Blood Saccharoid Content in Neuropsychiatric Patients

Abraham M. Balter, M.D., and Herman Y. Efron, Ph.D., Lyons, New Jersey

SUMMARY

Glucose tolerance tests were obtained in 430 psychiatric inpatients with both the Folin-Wu and Somogyi-Nelson methods on the same blood sample. Blood was drawn in the fasting state and at one-half, one, two and three hours after ingestion of glucose. By the Somogyi-Nelson method the curves of 170 subjects were classified as normal and 260 as abnormal. The saccharoid content of the blood was operationally defined as the Folin-Wu value minus the Somogyi-Nelson value with the latter taken as the "true" blood sugar. In marked contrast to previous studies of others with nonpsychiatric subjects the mean saccharoid values were not constant in either the normal or abnormal group but varied significantly from one time period to the next. The variations in saccharoids observed in the abnormal group over the testing interval were different from the variations for the normals. Within each group, there was no association between age and either saccharoid content or blood sugar level. Saccharoid content was not related to deviations from average weight. A "rule of thumb" suggested by the data is that if one wants to estimate "true glucose" from the Folin-Wu with 95 per cent certainty, then the constant to subtract varies with the time interval after glucose ingestion and is in the range of approximately 0 to 47 mg./100 ml. Estimation of true blood sugar content from a Folin-Wu reading that is close to the borderline range by subtraction of a constant is seen as an extremely dubious procedure. DIABETES *14*:719-23, November 1965.

The nonglucose reducing substances of the blood, first designated by Benedict[1] as "saccharoids," were described by Sunderman[2] as having been "extensively studied in the past." Sunderman noted that "no glucose reagent is completely specific for glucose" and that values obtained for the total saccharoid content of the blood and the different substances of which it is composed vary with the reagents used. Fashena and Stiff[3] found that the saccharoids in Folin-Wu tungstic acid filtrates which affect the Folin-Wu copper reagent are chiefly glutathion, glucuronic acid and glucuronids with much smaller amounts of creatinine, uric acid and ascorbic acid.

Mosenthal and Barry[4] found that in 200 consecutive determinations, the saccharoid content was greater than 30 mg. per cent in 38 per cent of their cases, and in four instances it was above 70 mg. per cent. They recommended that only "true" blood sugar estimations be used in the glucose tolerance test in order to avoid the erroneous diagnosis of diabetes. Wilkerson and associates[5] tested 573 subjects using both the Folin-Wu and Somogyi-Nelson methods. Each subject was evaluated with a standard 100-gm. oral glucose tolerance test, and again following a standard test meal. They found that the mean difference obtained by the two methods was 20.4 mg./100 ml. with a standard deviation of 7.7 mg. No appreciable differences in saccharoid content from hour to hour were observed in either test, but they were able to "detect individual differences among the subjects." They suggested that testing by methods which include the saccharoid content involves a degree of risk in misclassifying some individuals.

Psychotic patients may present a remarkable variability in behavior when compared with nonpsychotics both in response to various stimuli and to the presence of organic disease. The present study was made to determine whether the patients in this hospital would present predictably consistent variations in blood saccharoids following the ingestion of 100 gm. of glucose.

METHODS

The subjects in this study were 430 male inpatients of a 2,000-bed Veterans Administration Neuropsychiatric hospital. All newly admitted and re-admitted patients who entered the hospital after initiation of data collection were included (N-192). In order to increase both the number of subjects with abnormal tolerance curves and the total sample size, a group of patients already hospitalized were also included (N-238). The mean age of the combined group was 46.9 years with a standard deviation of 13.1 years. The subjects received a standard oral glucose tolerance test consisting of 100 gm. of glucose in 200 ml. of water. Blood speci-

From the Medical Service and the Program Evaluation Staff of the Veterans Administration Hospital, Lyons, New Jersey.

mens were obtained prior to ingestion of glucose and at one-half, one, two, and three hours thereafter. The blood from the same specimen was analyzed by both the Folin-Wu[6] procedure with readings being obtained after stabilization[7] and the Somogyi-Nelson procedure as described by Annino.[8] For both procedures readings were obtained with a Leitz Ruy photometer. Although Volk, Saifer and Lazarus[9] demonstrated that there is still a fraction of reducing substances which is not glucose and is measured by the Somogyi-Nelson method, for expediency it was taken as the measure of "true glucose." The saccharoid content of the blood was operationally defined as the Folin-Wu value minus the Somogyi-Nelson value with the latter taken as the "true" blood sugar.

