

# A New Carbohydrate Solution for Testing Glucose Tolerance

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## SUMMARY

During the standard 100 gm. glucose tolerance test, nausea or vomiting is a frequent side effect. In preparation for a large-scale survey for detection of diabetes a more palatable solution that causes no side effects was developed. The solution was made of partially hydrolyzed cornstarch, flavored with cola extract, and carbonated, yielding a product that tastes like a popular cola beverage. Glucose tolerance curves in sixty-three subjects after either 75 or 100 gm. of the new carbohydrate solution were, for practical purposes, identical to those after 100 gm. of glucose. Administration of the new solution was exceptionally well tolerated in 85,000 persons thus far tested for diabetes. *DIABETES* 14:96-99, February 1965.

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For many years, physicians, nurses, and medical technologists have been listening to patients' complaints of nausea after standard glucose tolerance tests with solutions containing 100 gm. of glucose. Commonly, such solutions cause vomiting; glucose frequently is not promptly absorbed, over 50 per cent being retained in the stomach for more than an hour.<sup>1</sup> Several other substances, such as galactose, mannose, and fructose, have been used in tolerance tests, but there have been no successful attempts to avoid the undesirable consequences of forcing a patient to drink from 200 to 600 ml. of a relatively concentrated glucose solution. In this study, among patients taking both tests, 20 per cent experienced nausea following the taking of 100 gm. of glucose.

Recent interest in improving methods for detecting abnormalities in glucose tolerance has led to the realization that the above-mentioned problems, although tolerable in occasional testing, would defeat attempts at mass screening for the presence of diabetes. The

urgent need is for an improved substance for the standard carbohydrate tolerance test.

This report describes the preparation and evaluation of a new *carbohydrate solution* that has a greatly improved palatability and that causes virtually no side reactions and, therefore, is suitable for mass-screening purposes. This new solution has been administered in mass screening to more than 85,000 persons. Although it has not been possible for the authors to interview each subject, reports from the technicians who drew the blood for testing state that nausea was a complaint in less than 0.1 per cent. *Not one person vomited.* It is also well tolerated by pregnant women and by children.

## MATERIALS

The carbohydrate employed was a commercially available partial hydrolysate of cornstarch.\* According to the manufacturer it contains 30 per cent dextrose, 18 per cent maltose, 13 per cent maltotriose, 39 per cent higher saccharides. It is a clear viscous solution, containing 81 per cent total solids, and is stable indefinitely at room temperature. The new solution is much less sweet and has a lower osmotic pressure than the glucose solutions commonly used. As a 30 per cent solution it has 40 per cent less sweetness and 40 per cent lower osmotic pressure than glucose, factors of primary importance in the prevention of nausea.

A flavored concentrate was prepared as follows: One hundred and twenty pounds of syrup was diluted with three and one-half gallons of water. To this was added 600 ml. of a concentrated cola flavor† or 400 ml. of cherry flavor.‡ After the addition of 120 gm. of sodium benzoate dissolved in one liter of water, the syrup was acidified by the addition of 65 ml. of 85 per cent phosphoric acid. This concentrate should have a spe-

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\*Intermediate conversion corn syrup, A. E. Staley Manufacturing Company, Decatur, Illinois.

†Virginia Dare Extract Company, Brooklyn, New York.

‡Brough Bottlers Supply Company, Cleveland, Ohio.

cific gravity of 1.32, and contain 65 per cent of carbohydrate by weight. A volume containing either 75 or 100 gm. of carbohydrate (either 87 or 116 ml.) is dispensed into a paper cup and is diluted with ice-cold carbonated water to a volume of 210 or 280 ml. Alternatively the product may be bottled as a carbonated beverage by usual commercial methods either in 7- or in 12-oz. bottles.\* Both the concentrate and the solution as described are stable at room temperature for at least a year.

The glucose equivalent of the carbohydrate present is determined by complete hydrolysis of the solution by boiling for thirty minutes with hydrochloric acid at a final concentration of 1.5 N. After neutralization with sodium hydroxide and suitable dilution the glucose is determined by any standard method.

