JCI The Journal of Clinical Investigation

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J Clin Invest. 1930;9(3):363-380. https://doi.org/10.1172/JCI100310.

THE TOLERANCE OF NORMAL SUBJECTS TO LEVULOSE

Factors Influencing the Variations in Rise in Blood Sugar

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(Received for publication July 7, 1930)

MacLean and de Wesselow (1) examined the type of blood sugar curves obtained in normal and diabetic subjects. They suggest that such curves rise very slowly or fail to rise during the second thirty minute period following administration of sugar by mouth, due to stimulation of the glycogen storage mechanism which abstracts the sugar from the blood more quickly than it enters. They believe that this dormant glycogen-forming function of the liver does not begin to act until the sugar concentration approaches 140 mgm. per cent. That the glycogen-storing function is stimulated by hyperglycemic levels is supported by Foster (2). He found that oral administration of glucose, when the concentration of the blood sugar is falling, results in little or no increase in blood sugar. This observation of Foster has been amply confirmed, especially by the work of du Vigneaud and Karr (3) and later by Lennox and Bellinger (4).

That there is a relation between the fasting blood sugar level and its rise above the fasting level following the administration of levulose by mouth seems borne out by this investigation. This relationship is intimately concerned with the mechanism by which the normal subject maintains his fairly constant blood sugar level as recently shown by Jonas and his associates (5), Trimble and Maddock (6) and Sweeney (7). They show that the normal subject maintains a blood sugar almost invariably between 80 and 140 mgm. per cent during such diverse activities as rest, sleep, mild exercise, work, and eating.

Schirokauer (8) was the first investigator who studied the rise in blood sugar following the oral administration of levulose. He found

in normal subjects little or no rise in blood sugar. This work was confirmed by other German investigators (9) (10). MacLean and de Wesselow (1) found levulose to be the only sugar which caused no definite rise in blood sugar in normal subjects. Following up this work, Spence and Brett (11) administered levulose according to body weight to fasting subjects. Using MacLean's blood sugar method and 30 minute samples for two hours, they found the maximum rise in blood sugar to be 12 mgm., and the highest blood sugar obtained to be 112 mgm. per cent. Five normal subjects were studied. Tallerman (12) giving 45 grams of levulose irrespective of the weight to 15 normal subjects concluded that the minimum criteria for an abnormal response to levulose to be: (*a*) a rise in blood sugar to 135 mgm. per cent, and, (*b*) an absolute rise of 30 mgm. above the fasting level. Brown (13) giving 20 to 30 grams of levulose to children considers a rise in blood sugar of 30 per cent of the fasting level as evidence of hepatic damage.

PURPOSE OF THIS STUDY

In attempting to evaluate the results of the levulose tolerance test in a group of patients suspected of having impaired liver function (14) it was found that there was no general agreement of the criteria for interpretation of the results. It was then decided to apply the test to a group of normal subjects, large enough to be statistically treated in order to determine:

(1) The average normal levulose tolerance test.
(2) Factors influencing the type of curve obtained.
(3) The changes in tolerance to levulose on repetition of the test.
(4) Criteria for interpretation of the test.

METHOD

This investigation extended over a period of eleven months from April, 1929. During this time 81 levulose tolerance tests were performed on 49 subjects. Forty of these tests were performed on 32 convalescent patients on the wards of The Third (New York University) Medical Division of Bellevue Hospital. The subjects selected were convalescing from acute infections, who had had normal temperature for ten days and who had been "up patient" for at least three

days. For normal subjects, 17 senior medical students were studied. Forty-one tolerance tests were performed on this group. On repetition of the test the same amount of levulose was given as on the first trial, and an interval of at least 7 days was allowed between tests. Prior to the test all subjects were fasted for 14 hours and reported to the laboratory without breakfast. After a sample of fasting venous blood was obtained, 30, 40, or 50 grams of levulose dissolved in 250 cc. of water were given by mouth. Subjects weighing between 50 and 75 kilos (110 and 165 lbs.) were given 40 grams. Those weighing over 75 kilos were given 50 grams, and those under 50 kilos were given 30 grams. Venous blood samples were obtained at 30, 60, and 120 minute intervals following the administration of the levulose. The protein was precipitated with tungstic acid by the method of Folin and Wu (15) within five minutes of obtaining the sample of blood. Sugar was determined by the method of Folin and Wu (15). A Klett biocolorimeter was used and all readings were made by the same individual. The levulose used was Pfanstiehl 90 per cent grade which is "practically free from all other sugars, the impurities being calcium levulosate and moisture" (16).

RESULTS

Table 1 gives each of the individual tests arranged according to the fasting blood sugar level. The maximum blood sugar reached was 121 mgm. per cent (Test 66) in a normal subject. The fasting level in this instance was 96 mgm. giving an absolute rise of 25 mgm. in blood sugar. In test 69 a maximum blood sugar of 117 mgm. per cent was obtained with a fasting level of 97 mgm., giving an absolute rise of 20 mgm. In the remaining 79 tests (97.5 per cent) the maximum blood sugar did not exceed 115 mgm. per cent. The maximum rise in blood sugar above the fasting level was 31 mgm. (Test 1) with a fasting level of 69 mgm. per cent. It is noted that rises in blood sugar of more than 25 mgm. above the fasting level occurred in only 6 tests, (Tests 1, 2, 3, 5, 7, 13), and in each instance the fasting blood sugar was 80 mgm. per cent or less.