RESULTS

Since five blood specimens were obtained from each of the 430 subjects, there was a grand total of 2,150 specimens. In a previous study[10] in this hospital, it was found that there was no clear demarcation between subjects with normal curves and abnormal curves, and that no definite line could be established beyond which the individual could be described as "diabetic." Consequently, normal and abnormal values are so described here only for purposes of convenience in making statistical comparisons. Subjects were divided into two groups on the basis of their Somogyi-Nelson curves: (a) those whose fasting, 2-hr. and 3-hr. blood specimens each contained less than 100 mg. of glucose/100 ml., and whose ½-hr. and 1-hr. specimens each contained less than 160 mg./100 ml. were classified as normal whereas (b) those who at any time period had glucose content at, or higher than, the levels specified above were classified as abnormal. The division resulted in 170 normal curves and 260 abnormal curves. Table 1 contains the means and standard deviations of saccharoid content, Somogyi-Nelson, and Folin-Wu values, before and at the various time intervals after ingestion of glucose for the normal, abnormal, and combined groups. Both groups had approximately a 40 per cent increase in saccharoid content at ½-hr., a peak at ½- or 1-hr., and a return to a level somewhat below their fasting values at 3 hrs. The fluctuations in saccharoid content from time period to time period are statistically significant* ($P < .0001$). In order to avoid the ambiguity that would result from combining data obtained from disparate groups, all subsequent analyses report the findings separately for the group with normal curves and the group with abnormal curves. Since saccharoid values were obtained at five different intervals there are ten distinct pairs of means that can be compared for each group, viz., fasting and ½-hr., fasting and 1-hr., etc., through 2-hr. and 3-hr. Within the normal group (first row of table 1) seven of the ten comparisons revealed significant differences ($P < .01$) in saccharoid content. The pairs of means that were not significantly different were the fasting and 2-hr., fasting and 3-hr., and the 1-hr. and 2-hr. The remaining seven comparisons attested to the fact that saccharoid content varies significantly from

*The statistical test was an analysis of variance for a two factor experiment having repeated measurements—unweighted means solution. This method of analysis was also used for the subsequent comparison of age and weight classifications.

TABLE 1

Means and (standard deviations) of saccharoid content, Somogyi-Nelson values, and Folin-Wu values in mg./100 ml.

Type of curve	Number of patients	Time after glucose (hours) 0	½	1	2	3	All hours
				Saccharoid content			
Normal	170	13.1(7.2)	18.8(10.3)	17.4(10.4)	14.1(8.4)	11.4(7.8)	15.0(9.3)
Abnormal	260	13.5(8.2)	18.5(11.5)	22.1(12.6)	18.0(12.1)	12.6(10.9)	17.0(11.7)
Combined	430	13.4(7.8)	18.7(11.0)	20.3(12.0)	16.4(10.9)	12.1(9.8)	16.2(10.8)
				Somogyi-Nelson values			
Normal	170	77 (7.6)	117 (18.5)	109 (23.3)	82 (13.2)	68 (13.9)	90 (25.0)
Abnormal	260	85 (15.1)	138 (25.3)	163 (34.0)	134 (37.5)	93 (36.8)	122 (42.7)
Combined	430	82 (13.4)	129 (25.0)	142 (40.1)	113 (39.7)	83 (32.3)	110 (39.9)
				Folin-Wu values			
Normal	170	90 (10.2)	136 (22.6)	127 (27.8)	96 (16.1)	79 (15.1)	105 (29.2)
Abnormal	260	99 (18.0)	156 (28.9)	185 (40.3)	152 (43.4)	105 (40.0)	139 (48.2)
Combined	430	95 (16.0)	148 (28.3)	162 (45.9)	130 (44.7)	95 (34.9)	126 (44.9)

one time period to the next. For the abnormal group (second row of table 1) eight of the ten possible comparisons of pairs yielded significant differences ($P < .01$). Only the mean at fasting did not differ from the 3-hr. mean, and the ½-hr. readings did not differ from the 2-hr. readings. Again it was found that saccharoid content varied with the different time periods. Normals differed from the abnormals in their 1- and 2-hr. specimens—the abnormals being higher, but they did not differ at the fasting, ½-hr., and 3-hr. intervals. The pattern of change that occurred in both the Somogyi-Nelson and Folin-Wu curves was essentially the same as that described above for the saccharoids.

Amount of Saccharoid Content. Of the 850 readings in the normal curve group, 53 (6 per cent) exceeded 30 mg./100 ml. and 5 (0.6 per cent) were negative values (M = —7 mg.). Of the 1,300 readings in the abnormal curve group 125 (10 per cent) exceeded 30 mg. and 8 (0.6 per cent) were negative values (M = —4 mg.). The 178 readings above 30 mg. that were found in both groups, were contributed by 119 patients and only two of the thirteen negative readings had absolute values equal to or greater than 10 mg.

