Reactive Hypoglycemia in Women

Results of a Health Survey

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SUMMARY

1. Reactive hypoglycemia (for the purpose of this evaluation: blood glucose levels of 59 mg. per 100 ml. or less at the second, third, fourth or fifth hours of an oral glucose tolerance test) occurred in about 17 per cent of a group of 285 adult females participating in a survey.

2. This degree of reactive hypoglycemia occurred more often in the younger members (twenty to forty-five years of age), i.e., in 19 per cent of those with body weight less than 146 lbs. and in 31 per cent of those whose weight was above this range. Hypoglycemia was distinctly less frequent in the older nonoverweight females (2 per cent) and in the older obese group (11 per cent).

3. The lesser frequency of this degree of reactive hypoglycemia in the older nonobese and obese groups is attributable to higher fasting levels of glucose and to greater increments in blood glucose levels following upon an oral glucose load and not to any decrease in the usual increments in insulin.

4. In the two younger groups (twenty to forty-five years of age and either less than 146 lbs. or 146 lbs. or more in weight), those with reactive hypoglycemia as defined above had lower fasting blood glucose levels. This fact alone accounted for the subsequent occurrence of hypoglycemia. This conclusion is supported by the finding that the responses of those with and those without the stated degree of hypoglycemia are indistinguishable in terms of increments in blood glucose, increments in insulin, and in the ratios of the two.

5. Our data permit the generalization that blood glucose levels between 59 and 41 mg. per 100 ml. in the later hours of an oral glucose tolerance test are so common in young individuals, nonobese and obese, that this must be taken into account in any evaluation of so-called functional or reactive hypoglycemia in persons of this age. This degree of hypoglycemia is much less frequent in persons above forty-five years of age. DIABETES *20*:428-34, June, 1971.

Decreases in blood sugar in the late phases of a glucose tolerance test often reach levels below the starting values. It is not known when such decreases represent an abnormal degree of hypoglycemia, for control data for the assessment of the origins and significance of low blood glucose levels during an oral glucose tolerance test are lacking.

The studies herein presented describe the frequency of an arbitrarily selected level of reactive hypoglycemia in a control population of adult females in relation to age, body weight, and glucose tolerance, and the serum insulin and growth hormone responses to oral carbohydrate.

MATERIALS AND METHODS

Oral glucose tolerance tests were performed in 285 adult female participants in a health survey. Glucose, 1.75 gm. per kilogram of body weight, was taken *per os* as a 50 per cent solution. Samples of venous blood withdrawn at the zero, one-half, one, two, three, four and five hour points of the test were analyzed for blood glucose[1] and serum insulin and growth hormone.[2]

The results of the oral glucose tolerance tests are expressed in terms of the Glucose Tolerance Sum for two and for five hours[3-5]: the sum of the venous blood glucose levels at zero, one-half, one, and two hours ($GTS_{0\text{-}2\ hr}$) and at zero, one-half, one, two, three, four and five hours ($GTS_{0\text{-}5\ hr}$). In previous publications,[3-5] we have related $GTS_{0\text{-}2\ hr.}$ values to the criteria of the World Health Organization,[6] the United States Public Health Service,[7] The British Diabetic Association,[8] and Fajans and Conn[9] for a normal and an abnormal glucose tolerance. We have found that when the $GTS_{0\text{-}2\ hr.}$ value is 500 or less, the probability of glucose intolerance based on these four sets of criteria is extremely low,

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TABLE 1

Age and body weight in all four subgroups of an adult female nonpatient population

Group	No.	Age (years) Min-Max	Age (years) X ± SD	Body Weight (lbs.) Min-Max	Body Weight (lbs.) X ± SD	*Reactive* Hypogly. Per cent
A	122	20-45	30.7 ± 6.7	95-145	124.6 ± 13.7	18.8
B	43	46-70	56.2 ± 6.9	90-145	124.7 ± 14.7	2.3
C	58	20-44	31.1 ± 6.5	148-270	179.8 ± 23.4	31.0
D	62	46-70	64.9 ± 3.0	146-219	170.0 ± 18.1	11.3

i.e., less than 2 per cent. As the $GTS_{0\text{-}2\ hr.}$ values increase above 500, the frequency of glucose intolerance rises progressively until at $GTS_{0\text{-}2\ hr.}$ values of 800, there is a high probability (greater than 98 per cent) that the test would be deemed abnormal by all four standards.[8-5]