The average or composite of all 81 tests is given in table 2, and is graphically shown in figure 1. In this curve it will be noted that the rise in blood sugar was 10.1 mgm. occurring at the 30 minute period.

TABLE 1

*The results of 81 levulose tolerance tests on 49 subjects arranged according to the height of the fasting blood sugar level**

Test	Blood sugar				
	Fasting	30 minutes	60 minutes	120 minutes	Rise
	mgm. per cent	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*
1	69	100	90	70	31
2	70	81	95	100	30
3	71	95	97	86	26
4	74	96	81	80	12
Composite of tests 1–4	71.0	93.0	90.7	84.0	22.0‡
5	76	83	104	80	28
6	76	90	84	79	14
7	76	92	105	88	29
8	77	98	100	96	23
9	77	91	86	84	14
Composite of tests 5–9	76.4	90.8	95.8	85.4	19.4‡
Composite of tests 10–25	81.8 ±1.7	93.5 ±6.8	92.8 ±7.1	87.8 ±9.2	12.0‡
Per cent of observations within range of 1σ†	75	59	68	50	
Per cent of observations within range of 2σ	100	100	87	100	
Per cent of observations within range of 3σ	100	100	100	100	
Composite of tests 26–40	87.0 ±1.4	98.0 ±6.2	96.2 ±7.9	86.0 ±6.7	11.0‡
Per cent of observations within range of 1σ	62	78	75	75	
Per cent of observations within range of 2σ	100	100	93	100	
Per cent of observations within range of 3σ	100	100	100	100	
Composite of tests 41–61	92.0 ±1.3	101.6 ±6.3	99.4 ±9.3	90.6 ±5.5	9.6‡
Per cent of observations within range of 1σ	71	66	76	76	
Per cent of observations within range of 2σ	100	95	100	95	
Per cent of observations within range of 3σ	100	100	100	100	
Composite of tests 62–75	96.8 ±1.3	104.8 ±7.0	99.7 ±7.3	91.0 ±5.6	8.0‡
Per cent of observations within range of 1σ	64	57	85	78	
Per cent of observations within range of 2σ	100	93	93	100	
Per cent of observations within range of 3σ	100	100	100	100	

* The individual tests are omitted in the groups of sufficient size to permit of statistical analysis.

† σ = Symbol meaning the Standard Deviation derived from the formula

$$\sigma = \sqrt{\frac{\Sigma \square^2}{N}}$$

when Σ = Symbol meaning the sum of.

$\square$ = Deviation from the mean.

N = Number of observations.

‡ The rise in the composite curve.

TABLE 1—*Concluded*

Test	Blood sugar				
	Fasting	30 minutes	60 minutes	120 minutes	Rise
	mgm. per cent	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*
76	100	103	111	98	11
77	100	100	115	86	15
78	100	109	90	86	9
79	103	109	104	103	6
Composite of tests 76–79	100.8	105.2	100.5	93.2	4.4‡
80	105	98	100	93	Nil
81	112	111	102	97	Nil
Composite of tests 80–81	108.5	104.5	101.0	95.0	Nil‡

At the 60 minute period the blood sugar is practically unchanged, but at the end of the 120 minutes it has returned to slightly below the fasting level. Statistical methods (17) were applied to these data to see if the sample was of sufficient size. The standard deviation from the mean was determined for each interval. To be statistically true about 66 per cent should fall within the range of the standard deviation, and 95 and 99 per cent of all observations should fall within the range of two and three times the standard deviation respectively. In this series (table 2) the above criteria are fulfilled. The maximum blood sugar allowed by three times the standard deviation is 124 mgm. per cent. Since 97.5 per cent of all tests did not exceed 115 mgm. per cent, and the maximum blood sugar actually obtained was 121 mgm. per cent, it seems safe to assume that blood sugar values reaching 125 mgm. per cent following administration of the specified amounts of levulose to be an abnormal response.

The choosing of convalescent patients as subjects to establish a normal response to a test may be open to criticism, so we included a number of normal subjects. Figure 2 compares the composites of the curves obtained in the normal and convalescent groups. It will be noted that the curves are, for all practical purposes, identical. The greatest deviation from each other is 3 mgm. at the 60 minute period. At this point the probable error of the two composite curves is 1.35

mgm. To be significant there must be a variation of at least three times this error. Therefore the convalescent patients chosen as normal