Constancy of Saccharoid Content. In order to investigate the consistency of the saccharoid level for an individual over the five time periods we calculated correlation coefficients. Table 2 shows that the relationships between saccharoid content and the various time periods are generally of moderate magnitude. The fasting and three-hour values show the least relationship with all other values for both groups. The highest interdependence was between the ½-, 1-, and 2-hr. determinations.

Age and Saccharoids. An analysis was done to determine whether there was any relationship between the age of the subject and his saccharoid level. Table 3 contains a summary of the relevant findings. Analysis of the data upon which table 3 was based revealed that there were generally no significant differences between the age groups within either the normal or abnormal curve groups. The only significant finding ($P < .01$) was that in the normal curve group, at one-half hour those who were less than fifty years of age had a higher saccharoid level (M = 19.9 mg.) than patients fifty years or older (M = 14.0 mg.). An analysis comparing age and Somogyi-Nelson levels within each curve type revealed no statistically significant differences between the age classifications in either group.

Weight and Saccharoids. Those persons who, for their height, weighed more than 5 per cent below the lower limit of their ideal weight[11] were classified as underweight; similarly those who weighed more than 5 per cent above the upper limit were classified as overweight. Comparisons yielded no significant differences between the weight classifications and saccharoid level. However, comparison between weight and Somogyi-Nelson level did yield some differences. For the normal curve group, at one hour, the underweight group had a lower Somogyi-Nelson value (M = 88 mg.) than either the normal weight group (M = 107 mg.; $P < .02$) or the overweight group (M = 113 mg.; $P < .001$). At the two-hour level the overweight group had higher Somogyi-Nelson values (M = 84 mg.) than the underweight group (M = 73 mg.; $P < .02$). At the other time periods no significant differences were found. For the abnormal curve group, the only noteworthy differences were at fasting. Both those of normal weight (M = 86 mg.), and the overweight (M = 85 mg.) had higher Somogyi-Nelson values than the underweight (M = 77 mg.; $P < .01$).

TABLE 2

Correlations between saccharoid contents at the various time periods

	0	½	1	2	3
0		.37	.32	.36	.44
½	.49		.59	.51	.31
1	.53	.66		.67	.48
2	.42	.53	.58		.51
3	.45	.49	.52	.49	

Abnormal curve group above diagonal: normal below. For all correlation coefficients $P < .001$

TABLE 3

Saccharoid level by curve type and age group

Age group (years)	Number of specimens	Saccharoid level (mg./100 ml.)	Standard deviation (mg.)
		Normal curves	
20-39*	430	15.5	9.9
40-49	265	15.0	9.6
50-59	90	13.9	6.7
60+	65	12.5	6.5
		Abnormal curves	
20-39*	355	17.7	12.7
40-49	325	17.2	11.7
50-59	230	17.1	12.3
60+	390	16.0	10.2

*This range was chosen because of the low frequency in the 20- to 29-yr. age group.

DISCUSSION

In both normal and abnormal groups the ingestion of glucose brought about a definite change in saccharoid values. In addition there was a statistically significant difference between the tolerance curves of the normal and abnormal groups. Not only was the magnitude of the saccharoid level different, but the shape of the curves also varied. From the ½ to the 1-hr. period saccharoid levels rose for the abnormal curves and declined for the normal.

The variability in saccharoid content in our sample of psychiatric patients is in sharp contrast to that of Wilkerson et al.[5] who found a remarkable constancy in the mean saccharoid value of normal subjects. The only hypothesis we have to explain these discrepant findings relates to the type of subjects tested. It appears that the psychiatric population reacts differently to the physiological stress of glucose loading than do normal subjects.

The variable nature of the saccharoid values at the different time intervals becomes more clear if an attempt is made to estimate the saccharoid level at one time period given the value at another period. The accuracy of the estimate would be a function of the closeness of the relationship between the known value and the one to be estimated. If they were highly related the estimate could be made with great accuracy, but if they were barely related the estimate would hardly be better than a guess made without benefit of the known value. If it were desired that the estimate be correct 95 per cent of the time, it would be necessary to allow a range of 24 mg. (± 12 mg.) for individuals with normal curves and a range of 32 mg. for those with abnormal curves.* The necessity for such a wide range to assure an adequate degree of accuracy indicates the variability of the saccharoid content during the glucose tolerance test.