The data are presented in terms of:

Zero-Hour Insulin Level;

Increment in insulin at the half-hour point of the test ($\Delta I_{0\text{-}1/2\ hr.}$);

Sum of the increments in insulin at the one-half, one and two hour points of the test ($\Delta I_{0\text{-}2\ hr.}$), at the third, fourth and fifth hours ($\Delta I_{3\text{-}5\ hr.}$), and during the entire test ($\Delta I_{0\text{-}5\ hr.}$);

Ratio of the sum of the increments in blood glucose (ΔBl.S.) to the sum of the increments in serum insulin (ΔI) during the intervals cited above:

$$\left(\frac{\Delta Bl.S.}{\Delta I}\right)_{0\text{-}2\ hr.} \quad \left(\frac{\Delta Bl.S.}{\Delta I}\right)_{3\text{-}5\ hr.} \quad \left(\frac{\Delta Bl.S.}{\Delta I}\right)_{0\text{-}5\ hr.}$$

Growth hormone at zero hour;

Growth hormone peak;

TABLE 2

Blood glucose and serum insulin and growth hormone levels prior to and during oral glucose tolerance test in nonoverweight (<146 lbs.) adult females participating in a survey

Index	Group A Age: 20-45 yrs. Body Weight: <146 lbs. X ± SD (n)	Group B Age: 46-70 yrs. Body Weight: <146 lbs. X ± SD (n)
Fasting Blood Sugar (mg. per 100 ml.)	*79.9 ± 10.8 (120)	*84.7 ± 12.3 (43)
Glucose Tolerance Sum (GTS)		
0-2 hrs.	†387.5 ± 45.9 (122)	†474.2 ± 111.4 (43)
0-5 hrs.	†613.3 ± 47.6 (122)	†741.5 ± 133.8 (43)
3-5 hrs.	†237.2 ± 24.5 (122)	†268.5 ± 35.8 (43)
ΔBlood Sugar (ΔBl.S.) (mg. per 100 ml.)		
0-2 hrs.	†71.2 ± 32.6 (122)	†137.2 ± 97.5 (43)
0-5 hrs.	†67.7 ± 53.7 (122)	†164.9 ± 110.2 (43)
3-5 hrs.	‡16.4 ± 21.7 (122)	‡28.9 ± 31.2 (43)
Fasting Insulin (microunits/ml.)	15.8 ± 11.3 (120)	18.9 ± 27.5 (43)
ΔInsulin (ΔI) (microunits/ml.)		
0-1/2 hr.	63.6 ± 50.6 (120)	52.3 ± 32.1 (43)
0-2 hrs.	165.0 ± 92.4 (122)	164.5 ± 92.7 (43)
0-5 hrs.	202.0 ± 112.6 (122)	215.9 ± 131.3 (43)
3-5 hrs.	39.3 ± 36.5 (122)	51.6 ± 57.2 (43)
$\frac{\Delta Blood\ Sugar}{\Delta Insulin}\ \left(\frac{\Delta Bl.S.}{\Delta I}\right)$		
0-2 hrs.	†0.58 ± 0.55 (122)	†1.14 ± 1.43 (43)
0-5 hrs.	‡0.66 ± 0.87 (122)	‡1.12 ± 1.45 (43)
3-5 hrs.	0.77 ± 1.49 (122)	0.68 ± 0.94 (43)
Growth Hormone, Fasting	9.2 ± 11.8 (120)	8.0 ± 10.4 (43)
Growth Hormone, Peak	17.0 ± 13.6 (120)	14.1 ± 13.4 (43)
Growth Hormone Sum (0-5 hrs.)	43.7 ± 26.2 (120)	43.2 ± 31.6 (43)

Differences between means on the same horizontal line marked by symbols are statistically significant by t or t-like test (Li, C.C.: Experimental Statistics. McGraw-Hill, 1964).