TABLE 2

Composite curves of various groups of 81 levulose tolerance tests on 49 subjects

Group	Blood sugar				
	Fasting	30 minutes	60 minutes	120 minutes	Rise
	mgm. per cent	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*
Entire group	88.7 ±8.3	98.8 ±8.3	97.2 ±8.6	87.6 ±7.6	10.1
Per cent of observations within range of 1σ*	77	68	69	68	
Per cent of observations within range of 2σ	95	96	98	98	
Per cent of observations within range of 3σ	100	100	100	100	
Normal subjects. 41 tests on 17 subjects	89.8 ±8.3	99.4 ±8.6	95.7 ±9.1	86.6 ±6.6	9.6
Per cent of observations within range of 1σ	78	56	75	68	
Per cent of observations within range of 2σ	97	97	95	100	
Per cent of observations within range of 3σ	100	100	100	100	
Convalescent subjects. 40 tests on 32 subjects	87.6 ±7.9	98.3 ±7.7	98.8 ±7.7	88.6 ±8.2	11.1
Per cent of observations within range of 1σ	77	65	70	72	
Per cent of observations within range of 2σ	95	97	97	97	
Per cent of observations within range of 3σ	100	100	100	100	
First test on 12 normal subjects	91.9 ±10.3	100.0 ±9.4	95.4 ±7.7	89.0 ±6.8	8.1
Per cent of observations within range of 1σ	58	67	67	58	
Per cent of observations within range of 2σ	100	100	92	100	
Per cent of observations within range of 3σ	100	100	100	100	
Second test on 12 normal subjects	92.7 ±5.0	100.0 ±6.3	93.7 ±7.9	86.8 ±6.8	7.3
Per cent of observations within range of 1σ	75	67	83	75	
Per cent of observations within range of 2σ	100	92	92	92	
Per cent of observations within range of 3σ	100	100	100	100	
Third test on 12 normal subjects	89.6 ±6.2	100.9 ±8.2	97.5 ±10.1	85.2 ±5.7	11.3
Per cent of observations within range of 1σ	58	75	67	75	
Per cent of observations within range of 2σ	100	100	92	92	
Per cent of observations within range of 3σ	100	100	100	100	

* Symbol meaning the standard deviation.

subjects gave a response identical to normals, providing the two composite curves are statistically true. The curve of the convalescent

group fulfills these criteria. In the normal group at the 30 minute period not quite 66 per cent of all observations fall within the standard deviation. However, at all other points this is true. Also 95 per cent and 100 per cent fall within two and three times the standard deviation respectively. That these curves are statistically true is even more probable when it is observed that neither curve deviates more than 2 mgm. from the composite of the entire group.

Lennox and Bellinger (4) by triplicate glucose tolerance curves in non-diabetic subjects, in whom the original curve was of the pre-diabetic type, found the average of the second curves lower than the

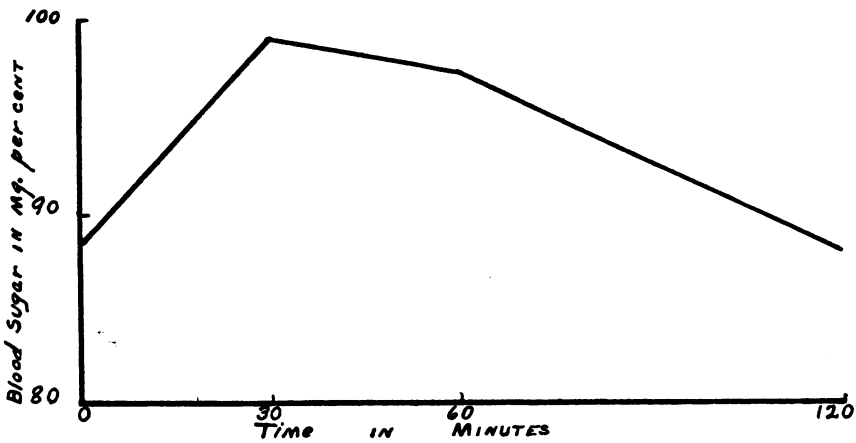

FIG. 1. COMPOSITE OF 81 LEVULOSE TOLERANCE TESTS ON 49 SUBJECTS

first, and the third lower than the second. To see if this apparent improvement in tolerance to glucose was also true for levulose the test was repeated three times on twelve normal subjects at intervals of 7 days or longer. If the tolerance to levulose can be measured by the absolute rise above the fasting level 4 subjects showed a progressive improvement in tolerance to levulose. Three subjects showed a progressive fall in tolerance by the same criterion. If one takes a progressive lowering of the height of the maximum blood sugar as improvement in tolerance, the figures for only one subject show this. By the same criterion one subject showed a progressive impairment in tolerance. By the above methods of analysis there is no evidence of a progressive

improvement in tolerance. If the composite curves for the three groups are examined (fig. 3) we find the three curves almost superimposed. The composite curves of the first tests rises 8.1 mgm., the second rises 7.3 mgm., while the third rises 11.3 mgm. above the fasting level. It is noted, however, that the maximum blood sugar in each of the three composite curves reaches approximately the same level, and variations in the rise are due to changes in the fasting blood sugar level. In all except the fasting period the greatest deviation from the composite curve of all 81 tests is 2.5 mgm. These three curves are statistically