The adequacy of Folin-Wu results for measuring true blood sugar varies with the time interval after glucose ingestion. A "rule of thumb" suggested by the range of saccharoid content in our data is that if one wants to ascertain true blood sugar from the Folin-Wu with 95 per cent certainty, the constants to subtract from Folin-Wu readings are as follows:

(a) Fasting: 1 and 34 mg./100 ml.
(b) ½-hour: 1 and 47 mg./100 ml.
(c) 1-hour: 2 and 47 mg./100 ml.
(d) 2-hour: 2 and 41 mg./100 ml.
(e) 3-hour: 0 and 37 mg./100 ml.

*These results were obtained using the intraclass correlation adjusted for trend and the standard error of measurement.

To illustrate, if subtracting 2 mg. from a 2-hr. Folin-Wu value supports a different diagnosis than subtracting 41 mg. the test results should be considered equivocal. However, if subtraction of both constants (for a given time period) results in two values that are both normal or both abnormal then the results may be accepted as being equivalent to true blood sugar measurement with 95 per cent certainty. If one insisted on being wrong not more than once per hundred times (99 per cent certainty) the range of constants would be much greater. For example, the 2-hr. constants would be 0 to 76 mg./100 ml. instead of 2 and 41 mg./100 ml. This is seen as corroborating the findings of Haunz and Keranen[12] who concluded that saccharoid content was not predictable from the level of blood sugar. Obviously in those instances where the Folin-Wu value is close to the borderline range between pathological and normal functioning the subtraction of a constant from the Folin-Wu value to arrive at the Somogyi-Nelson value would be a highly dubious practice.

Age: There is no significant difference in the saccharoid values for subgroups based on age. Again we find that the results in our sample differ from those of Wilkerson et al.[5] who found a slight increase in saccharoids with age. When the effect of age on Somogyi-Nelson readings was studied in both curve type groups, we found no indication that the quantity of blood sugar was influenced by age. A previous study[10] showed that an abnormal response to the glucose tolerance test occurs more frequently among the older subjects. The present study shows that once the individual is in the abnormal group, the degree of abnormality is not related to age.

Weight: The independence of weight and saccharoids in our subjects is consistent with a previously reported large scale study.[5] However, we find that the glucose content of the blood was related to weight. At certain time periods underweight subjects had significantly lower Somogyi-Nelson readings. Whether this holds true for only a psychiatric population is not known.

Frequency of Extreme Values of Saccharoids. Previous studies have reported a relatively large discrepancy between the number of instances when the saccharoid value was greater than 30 mg./100 ml. It has been variously reported as 38 per cent (N = 200),[4] 27 per cent (N = 50),[13] 39 per cent (N = 100),[12] and 11 per cent (N = 4,584).[5] Our study found 8 per cent (N = 2,150) of the saccharoid values to be 30 mg./100 ml. or greater.

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Project Head Start—A Beginning

Through July and August this past summer Project Head Start Child Development Centers in over 2,000 U. S. towns and cities worked to help children from deprived families prepare for kindergarten and first grade. The centers were set up and run by the communities, with advice and financial assistance from the Office of Economic Opportunity. They provided health, social, and teaching services of personnel ranging from highly trained professionals to local volunteers, including parents of the children, who were urged to participate.

Ninety per cent of the children had never had a physical examination, and as the project opened it was expected that every group of 100 would show some tuberculosis, four partially blind, fifteen with some sort of eye difficulties, ten partially deaf, as many as half who had never been immunized against diphtheria or tetanus, and many with dental problems. Families were often referred to available welfare services and programs for special assistance.

The continuing project covers creative, supervised play, health, and feeding programs, with a special emphasis on good nutrition. Children of the poor are often improperly or inadequately nourished; the centers try to plan, with family cooperation, a feeding program which will instill good lifetime eating habits. It may include both breakfast and lunch planned by professional nutritionists and eaten at the center.

A number of federal agencies are involved in Project Head Start. The centers are eligible for the USDA Special Milk Program and appropriate surplus foods. Personnel from the Office of Education, the Departments of Labor, Agriculture, Interior, and other agencies are on loan to the Office of Economic Opportunity to help in planning, organizing, and funding the programs. The federal financial contribution averages 90 per cent of the total cost.

Project personnel are recruited from the communities—professional doctors, dentists, and nutritionists, and nonprofessional volunteers. The National University Extension Association trained over 12,000 teachers for Project Head Start centers last spring.

The Office of Economic Opportunity hopes that Project Head Start will be the nucleus for continuing help for children from poverty stricken families, and an incentive to apply for community action grants to finance nine- to twelve-month programs of a similar nature.

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