*$p < 0.05$

†$p < 0.001$

‡$p < 0.01$

TABLE 3

Blood glucose and serum insulin and growth hormone levels prior to and during oral glucose tolerance test in overweight (> 145 lbs.) adult females participating in a survey

Index	Group C (Age 20-45 yrs.) Body Weight: > 145 lbs. X ± SD (n)	Group D (Age 46-70 yrs.) Body Weight: > 145 lbs. X ± SD (n)
Fasting Blood Sugar (mg. per 100 ml.)	*81.5 ± 9.6 (58)	*94.1 ± 26.6 (62)
Glucose Tolerance Sum (GTS)		
0-2 hrs.	*418.9 ± 88.4 (58)	*512.9 ± 166.9 (62)
0-5 hrs.	*666.6 ± 111.5 (58)	*812.0 ± 268.8 (62)
3-5 hrs.	*247.0 ± 32.9 (58)	*299.2 ± 111.1 (62)
ΔBlood Sugar (ΔBl.S.) (mg. per 100 ml.)		
0-2 hrs.	†92.4 ± 64.6 (58)	†135.1 ± 93.4 (62)
0-5 hrs.	†111.9 ± 80.3 (58)	†174.5 ± 137.8 (62)
3-5 hrs.	‡18.9 ± 23.2 (58)	‡39.4 ± 56.2 (62)
Fasting Insulin	21.7 ± 20.1 (58)	24.7 ± 37.1 (62)
ΔInsulin (ΔI) (microunits/ml.)		
0-1/2 hr.	72.9 ± 55.6 (58)	64.6 ± 56.0 (62)
0-2 hrs.	251.6 ± 219.9 (58)	224.6 ± 154.2 (62)
0-5 hrs.	345.1 ± 260.0 (58)	304.9 ± 187.6 (62)
3-5 hrs.	95.3 ± 77.4 (58)	70.4 ± 72.8 (62)
$\frac{\Delta\text{Blood Sugar}}{\Delta\text{Insulin}}$ $\left(\frac{\Delta\text{Bl.S.}}{\Delta\text{I}}\right)$		
0-2 hrs.	0.71 ± 1.51 (58)	1.06 ± 1.70 (62)
0-5 hrs.	0.66 ± 1.57 (58)	0.96 ± 1.56 (62)
3-5 hrs.	0.52 ± 1.32 (58)	0.78 ± 1.57 (62)
Growth Hormone, Fasting	5.3 ± 5.2 (58)	5.4 ± 5.1 (62)
Growth Hormone, Peak	12.3 ± 9.7 (58)	10.1 ± 7.0 (62)
Growth Hormone Sum (0-5 hrs.)	41.1 ± 36.2 (58)	36.2 ± 22.7 (62)

*$p < 0.001$
†$p < 0.01$
‡$p < 0.05$

Growth hormone sum at the zero, one-half, one, two, three, four and five hours.

RESULTS

In search for factors predisposing to or protecting against low blood glucose levels following an oral carbohydrate load, we have arbitrarily taken glucose levels of 59 mg. per 100 ml. or less recorded during the second to the fifth hours of the oral glucose tolerance test to represent "undue reactive hypoglycemia." None of the subjects developed symptoms in association with decreases of this magnitude.

The frequency of this degree of hypoglycemia in the total population of 285 women ranged from 2 to 31 per cent, depending on age. Thus, in persons below the age of forty-six years, undue hypoglycemia occurred in 19 per cent of those who were not overweight and in 31 per cent of those who were overweight (table 1). In individuals above the age of forty-five years, reactive hypoglycemia of the degree designated above developed in 2 per cent of those below 146 lbs. and in 11 per cent of those whose body weight was 146 lbs. or higher. The lowest blood glucose levels in the patients with reactive hypoglycemia as defined above during the second to the fifth hour of the test ranged from 59 to 41 mg. per 100 ml. with a mean of 54 ± 4 mg. per 100 ml.

