject's normal carbohydrate intake was calculated to be less than 140 gm.

A standard three-hour, 100-gm. oral glucose tolerance test was given to both men and women without prior dietary preparation. Specimens of venous blood drawn at fasting and one, two, and three hours after glucose ingestion were analyzed by the Somogyi-Nelson method.[2] The subjects were tested for glycosuria and acetonuria at each hour of the test by Clinitest and Acetest methods.

On the day following the first glucose tolerance test, the study groups were placed on a 20-gm. carbohydrate, 50-gm. protein, 1600-calorie daily diet for five days, after which the glucose tolerance tests were repeated with blood sugars analyzed in duplicate. Body weights were recorded at the inception of the diet and just

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prior to the glucose tolerance test.

All participants then were given a 150-gm. carbohydrate, 80-gm. protein, 1640-calorie diet for four days, similarly followed by glucose tolerance tests.

RESULTS

Table 1 presents, by male and female groups, individual and mean blood sugar determinations of oral glucose tolerance tests following various levels of carbohydrate intake.

Male group. After five days on 20 gm. of carbohydrate, impaired glucose tolerance was observed in all of the men. Increases were recorded at the one- and two-hour levels which averaged 140 to 125 mg./100 ml., respectively. Normal glucose removal was obtained following four days on the 150-gm. carbohydrate, 1640-calorie diets.

Table 2 shows the statistical significance of blood sugar differences observed between the various diets. Practically at all hours of blood analysis, the 20-gm. carbohydrate diet may be distinguished from the 150-gm. carbohydrate diet and the normal diet of the men. The differences indicated by "yes" are statistically significant at the 5 per cent probability level. At one and two hours after ingestion of glucose no significant blood sugar differences were observed between the normal and the 150-gm. carbohydrate diets.

Glycosuria was noted to a minor degree at various times after glucose ingestion in specimens of eight of the nine men during the glucose tolerance test following the 20-gm. carbohydrate diet. After the normal or 150-gm. carbohydrate diet, no glycosuria was evident at the time of the glucose tolerance test.

Weight loss during the restricted carbohydrate diet averaged 6.6 pounds, while weight gain during the 150-gm. carbohydrate diet averaged 1.0 pound.

Female group. Test results of the nine women followed a pattern similar to that of the men except that the glucose tolerance curves of the 20- and 150-gm. carbohydrate diets were generally higher.

Blood sugar values following the 150-gm. carbohydrate diet approached normalcy but were not restored as dramatically as they were in the men. However, the two groups experienced a similar percentage decrease in blood sugar values at the one-hour level when the 20-gm. and 150-gm. carbohydrate diets were compared (table 1).

Statistically significant differences were again ob-

TABLE 1

Individual and mean blood sugar results, mg./100 ml., following various levels of carbohydrate intake at fasting, and one, two, and three hours after glucose ingestion

Subject	Usual carbohydrate diet*				20 gm. carbohydrate diet for five days				150 gm. carbohydrate diet for four days			
	Fasting	One hour	Two hours	Three hours	Fasting	One hour	Two hours	Three hours	Fasting	One hour	Two hours	Three hours
						Male						
1	84	139	89	34	60	193	173	Clot	83	155	110	56
2	61	89	95	35	41	155	139	46	68	103	80	41
3	76	105	56	43	53	148	125	44	76	130	82	50
4	84	49	56	76	93	91	86	69	98	82	78	80
5	75	61	77	55	64	118	100	95	78	82	73	82
6	74	35	56	60	53	85	70	58	75	57	63	77
7	84	99	76	44	71	124	91	115	70	74	63	46
8	77	139	71	26	45	213	175	104	78	122	75	58
9	74	71	59	33	53	135	165	126	66	112	63	70
Mean	76	88	70	45	59	140	125	82	77	101	76	62
Standard Deviation	7.3	36.8	14.9	15.9	15.6	32.7	30.8	32.0	9.6	31.0	14.7	15.4
						Female						
1	75	71	65	39	65	166	133	75	64	119	66	34
2	74	67	71	78	63	181	200	160	65	148	145	29
3	75	72	70	69	59	161	125	111	63	109	80	40
4	75	49	81	66	63	141	130	113	55	75	65	46
5	78	80	67	47	55	155	113	57	69	145	69	24
6	78	84	95	49	71	130	135	81	70	134	109	73
7	69	95	45	63	55	276	148	69	56	131	36	36
8	75	94	55	66	67	173	107	45	63	170	36	43
9	86	101	89	91	77	219	200	155	71	144	109	76
Mean	76	79	71	63	64	178	143	96	64	130	79	44
Standard Deviation	4.5	16.4	15.7	16.2	7.2	44.8	34.2	41.2	5.7	27.3	35.0	18.5