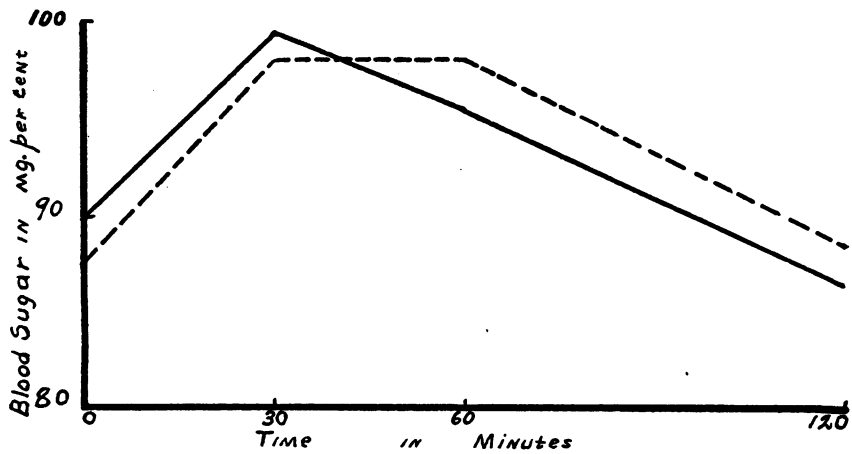

FIG. 2. COMPARISON OF THE COMPOSITE CURVES OBTAINED IN NORMAL AND CONVALESCENT SUBJECTS

Solid line: Normal subjects.
Broken line: Convalescent subjects.

analyzed in table 2. It therefore seems probable that there is no progressive improvement in tolerance to levulose in normal subjects if the tests are repeated at intervals of 7 days or greater.

It soon became apparent that there are great variations in the rise in blood sugar above the fasting level, from individual to individual, and to a less extent in the same individual. It has been previously noted in this paper that rises of more than 25 mgm. above the fasting level occurred only when the fasting blood sugar was 80 mgm. per cent or less. It was also noted that the differences in rise in blood sugar in the

composite curves in the subjects on whom triplicate curves were performed were due mainly to changes in the fasting blood sugar level, rather than to the height to which the curve rose. It appears, therefore, that after administration of levulose the blood sugar rises from whatever fasting value it may have, high or low, toward a constant "ceiling," and then falls as sugar storage is acclerated. Following this idea our data have been tabulated according to the height of the fasting blood sugar, and composites made for each group of 5 mgm. from 75 to 104 mgm. per cent. Fasting values below 75 mgm. were in-

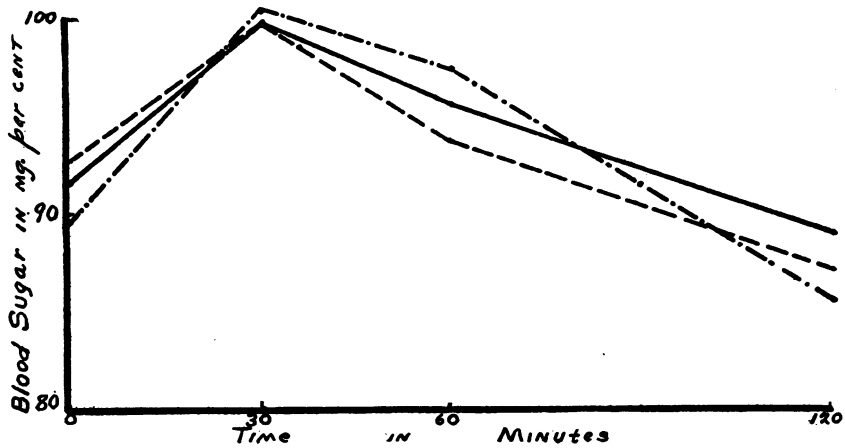

FIG. 3. TRIPLICATE LEVULOSE TOLERANCE CURVES ON 12 NORMAL SUBJECTS
Solid line: Composite curve of the first tests.
Broken line: Composite curve of the second tests.
Dash-dot-dash line: Composite curve of the third tests.

cluded in one group, as were those of 105 mgm. or over. Figure 4 gives the various composite curves obtained. It is clear that the higher the fasting blood sugar level the smaller is the rise in blood sugar above that level. This relationship is better shown in the ogive correlation in figure 5. With a fasting level below 75 mgm. note that the rise is 22 mgm., while in the group with a fasting level above 104 mgm. note that the rise is nil. In the groups between 80 and 99 mgm. this relationship is statistically true, and therefore probably not the result of random sampling. However, for the two ex-

treme groups of high and low fasting values the number of curves is too small to permit conclusions to be drawn. It may be calculated that 400 tolerance tests would be required to produce a minimum of ten cases in each of these groups if the distribution of the fasting blood sugar values remained as in this group of 81 tests.