CLINICAL TESTING

Sixty-three men, ranging from twenty-two to seventy-five years of age, comprising medical students and convalescent patients in medical, surgical, and orthopedic wards were selected to receive the new carbohydrate solution for testing glucose tolerance. In no case was diabetes mellitus a diagnosis listed in the medical records. However, as will be noted, some of the patients were subsequently shown to have diabetic types of glucose tolerance curves. Tests were performed from three to seven days apart. The patients were not prepared by regulation of the amount of carbohydrate in their diets or by increasing the daily carbohydrate intake. They were eating well, were served a general hospital diet, and they were living and eating under the same conditions during the period of time during which the two tests were done. Approximately half of the subjects received the glucose first and the other half the new solution first. Venous blood samples were obtained after an overnight fast and at intervals of one half, one, one and one-half, and two hours after ingestion either of glucose or of the new solution. When 100 gm. of glucose was used, the volume of the solution was 250 ml. When 100 gm. of the new carbohydrate solution was used the volume was 280 ml., and for 75 gm. of carbohydrate it was 210 ml. Blood was collected in sodium fluoride, refrigerated within two hours after collection, and analyzed for glucose within forty-eight hours by the method of Hoffman,<sup>2</sup> employing an AutoAnalyzer.†

\*The bottled product is now commercially available from Glucola, Ames Company, Elkhart, Indiana.

†Technicon Company.

RESULTS

The raw data as well as the statistical analyses of variants are presented in tables 1 and 2. It will be noted that blood glucose levels over 120 mg. per 100 ml. at two hours occur in eleven of the twenty-five subjects listed in table 1. This may seem to many, as it did to us, to be a high incidence of elevated levels. It should be kept in mind that this was a hospital population. How these data may compare with others in the study of a randomly selected group remains to be shown. Results after 100 gm. of carbohydrate as the new solution were compared with those after 100 gm. of glucose (table 1), and the average results of the two tests in the same twenty-five subjects were nearly identical. Since we propose to use the equivalent of 75 gm. of glucose as a standard test, it was compared with the 100 gm. of glucose, as commonly used, in thirty-eight other subjects. In this comparison there was a slight difference in blood glucose levels at two hours, the concentration averaging 110 mg. per 100 ml. after the starch hydrolysate, and 121 mg. per 100 ml. after the glucose. This difference was at the

TABLE 1  
Comparison of blood glucose levels after 100 gm. of glucose, and after 100 gm. of carbohydrate as a new tolerance solution

Subject no.	Time (minutes)									
	0		30		60		90		120	
	G*	C†	G	C	G	C	G	C	G	C
1	70	80	120	110	127	120	88	85	86	110
2	97	81	106	100	136	140	177	184	160	190
3	76	85	78	106	112	135	120	117	120	124
4	81	85	120	142	127	182	150	180	140	160
5	80	76	160	95	222	145	235	213	227	215
6	85	76	245	155	202	120	121	93	95	167
7	70	75	112	122	205	152	238	165	187	177
8	120	110	163	145	225	168	220	183	230	155
9	83	88	132	130	150	155	160	163	145	150
10	77	83	145	168	161	183	115	146	87	135
11	79	77	117	126	123	151	88	143	83	108
12	70	71	135	145	129	126	83	102	94	85
13	65	73	107	97	101	88	107	95	100	95
14	88	90	156	155	193	166	191	172	185	180
15	82	76	135	105	162	73	110	95	88	92
16	76	75	130	127	150	131	114	90	80	102
17	73	70	83	112	92	90	65	70	80	88
18	92	79	163	128	172	160	155	135	140	112
19	75	76	121	131	121	118	119	100	105	92
20	86	87	110	103	155	143	140	139	130	117
21	75	85	114	145	124	143	120	125	108	123
22	105	65	113	166	126	195	149	184	149	168
23	80	88	158	173	168	194	142	165	100	109
24	69	77	118	105	120	88	99	102	85	93
25	76	70	118	165	132	87	155	83	75	106
Average	81	80	130	130	149	138	138	133	123	130
P value	>0.5		>0.5		>0.1		>0.3		>0.2	

\*G = Glucose.

†C = Carbohydrate solution.

TABLE 2

Comparison of blood glucose levels after 100 gm. of glucose, and after 75 gm. of carbohydrate as a new tolerance solution