*Calculated average carbohydrate intake: male 311 gm. and female 207 gm.

TABLE 2

Statistical significance of blood sugar differences observed between various diets
(Mean differences in mg./100 ml. and level of significance: P=.95)

Carbohydrate intakes differentiated	Fasting		Hours after glucose ingestion: One hour		Two hours		Three hours	
	Mean diff.	Significant	Mean diff.	Significant	Mean diff.	Significant	Mean diff.	Significant
			Nine males					
311 gm.* less 20 gm.	+17	Yes	—52	Yes	—55	Yes	—37	Yes
20 gm. less 150 gm.	—18	Yes	+39	Yes	+49	Yes	+20	No
311 gm.* less 150 gm.	—1	No	—13	No	—6	No	—17	Yes
			Nine females					
207 gm.* less 20 gm.	+12	Yes	—99	Yes	—72	Yes	—33	Yes
20 gm. less 150 gm.	0	No	+48	Yes	+64	Yes	+52	Yes
207 gm.* less 150 gm.	+12	Yes	—51	Yes	—8	No	+19	Yes

*Calculated average of usual carbohydrate intake.

served in the majority of comparisons between the restricted carbohydrate diet and the other two diets (table 2).

All the female participants showed glycosuria in urine specimens taken at the time of the glucose tolerance test following the 20-gm. carbohydrate diet; however, this cleared after four days on 150 gm. of carbohydrate.

Weight loss during the restricted diet averaged 3.7 pounds while weight gains during the 150-gm. carbohydrate diet averaged 2.2 pounds.

Individual Diagnoses, Male and Female. Individual glucose tolerance curves obtained have been tested against criteria for diabetes and "possible" diabetes set up in collaboration with consultants to the U. S. Public Health Service, Chronic Disease Program, Diabetes Field Research Unit. These criteria are based on a point system where venous blood sugar values by Somogyi-Nelson method (mg./100 ml.) equaling or exceeding specified levels are assigned as follows:

Time interval in relation to glucose loading	Elevated blood sugar values	Borderline blood sugar values	Diagnostic points
Fasting	110	100	1
1 hour after glucose	170	150	½
2 hours after glucose	120	110	½
3 hours after glucose	110	100	1

When data are applied to the "Elevated blood sugar values" two or more points indicate diabetes and one point indicates "possible diabetes." Lacking applicability to elevated levels two points under the "Borderline blood sugar values" indicates "possible diabetes." A case not meeting any of the above criteria is classified as "no diabetes."

On the 20-gm. carbohydrate diet none of the male participants met our diagnostic criteria for diabetes, but there were four who did meet the criteria for "possible diabetes" (table 1, Subjects 1, 7, 8 and 9). Two female participants (numbered 2 and 9) would have been considered diabetic and three others (numbered 3, 4 and 7) met the criteria for "possible diabetes."

Figures 1 and 2 graphically show composite glucose tolerance curves of male and female participants following each of the diets.

DISCUSSION

A few blood sugar values three hours after glucose seem unusually low. The blood preservative used prevents glycolysis for four days and all analyses were made from duplicate filtrates. The low values therefore are believed to be valid. Data on the clinical status of the subjects with low blood sugar values show no evidence of cause.

Blood sugar values recorded following the 20-gm. and 150-gm. carbohydrate diets may be analyzed by two different approaches.