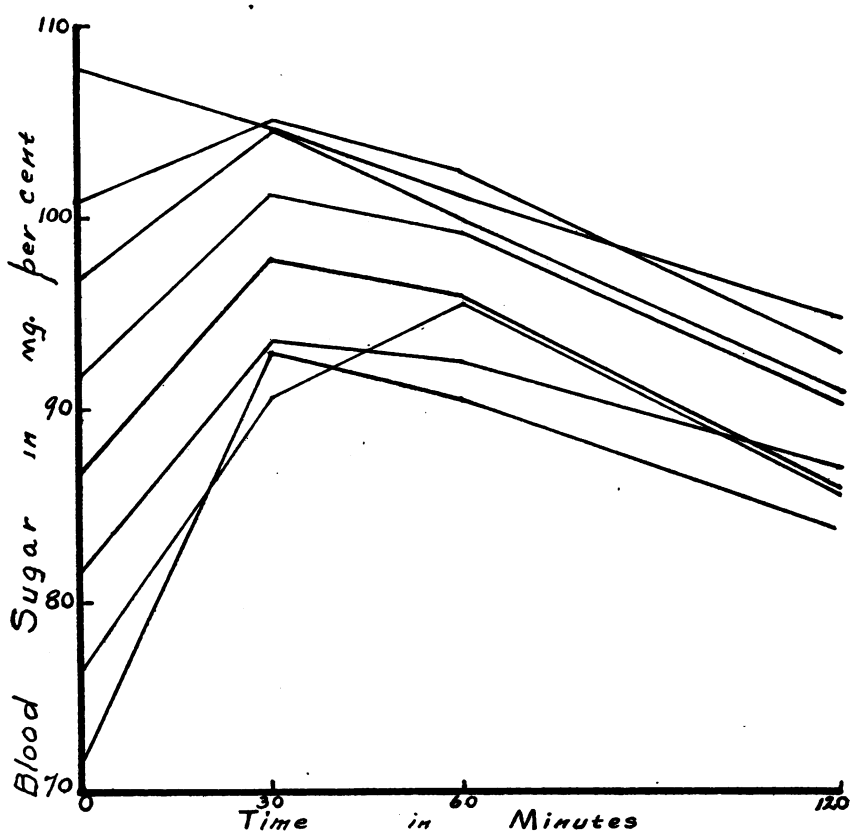

FIG. 4. RELATION OF THE FASTING BLOOD SUGAR LEVEL TO THE RISE IN BLOOD SUGAR FOLLOWING ORAL ADMINISTRATION OF LEVULOSE

Since extremely low and extremely high fasting levels cannot be obtained spontaneously with sufficient frequency, we extended this series by raising the fasting blood sugar to slightly over 100 mgm. per cent by giving glucose prior to the administration of levulose. In a

preliminary test on a normal subject using 20 grams of glucose the blood sugar rose from a fasting level of 89 mgm. to 109 mgm. in 30 minutes, and then progressively fell to 81 mgm. in two hours (Curve 2, fig. 6). Ten days later this same individual was tested to 40 grams of glucose when the blood sugar rose to 104 mgm. in 15 minutes, to 138 in 30 minutes, and then progressively fell, reaching 85 mgm. at the two hour period (Curve 1, fig. 6). It therefore seemed that 20 grams of glucose administered by mouth would raise the blood sugar sufficiently

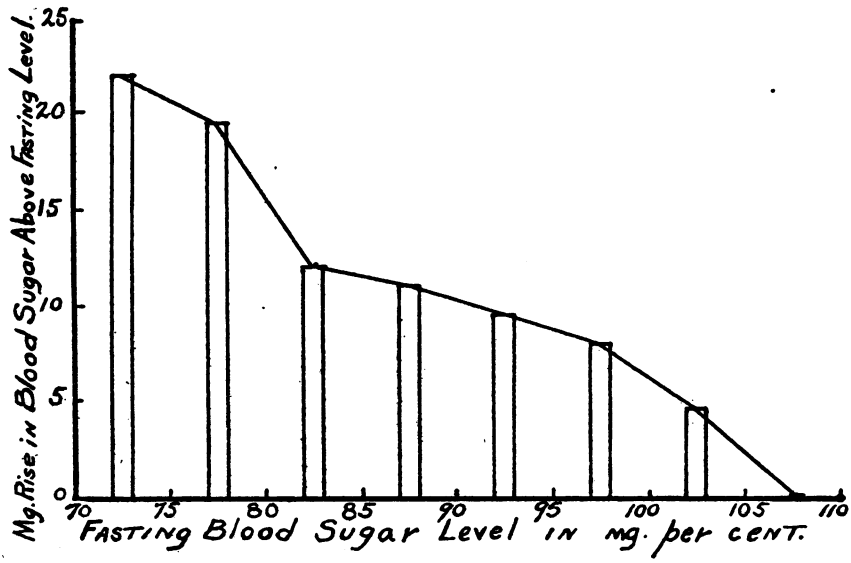

FIG. 5. OGIVE CORRELATION OF THE FASTING BLOOD SUGAR LEVEL TO THE RISE IN BLOOD SUGAR FOLLOWING ORAL ADMINISTRATION OF LEVULOSE

to obtain a "fasting" blood sugar of over 100 mgm. per cent within 30 minutes. Ten normal subjects volunteered for this study. In each of these subjects the administration of the preliminary dose of 20 grams of glucose preceded the administration of the levulose by 30 minutes. In the composite curve of the results obtained (Curve 4, fig. 6) the blood sugar rose from a fasting level of 84.4 mgm. to slightly over 100 grams per cent in thirty minutes. At this time 40 mgm. of levulose were given. There was in the composite curve no rise following the administration of the levulose, but a progressive fall very much like the

curve obtained when only 20 grams of glucose (Curve 2, fig. 6) was given alone. The individual curves are given in table 3. In 4 sub-