From our studies we are unable to state whether or not mild glucose intolerance increases the frequency of this type of reactive hypoglycemia since $GTS_{0\text{-}2\ hr.}$ values > 500 occurred in only four of our subjects, i.e., one in Group C and three in Group D.

A. *Variables Protective Against Reactive Hypoglycemia*

Comparison with their younger nonoverweight counterparts (Group A) reveals that the lesser frequency of reactive hypoglycemia as defined above in the older nonoverweight subjects (Group B) may be related to higher zero-hour blood glucose levels and to greater blood glucose increments (ΔBl.S.) during the oral glucose tolerance tests, and not to changes in insulin levels. The insulin increments (ΔI) following oral glucose were about the same in the two groups (table 2). The blood glucose increments in Group B were high enough to increase the $\frac{\Delta\text{Bl.S.}}{\Delta\text{I}}$ ratios for 0.2 and 0.5 hours.

TABLE 4

Blood glucose and serum insulin and growth hormone levels in nonoverweight females during oral glucose tolerance tests without and with reactive hypoglycemia (*Bl. Glucose < 59 mg. per 100 ml.*)

Index		Group A Age 20-45 yrs.; B. Wgt. < 146 lbs. Bl. Gluc. >60 mg. per 100 ml. X ± SD (n)	Group A Age 20-45 yrs.; B. Wgt. < 146 lbs. Bl. Gluc. <59 mg. per 100 ml. X ± SD (n)	Group B Age 46-70 yrs.; B. Wgt. < 146 lbs. Bl. Gluc. > 60 mg. per 100 ml. X ± SD (n)	Group B Age 46-70 yrs.; B. Wgt. < 146 lbs. Bl. Gluc. < 59 mg. per 100 ml. X ± SD (n)
Fasting Blood Sugar		*81.6 ± 10.4 (97)	*72.8 ± 11.4 (23)	85.4 ± 12.4 (42)	70 (1)
GTS	0-2 hr.	391.6 ± 47.0 (99)	370.1 ± 45.3 (23)	473.5 ± 112.0 (42)	478 (1)
	0-5 hr.	*634.9 ± 64.8 (99)	*580.2 ± 50.8 (23)	744.1 ± 134.9 (42)	702 (1)
	3-5 hr.	*243.3 ± 27.0 (99)	*210.1 ± 14.8 (23)	270.6 ± 36.6 (42)	224 (1)
ΔBl.S.	0-2 hr.	67.6 ± 39.8 (99)	83.8 ± 41.6 (23)	134.8 ± 94.4 (42)	198 (1)
	0-5 hr.	83.5 ± 53.6 (99)	99.3 ± 54.5 (23)	163.6 ± 109.6 (42)	223 (1)
	3-5 hr.	16.7 ± 22.1 (99)	15.4 ± 20.0 (23)	29.0 ± 31.3 (42)	25 (1)
Fasting Insulin		16.9 ± 13.1 (97)	11.6 ± 3.8 (23)	19.3 ± 27.1 (42)	4 (1)
ΔI	0-1/2 hr.	62.8 ± 52.6 (97)	67.1 ± 42.5 (23)	52.7 ± 33.6 (42)	42 (1)
	0-2 hr.	164.0 ± 96.9 (99)	171.6 ± 73.3 (23)	165.4 ± 91.1 (42)	132 (1)
	0-5 hr.	202.4 ± 117.4 (99)	212.0 ± 98.6 (23)	217.8 ± 129.7 (42)	164 (1)
	3-5 hr.	39.4 ± 36.3 (99)	40.4 ± 30.1 (23)	52.4 ± 56.1 (42)	32 (1)
$\frac{\Delta Bl.S.}{\Delta I}$					
	0-2 hr.	0.59 ± 0.60 (99)	0.56 ± 0.34 (23)	1.13 ± 1.44 (42)	1.50 (1)
	0-5 hr.	0.62 ± 0.85 (99)	0.81 ± 0.96 (23)	1.10 ± 1.46 (42)	1.36 (1)
	3-5 hr.	0.78 ± 1.56 (99)	0.70 ± 1.18 (23)	0.67 ± 0.95 (42)	0.78 (1)
Growth Hormone, Fasting		9.5 ± 13.0 (97)	7.8 ± 6.8 (23)	8.0 ± 10.5 (42)	6 (1)
Growth Hormone, Peak		17.1 ± 14.7 (97)	16.6 ± 9.3 (23)	14.2 ± 13.5 (42)	11 (1)
Growth Hormone Sum		44.1 ± 28.2 (97)	41.8 ± 17.9 (23)	43.5 ± 31.8 (42)	31 (1)