One approach, previously discussed (table 2), is to interpret results in terms of statistical significance of increases and decreases in blood sugar values following the various diets. Using this method, it can be said first that generally the blood sugar differences between the usual and the prepared 150-gm. carbohydrate diets are not diagnostically important. Secondly, the 20-gm. carbohydrate diet differs significantly by statistical analysis from both the usual and 150-gm. carbohydrate diets for practically all blood sugar readings.

Another approach is to test the glucose tolerance curves of both diets against the diagnostic criteria for

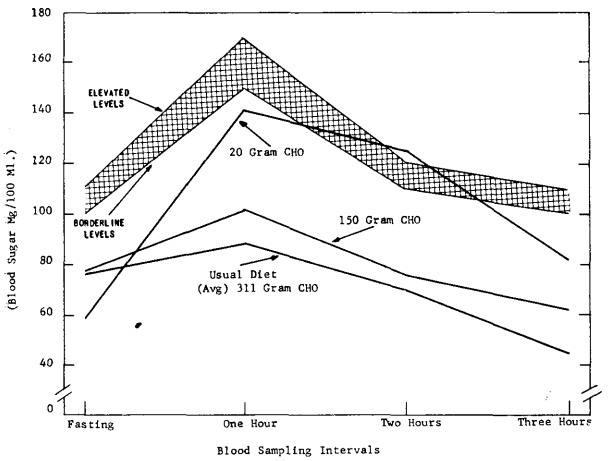

FIG. 1. Composite glucose tolerance curves by various levels of carbohydrate intake for nine males.

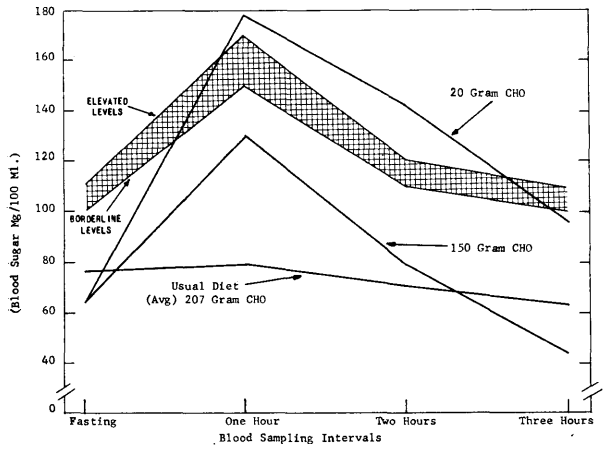

FIG. 2. Composite glucose tolerance curves by various levels of carbohydrate intake for nine females.

diabetes and "possible" diabetes used by various authorities. Table 3 shows how the subjects would have fared under varying criteria for diagnosis.[3-5] The exceptionally low carbohydrate diet impaired glucose tolerance to diagnostic levels; however, the 150-gm. carbohydrate diet restored practically all the subjects to nondiagnostic levels.

TABLE 3

Number of persons designated as having diabetes or possible diabetes, by the criteria of various authorities at different levels of carbohydrate intake

	Usual diet		20 gm. CHO diet		150 gm. CHO diet	
	Diabetes	Possible diabetes	Diabetes	Possible diabetes	Diabetes	Possible diabetes
Consultants to CD Program USPHS	0	0	2	7	0	0
Conn[3]	0	0	7	6	0	2
Mosenthal and Barry[4]	0	*	10	*	1	*
Joslin Clinic[5]	0	*	8	*	0	*

*Specific criteria for "possible" diabetes not presented.