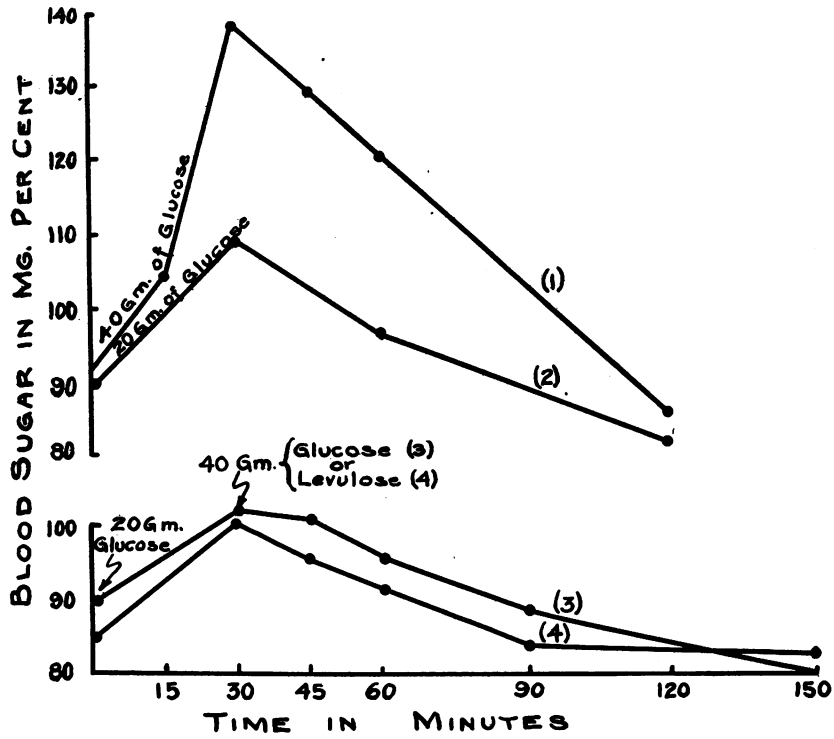

FIG. 6. CURVES ILLUSRTATING THE EFFECT OF ARTIFICIAL ELEVATION OF THE BLOOD SUGAR LEVEL PRIOR TO THE LEVULOSE OF GLUCOSE TOLERANCE TESTS

Curve 1. Blood sugar curve following oral administration of 40 grams of glucose.

Curve 2. Blood sugar curve following oral administration of 20 grams of glucose.

Curve 3. Composite curve of the effect of administering 20 grams of glucose 30 minutes prior to the glucose tolerance test in 10 normal subjects.

Curve 4. Composite curve of the effect of administering 20 grams of glucose 30 minutes prior to the levulose tolerance test in 10 normal subjects.

jects there was a slight rise at the 45 minute period above the 30 minute period. In these subjects, however, the 30 minute blood sugar did not exceed the average for the group, thus agreeing very closely

TABLE 3

Effect of administration of 20 grams of glucose thirty minutes prior to levulose tolerance test

Subject	Blood sugar							
	Fasting		30 minutes		45 minutes	60 minutes	90 minutes	150 minutes
	mgm. per cent	20 grams glucose	*mgm. per cent*	40 grams levulose	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*
50	87		94		88	100	82	87
51	88		116		98	96	102	102
52	87		89		93	82	80	86
53	78		98		93	80	80	76
54	80		95		96	87	76	79
55	75		100		87	82	80	80
56	86		103		84	86	80	74
57	94		109		100	92	86	80
58	88		100		106	100	91	82
59	81		98		100	97	80	81
Composite...	84.4		100.2		94.5	91.2	83.7	82.4

TABLE 4

Effect of administration of 20 grams of glucose thirty minutes prior to glucose tolerance test

Subject	Blood sugar							
	Fasting		30 minutes		45 minutes	60 minutes	90 minutes	150 minutes
	mgm. per cent	20 grams glucose	*mgm. per cent*	40 grams glucose	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*	*mgm. per cent*
50	101		103		105	93	71	90
51	95		111		105	100	93	83
52	86		114		104	96	92	77
53	90		114		112	105	84	83
54	83		90		103	95	94	58
55	83		88		90	94	94	75
56	89		89		81	80	81	80
57	96		109		100	90	82	71
58	94		99		101	100	92	68
59	84		102		100	98	90	86
Composite...	90.1		101.9		100.1	95.1	87.3	79.8

with the results obtained in those tests having a "natural" fasting blood sugar of 95 to 104 mgm. The individuals having a blood sugar at the thirty minute period above the average for the group invariably

showed a lowering at the 45 minute period, agreeing very closely with the composite curve of those individuals having a "natural' fasting blood sugar of 105 mgm. or over. These results were so consistent that it was decided to substitute the same amount of glucose for the levulose administered at the thirty minute period. The same subjects again volunteered and a glucose tolerance test was preceded by thirty minutes by 20 grams of glucose. It was our purpose to show that if glucose was administered to subjects with a high normal blood sugar that a hyperglycemia would result. Curve 3 in figure 6 shows that such was not the case, but the curve was practically identical with the case when levulose was administered. Table 4 gives the individual curves. It is noted, however, that when glucose was given the fall during the first portion of the curve was possibly not as rapid as when levulose was given.