*$p < 0.01$

Similarly, the relative rarity of reactive hypoglycemia of this degree in the older overweight category (Group D) compared to the younger overweight individuals (Group C) is related to the same reasons, i.e. higher zero-hour blood glucose levels and higher increments in blood sugar following the oral administration of glucose (table 3).

As in the younger and older nonoverweight individuals comprising Groups A and B, the insulin responses of Groups C and D to the rises in blood glucose were of the same orders of magnitude (table 3). Hence, as in Groups A and B, increased insulinemia was not a factor predisposing to reactive hypoglycemia in Groups C and D.

In neither the nonobese nor the obese groups can changes in serum growth hormone, i.e., in the fasting level, in the peak value, or in the sum of growth hormone levels recorded during the glucose tolerance test, be invoked as variables in the presence or absence of this degree of reactive hypoglycemia.

B. *Findings in Younger Nonoverweight Subjects Without and with Reactive Hypoglycemia*

Reactive hypoglycemia of the magnitude cited occurred in approximately 19 per cent of these young nonoverweight adult females. Fasting blood glucose levels were slightly lower in those in Group A (twenty to forty-five years of age and body weight between 101 and 145 lbs.) who developed reactive hypoglycemia following an oral carbohydrate load, i.e. 72.8 versus 81.6 mg. per 100 ml. in those without reactive hypoglycemia (table 4). Also, during the latter hours of this five-hour test, the blood glucose values were significantly lower in those with the reactive hypoglycemia. This is reflected in the $GTS_{0\text{-}5\ hr.}$ values of 580 versus 634 and in the $GTS_{3\text{-}5\ hr.}$ values of 210 and 243 in those with and those without reactive hypoglycemia. Such lower blood glucose levels in the latter part of the test could be anticipated from the criterion of reactive hypoglycemia selected for this study, i.e. blood glucose values at 59 mg. per 100 ml. or less between the second and fifth hours of an oral glucose tolerance test. However, the mean increment in blood glucose following oral carbohydrate was the same in the two groups.

The zero-hour insulin levels, the increments in insulin induced by the oral carbohydrate, and the ratios of the increments in blood glucose to the increments in

TABLE 5

Blood glucose and serum insulin and growth hormone levels in overweight females during oral glucose tolerance tests without and with reactive hypoglycemia (Bl. Glucose < 59 mg. per 100 ml.)