One subject, who would have been considered diabetic after the 150-gm. carbohydrate diet for four days, according to the criteria of Mosenthal and Barry,[4] had the following glucose tolerance test readings: Fasting, eighty-three; one hour, 155; two hours, 110; three hours, fifty-six. In view of the blood sugar level three hours after glucose ingestion, it could be contended that the one- and two-hour values are of borderline significance. This person is also one of the two designated as having "possible" diabetes under the 150-gm. carbohydrate diet according to Conn's criteria.[3]

A pertinent question recently asked by Conn[3] is: "What, under conditions of standard dietary preparation, is the smallest decrease in carbohydrate tolerance which can be confidently diagnosed as indicative of the presence of diabetes mellitus?" In our study, we have attempted to determine the adequacy of a low carbohydrate diet which would be practicable for most persons. The increases and decreases in glucose tolerance shown are not based on diets of long duration nor on a large study population. Therefore, the question raised cannot be completely answered by the data in this report. Findings in this study, however, do indicate that a normally nourished person may eat as little as 150 gm. of carbohydrate in a 1600-calorie daily diet for four days prior to a glucose tolerance test and the resulting glucose tolerance curve will not lead to a false diagnosis of diabetes or "possible" diabetes, using either the criteria of the UPHS consultants or those of other workers.

The actual carbohydrate intake of the general population is of practical importance in considering dietary preparation for glucose tolerance tests. An indication as to the possible carbohydrate intake of the population was obtained by the authors in a survey of 441 nondiabetic persons in a hospital outpatient clinic who were interviewed regarding their usual dietary intake. Eighty-two per cent had a daily carbohydrate intake of 150 gm. or more; 17 per cent, 100 to 149 gm.; and only 1 per cent had an intake under 100 gm. The men averaged 221 gm. while the women averaged 192 gm.

If we may then assume that most persons consume an average daily minimum of 150 gm. carbohydrate, a person requiring 150 gm. or more for normal sustenance and weight maintenance who had restricted himself to less than that requirement easily could be

isolated by inspection or brief questioning. One could be reasonably certain then that a dietary preparation as low as 150 gm. of carbohydrate daily for four days would be enough to correct the carbohydrate deficiency. Dietary preparation around this level ordinarily would not be time-consuming nor would it impose changes in the usual eating habits of the patient. These observations are similar to those offered by Irving and Wang.[6]

The point which may be emphasized here has been alluded to by Mosenthal and Barry[4] who state "the diet preceding a glucose tolerance test in nondiabetics has a profound effect on the character of the resulting curve, though a closer scrutiny of the published observations points to a probable exaggeration of this influence . . . where the crucial figure, between 50 and 125 gm. carbohydrate, lies is undetermined. However, it is scarcely conceivable that anyone who eats at all will consume less than 125 gm. of carbohydrate. On the other hand, an emaciated person will, as stressed by Conn, have a lowered carbohydrate tolerance." It is felt that this emaciated person can readily be detected by inspection or brief questioning.

We emphasize our purpose would be not to preclude any standard dietary preparation for glucose tolerance tests, but to suggest that the standard preparation requirement need not be at an unusually high level. We would suggest that a diagnostically safe minimum daily carbohydrate intake is about 150 gm.

SUMMARY

1. Eighteen healthy men and women, after showing normal glucose tolerance curves without any previous dietary preparation, were placed on a 20-gm. carbohydrate, 1600-calorie daily diet for five days. Impaired carbohydrate tolerance on the 20-gm. carbohydrate diet was observed in both male and female participants, however, only two females showed curves diagnostic of diabetes by the criteria currently used in Public Health Service diabetes studies. Carbohydrate restriction in the females produced a greater loss of carbohydrate tolerance than it did in the males.

2. In an effort to restore normal glucose tolerance, the subjects were placed on a 150-gm. carbohydrate, 1640-calorie daily diet for four days. At the end of that period, normal carbohydrate tolerance (in terms of United States Public Health Service criteria) was fully restored and none of the subjects had curves indicative of diabetes or "possible" diabetes.

3. It is believed that adequately nourished individuals need no special high carbohydrate preparation prior to administration of an oral glucose tolerance test. A minimum of 150 gm. of carbohydrate daily for four days is considered sufficient to restore normal carbohydrate tolerance in persons who have restricted their carbohydrate intake.