DISCUSSION

The factor or factors influencing the type of blood sugar curve obtained by various sugars, notably glucose, levulose, and galactose have been variously explained. Folin and Berglund (18) consider absorption of sugar from the blood by the tissues rather than glycogen formation the immediate reason the administered sugar fails to accumulate in the blood. The slight rise in blood sugar when levulose is administered is explained by the fact that the tissues are practically free from levulose, and relatively "saturated" with glucose. This hypothesis has been questioned by Foster (2), Reinhold and Karr (19) and by Bodansky (20) who show that there is a greater rise in blood sugar with galactose than with glucose. Rienhold and Karr (19) believe that the ability of various carbohydrates to produce hyperglycemia varies directly with their rate of absorption, and inversely with their ability to form glycogen and their ease of being oxidized. Levulose is absorbed slowly but, being a good glycogen former and readily oxidized, causes only a slight rise in blood sugar. Cori and Cori (21) have shown in rats that levulose is absorbed more slowly than glucose and that galactose is absorbed more rapidly than glucose after oral administration. In four hours time approximately 16 per cent of the glucose absorbed is deposited in the liver as glycogen (21) while 40 per cent of the levulose and 5 per cent of the galactose absorbed are deposited in the liver as glycogen.

The facts presented in this paper seem to add additional information upon the type of blood sugar curve obtained by glucose and levulose, and by inference the explanation for the type of curve obtained with galactose. We may assume first, that there is an excitatory ceiling or level of blood sugar in normal subjects between 95 and 110 mgm. per cent at which the sugar storage mechanism is stimulated. We may further assume, since crystalline insulin itself shows a latent period when injected intravenously (22), that an interval of 10 to 15 minutes elapses after this excitatory ceiling is reached before the sugar storage mechanism begins to effect a significant fall in blood sugar. In this view sugar administered per os would drive the blood sugar above the excitatory ceiling because of the continued absorption during the latent period. Those sugars which are most rapidly absorbed (galactose) would overshoot the ceiling considerably and the blood sugar curve would not start to fall until a level of about 160 mgm. per cent had been reached: sugars of slower absorption (glucose) would overshoot the ceiling less (140 mgm. per cent) and slowly absorbed sugar (levulose) would overshoot it but little (115 mgm. per cent). MacLean and de Wesselow (1) believe the level of blood sugar at which the carbohydrate mechanism is stimulated to be about 140 mgm. following administration of glucose. We have shown that if the blood sugar is raised by a preliminary dose of 20 grams of glucose to 100 mgm. per cent, a second dose of 40 grams is followed by an immediate fall, and not a rise to about 140 mgm. as would be expected by the explanation of MacLean and de Wesselow. This result agrees with our interpretation that the sugar storage mechanism is stimulated at a blood sugar level of 95 to 110 mgm. per cent, and was therefore active when the second dose of sugar was given. The high blood sugar level obtained at the thirty minute period when 40 grams of glucose alone was given (fig. 6, Curve I) is the result of an overshooting of the excitatory ceiling during the latent period in consequence of its absorption during the 15 to 30 minute period.

This hypothesis also explains why the rise in the blood sugar above the fasting level following the administration of levulose varies inversely with the height of the fasting blood sugar level. In an individual having a very low fasting level the rise must of necessity be comparatively great before a fall occurs since the storage mechanism

probably remains dormant until a level of 95 to 110 mgm. has been reached. This hypothesis seems to explain the progressive fall in blood sugar in the group having a fasting level of 105 mgm. or more.

SUMMARY AND CONCLUSIONS

Ninety-one levulose tolerance tests and 12 glucose tolerance tests have been performed on normal subjects under a variety of conditions. Results have been tabulated according to the fasting blood sugar level with the following conclusions:

1. In normal subjects the maximum blood sugar following administration of 30 to 50 grams (based on body weight) of levulose by mouth rarely exceeds 115 mgm. per cent.

2. A rise in blood sugar to 125 mgm. per cent or over should be considered an abnormal response to the oral administration of levulose.

3. In the group of convalescent subjects included in this study the levulose tolerance was the same as in the normal subjects studied.

4. Triplicate levulose tolerance tests performed on normal subjects 7 or more days apart show no significant variation in their blood sugar curves.

5. In normal subjects the rise in blood sugar above the fasting level following the oral administration of levulose varies inversely with the height of the fasting blood sugar level.

6. It seems probable that there is a level of blood sugar varying from 95 to 110 mgm. per cent, which when exceeded stimulates the sugar storage mechanism to clear the blood rapidly of its excess sugar. A period of 10 to 15 minutes elapses after this excitatory ceiling is reached before the sugar storage mechanism begins to cause a significant fall in blood sugar. The rise in blood sugar above this level depends upon the rapidity of absorption of the sugar administered. The rapidity with which the blood sugar falls from its peak probably depends upon the glycogen forming ability of the sugar used.