Subject no.	Time (minutes)									
	0		30		60		90		120	
	G*	C†	G	C	G	C	G	C	G	C
26	75	76	154	162	178	196	170	170	153	162
27	80	102	131	154	131	152	132	182	157	188
28	86	57	160	184	228	220	232	232	188	208
29	62	54	86	91	84	80	78	96	96	91
30	92	80	140	164	200	232	232	236	197	196
31	74	96	160	142	148	145	149	106	144	104
32	69	72	130	136	142	150	145	127	134	140
33	72	70	134	140	134	146	124	158	124	130
34	74	86	142	150	180	162	180	152	154	102
35	64	74	108	122	114	102	68	74	80	78
36	82	83	150	135	187	145	164	115	120	118
37	65	67	95	113	89	91	89	85	89	91
38	75	66	100	100	140	136	150	122	142	88
39	73	73	117	103	87	98	110	79	101	76
40	75	75	100	83	65	83	92	83	73	72
41	83	75	123	127	97	120	103	110	103	100
42	77	75	100	83	121	89	143	123	125	115
43	88	85	113	133	128	158	136	160	128	128
44	95	84	115	170	162	188	210	232	231	230
45	91	90	162	152	178	188	198	165	152	152
46	81	80	112	145	137	163	138	175	150	150
47	83	80	118	118	149	118	130	83	120	90
48	80	86	121	140	142	140	123	142	129	92
49	77	73	132	147	142	158	180	163	170	142
50	69	75	160	152	141	118	105	62	103	62
51	78	75	155	135	173	175	235	195	273	173
52	82	87	130	107	90	63	79	77	72	65
53	78	78	115	113	75	56	111	75	68	83
54	73	77	125	142	107	121	77	80	84	100
55	80	75	124	87	89	62	84	81	71	62
56	79	77	133	110	82	82	95	68	98	71
57	65	78	93	136	69	81	56	73	71	68
58	76	75	169	121	154	80	98	90	92	75
59	90	78	110	84	77	54	71	68	65	62
60	89	87	120	110	104	90	89	69	108	77
61	86	78	126	129	150	114	110	84	90	73
62	68	73	117	106	69	71	69	56	62	69
63	87	82	117	116	90	76	80	85	65	87
Average	78	78	126	127	127	124	127	119	121	110
P value	>0.5		>0.5		>0.5		>0.05		>0.02	

\*G = Glucose.  
†C = Carbohydrate solution.

borderline of statistical significance with a P value of 0.02. If a blood glucose level of 120 mg. per 100 ml. is arbitrarily set as the upper limit of normal two hours after the loading dose, then five tests would have been labeled "diabetic" when glucose was used, but "normal" when the new solution was used; the clinical significance of such a sharp dividing line is questionable.

In figures 1 and 2, subjects receiving 100 gm. of both types of carbohydrates were arbitrarily divided into two groups, those having blood glucose levels below 120 mg. per 100 ml. at two hours and those having levels above 120 mg. per 100 ml. The difference in the results was not of statistical significance.

In figures 3 and 4 the above-described arbitrary

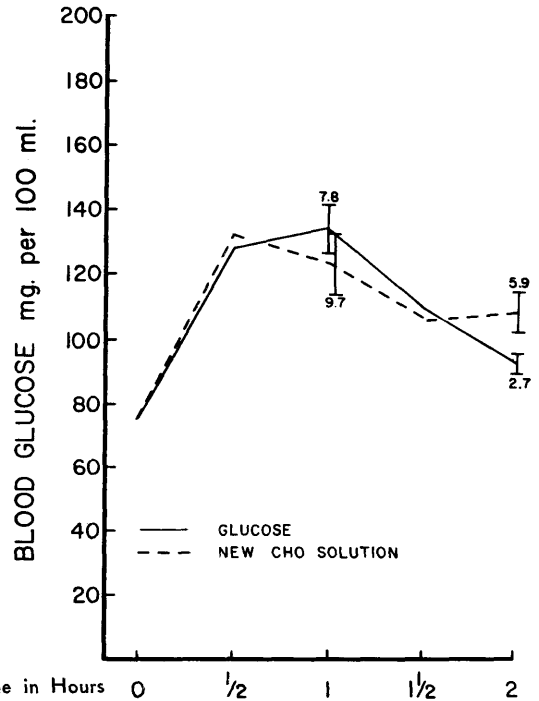


FIG. 1. Blood glucose levels after ingestion of 100 gm. of glucose or 100 gm. of new carbohydrate solution in fifteen subjects in whom the blood glucose levels at two hours were less than 120 mg. per 100 ml.