SUMMARIO IN INTERLINGUA

Le Effecto de Un Antecedente Ingestion de Hydrato de Carbon Super le Test del Tolerantia pro Glucosa Oral

1. Dece-octo normal homines e feminas, qui habeva monstrate normal curvas de tolerantia pro glucosa sin previe preparation dietari, esseva restringite durante cinque dies a dietas de 1.600 calorias e 20 g de hydrato de carbon per die. Vitiate tolerantias pro glucosa durante le application del dieta a 20 g de hydrato de carbon esseva observate in participantes tanto mascule como etiam feminin, sed solmente duo femininas monstrava curvas que haberea supportate un diagnose de diabete secundo le criterios que es currentemente in uso in le studios de diabete per le Servicio de Sanitate Public. Le restriction de hydrato de carbon produceva un plus marcate perdita de tolerantia pro glucosa in femininas que in masculos.

2. In le effortio de restaurar normal tolerantias pro glucosa, le subjectos esseva tractate durante quatro dies con dietas de 1.640 calorias e 150 g de hydrato de carbon. Al fin de iste periodo, normal tolerantias pro glucosa (secundo le criterios del Servicio de Sanitate Public) esseva restaurate completemente, e nulle del subjectos habeva curvas indicante diabete o mesmo le possibilitate de diabete.

3. Es opinate que adequatemente nutrite subjectos non require un preparation special a alte ingestion de hydrato de carbon ante le administration de un test oral de tolerantia pro glucosa. Un minimo de 150 g de hydrato de carbon per die durante quatro dies es considerate como sufficiente pro restaurar un normal tolerantia pro hydrato de carbon in subjectos qui ha restringite lor ingestion de hydrato de carbon.

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Sorbitol and Vitamin B_{12} Absorption

Observations on the vitamin sparing action of D-sorbitol (Morgan and Yudkin, *Nature 180*:543, 1957); (*Nutrition Reviews 16*:126, 1958) have stimulated interest in this carbohydrate as a factor influencing intestinal synthesis of vitamins (Jones and Baumann, *J. Nutrition 66*:383, 1958) and the absorption of vitamins such as vitamin B_{12} (Greenberg et al., *Nature 180*:1401, 1957) in animals. During the past year studies on vitamin B_{12} absorption have been extended to normal human subjects and to subjects suffering from pernicious anemia.

The interest of B. F. Chow and associates in the problem of factors affecting vitamin B_{12} absorption was broadened when they observed that an experimental lipotropic elixir enhanced the absorption of vitamin B_{12} in man and in the rat (*Am. J. Clin. Nutrition 4*:434, 1956). They later studied the effects of the individual components of the lipotropic elixir (B. F. Chow, P. Meier and S. M. Free, Jr., *Ibid. 6*:30, 1958) on vitamin B_{12} absorption.

In a further study (Chow et al., *Am. J. Clin. Nutrition 6*:386, 1958) the serum vitamin B_{12} levels of subjects receiving 25 μg. of vitamin B_{12} per day administered orally in a capsule containing sorbitol were found to be considerably higher after four months of treatment than those of comparable subjects receiving 100 μg. of vitamin B_{12} without sorbitol.

In every case more radioactivity from vitamin B_{12} was found in the blood, kidneys, livers, and gastrointestinal tracts of rats receiving sorbitol, indicating again the enhancing effect of sorbitol on vitamin B_{12} absorption. Pregnancy, in agreement with observations of Hellegers et al. (*Am. J. Clin. Nutrition 5*:327, 1957) also increased vitamin B_{12} absorption but not to the extent that D-sorbitol did. The results also show very clearly the shift of vitamin B_{12} from the maternal tissues to the fetus during the third trimester of pregnancy, but even here the effect of administering D-sorbitol was marked. Fetuses of mothers receiving sorbitol contained about 7 per cent of the administered radioactivity whereas those from mothers receiving no sorbitol contained only about 2.5 per cent of the administered radioactivity. This provides support for the observation of Izak et al. (*Arch. Int. Med. 99*:346, 1957) that the great fetal demand for vitamin B_{12} may lead to the development of vitamin B_{12} deficiency in the pregnant female.

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