BIBLIOGRAPHY

1. MacLean, H., and de Wesselow, O. L. V., Quart. J. Med., 1921, xiv, 103. The Estimation of Sugar Tolerance.
2. Foster, G. L., Proc. Soc. Exp. Biol. and Med., 1921–22, xix, 408. Blood Sugar Studies.

Ibid., J. Biol. Chem., 1923, lv, 291. Studies of Carbohydrate Metabolism. I. Some Comparisons of Blood Sugar Concentrations in Venous Blood and in Finger Blood.

Ibid., J. Biol. Chem., 1923, lv, 203. Studies on Carbohydrate Metabolism. II. An Interpretation of the Blood Sugar Phenomena Following the Ingestion of Glucose.

3. du Vigneaud, V., and Karr., W. J., J. Biol. Chem., 1925, lxvi, 281. Carbohydrate Utilization. Rate of Disappearance of d-Glucose from the Blood.
4. Lennox, W. G., and Bellinger, M., J. Biol. Chem., 1927, lxxiii, 237. Stimulation of the Sugar Regulating Mechanism as Shown by Duplicate Blood Sugar Curves.

Ibid., J. Clin. Invest., 1927, iv, 331. Repeated Blood Sugar Curves in Non-Diabetic Subjects.

5. Jonas, L., Miller, T. G., and Teller, I., Arch. Int. Med., 1925, xxxv, 289. All Day Blood Sugar Curves in NonDiabetic Individuals and in Diabetic Patients with and without Insulin.
6. Trimble, H. C., and Maddock, S. J., J. Biol. Chem., 1929, lxxxi, 595. The Fluctuations of the Capillary Blood Sugar in Normal Young Men During a Twenty-four Hour Period (Including a Discussion of the Effect of Sleep and Mild Exercise).
7. Sweeney, J. S., Arch. Int. Med., 1930, xlv, 257. Twenty-four-hour Blood Sugar Variations in Fasting and Non Fasting Subjects.
8. Schirokauer, H., Ztschr. f. klin. Med., 1913, lxxviii, 462. Zur Funktionsprüfung der Leber. Die alimentäre Lävulose- Hyperglykämie.
9. Bergmark, G., Jahrb. f. kinderh., 1914, lxxx, 373. Zuckerresportion und Blutzuckerspiegel.
10. Isaac, S., Med. Klin., 1920, xvi, 1211. Theoretisches und klinisches zur Stellung der Lävulose im Stoffwechsel.
11. Spence, J. C., and Brett, P. C., Lancet, 1921, ii, 1362. The Use of Laevulose as a Test for Hepatic Inefficiency.
12. Tallerman, K. H., Quart. J. Med., 1923, xvii, 37. The Laevulose Test for Liver Efficiency and an Investigation of the Hepatic Condition in Pregnancy.
13. Brown, M. J., Arch. Dis. Childhood, 1928, iii, 81. Hepatic Efficiency. The Value of the Haemoclastic and the Laevulose Tests in Childhood.

Ibid., 1929, iv, 76. Laevulose Tests in Rheumatic and Choreic Children.

14. Jolliffe, N., J. Clin. Invest., 1930, viii, 419. Liver Function in Congestive Heart Failure.
15. Folin, O., and Wu. H., J. Biol. Chem., 1920, xli, 367. A Simplified and Improved Method for Determination of Sugar.
16. Pfanstiehl Chemical Co., Personal Communication.
17. Dunn, H. L., Physiol. Rev., 1929, ix, 275. Application of Statistical Methods in Physiology.

18. Folin, O., and Berglund, H., J. Biol. Chem., 1927, li, 213. Some New Observations and Interpretations with Reference to Transportation, Retention, and Excretion of Carbohydrates.
19. Reinhold, J. G., and Karr, W. J., J. Biol. Chem., 1927, lxxii, 345. Carbohydrate Utilization. II. Rate of Disappearance of Various Carbohydrates from the Blood.
20. Bodansky, M., J. Biol. Chem., 1923, lvi, 387. Fructose, Glucose, and Galactose Tolerance in Dogs.
Ibid., 1923, lviii, 515. The Effect of Chloroform and Phosphorus Poisoning on Carbohydrate Tolerance.
Ibid., 1924, lviii, 799. The Action of Hydrazine and Some of Its Derivatives in Producing Liver Injury as Measured By the Effect on Levulose Tolerance.
21. Cori, C. F., and Cori, G. T., J. Biol. Chem., 1927, lxxii, 597. The Fate of Sugar in the Animal Body. IV. The Tolerance of Normal and Insulinized Rats for Intravenously Injected Glucose and Fructose.
Ibid., 1928, lxxvi, 755. VIII. The Influence of Insulin on Utilization of Glucose, Fructose, and Dihydroxyacetone.
Ibid., 1929, lxxxv, 275. The Influence of Insulin and Epinepherine on Glycogen Formation in the Liver.
Ibid., J. Biol. Chem., 1927, lxxiii, 555. VI. Sugar Oxidation and Glycogen Formation in Normal and Insulinized Rats during Absorption of Fructose.
22. Neuwirth, I., Co Tui, F., and Wallace, G. B., Proc. Soc. Exp. Biol. and Med., 1929, xxvii, 194. The So-called Hyperglycemic Action of Insulin.