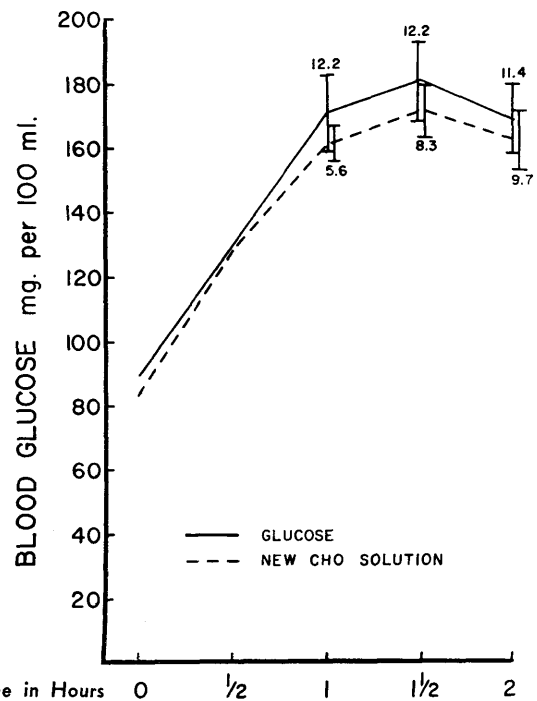


FIG. 2. Blood glucose levels after ingestion of 100 gm. of glucose or 100 gm. of new carbohydrate solution in ten subjects in whom the blood glucose levels at two hours were more than 120 mg. per 100 ml.

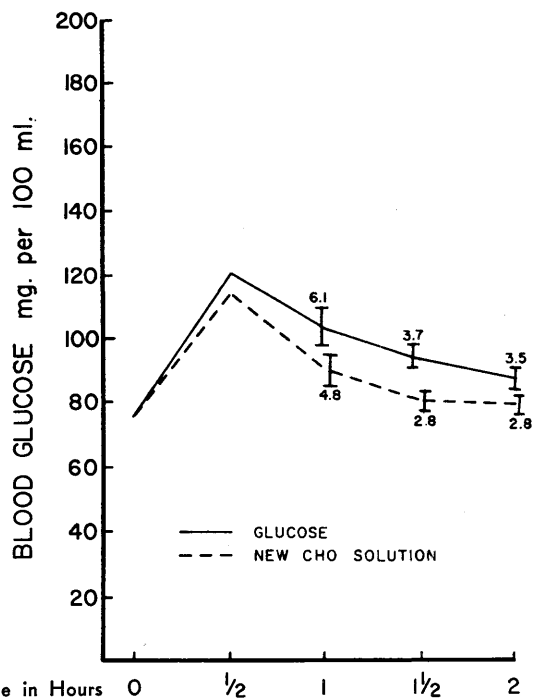


FIG. 3. Blood glucose levels after ingestion of 100 gm. of glucose or 75 gm. of new carbohydrate solution in twenty-two subjects in whom the blood glucose levels at two hours were less than 120 mg. per 100 ml.

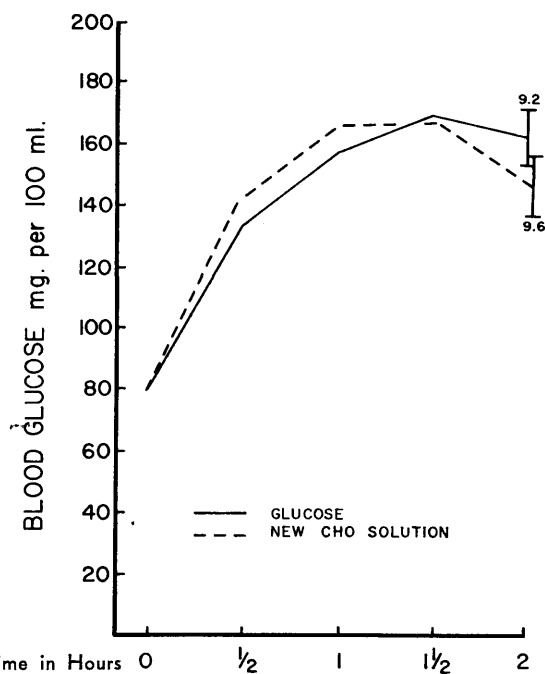


FIG. 4. Blood glucose levels after ingestion of 100 gm. of glucose or 75 gm. of new carbohydrate solution in sixteen subjects in whom the blood glucose levels at two hours were more than 120 mg. per 100 ml.

division was made in subjects in whom 100 gm. of glucose was compared with 75 gm. of the carbohydrate as the new solution. Here again, both in "normal" and in "diabetic" groups the results with the two solutions were not statistically different.

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#### REFERENCES

- Leonards, J. R., and Free, A. H.: Note on gastric retention on one-hour, two-dose glucose tolerance tests. *J. Lab. Clin. Med.* 30:1070-71, 1945.
- Hoffman, W. S.: Rapid photoelectric method for the determination of glucose in blood and urine. *J. Biol. Chem.* 120:51-55, 1937.