Index	Group C Age 20-45 yrs.; B Wgt. > 145 lbs. Bl. Gluc. > 60 mg. per 100 ml. X ± SD (n)	Group C Age 20-45 yrs.; B Wgt. > 145 lbs. Bl. Gluc. < 59 mg. per 100 ml. X ± SD (n)	Group D Age 46-70 yrs.; B. Wgt. > 145 lbs. Bl. Gluc. > 60 mg. per 100 ml. X ± SD (n)	Group D Age 46-70 yrs.; B. Wgt. > 145 lbs. Bl. Gluc. <59 mg. per 100 ml. X ± SD (n)
Fasting Blood Sugar	*85.0 ± 8.9 (40)	*76.3 ± 11.7 (18)	96.0 ± 28.5 (55)	87.4 ± 12.4 (7)
GTS 0-2 hr.	†436.7 ± 92.2 (40)	†381.1 ± 80.2 (18)	515.4 ± 173.9 (55)	496.1 ± 119.6 (7)
0-5 hr.	†692.7 ± 118.8 (40)	†610.4 ± 97.4 (18)	824.3 ± 287.8 (55)	718.4 ± 126.5 (7)
3-5 hr.	†256.0 ± 32.9 (40)	†229.3 ± 35.2 (18)	309.5 ± 123.4 (55)	222.3 ± 18.7 (7)
ΔBl.S. 0-2 hr.	98.8 ± 72.4 (40)	80.7 ± 48.9 (18)	133.2 ± 94.4 (55)	152.7 ± 89.5 (7)
0-5 hr.	116.3 ± 85.6 (40)	103.8 ± 70.3 (18)	176.3 ± 144.8 (55)	163.7 ± 89.6 (7)
3-5 hr.	17.5 ± 17.0 (40)	23.1 ± 37.3 (18)	43.1 ± 62.1 (55)	11.0 ± 9.9 (7)
Fasting Insulin	20.8 ± 18.5 (40)	24.4 ± 23.7 (18)	25.9 ± 40.7 (55)	15.6 ± 9.0 (7)
ΔI 0-1/2 hr.	70.8 ± 46.9 (40)	77.1 ± 77.4 (18)	65.3 ± 58.7 (55)	61.1 ± 40.4 (7)
0-2 hr.	255.3 ± 205.5 (40)	244.2 ± 253.9 (18)	225.2 ± 156.4 (55)	221.9 ± 140.6 (7)
0-5 hr.	351.8 ± 256.5 (40)	332.1 ± 269.4 (18)	304.1 ± 186.5 (55)	312.4 ± 200.2 (7)
3-5 hr.	99.0 ± 77.0 (40)	87.9 ± 80.1 (18)	78.9 ± 74.7 (55)	90.6 ± 64.1 (7)
$\frac{\Delta Bl.S.}{\Delta I}$				
0-2 hr.	0.82 ± 2.03 (40)	0.48 ± 0.37 (18)	1.06 ± 1.79 (55)	0.97 ± 0.99 (7)
0-5 hr.	0.77 ± 2.21 (40)	0.42 ± 0.34 (18)	0.99 ± 1.65 (55)	0.76 ± 0.81 (7)
3-5 hr.	0.28 ± 0.45 (40)	1.05 ± 3.25 (18)	0.87 ± 1.76 (55)	0.10 ± 0.10 (7)
Growth Hormone, Fasting	5.6 ± 4.8 (40)	4.8 ± 6.0 (18)	5.7 ± 5.4 (55)	3.0 ± 2.5 (7)
Growth Hormone, Peak	12.9 ± 11.1 (40)	11.3 ± 6.6 (18)	10.6 ± 7.4 (55)	6.1 ± 4.2 (7)
Growth Hormone Sum	45.1 ± 46.6 (40)	32.2 ± 15.5 (18)	37.7 ± 23.5 (55)	24.4 ± 16.5 (7)

*$p < 0.01$
†$p < 0.05$

insulin were the same in the two subgroups in Group A, i.e. those without and those with reactive hypoglycemia (table 4).

Also, the growth hormone patterns were comparable in those with and those without reactive hypoglycemia. This was true of the zero-hour and peak growth hormone levels recorded in the glucose tolerance test as well as the sum of the growth hormone levels between the zero and fifth hours, inclusive. Hence, there is no evidence that the presence or absence of this degree of reactive hypoglycemia was causally related to growth hormone levels or evoked changes in growth hormone (table 4).

C. *Findings in Younger Overweight Persons with and Without Reactive Hypoglycemia*

Reactive hypoglycemia was surprisingly common in the younger overweight subjects who comprised Group C, occurring in 31 per cent of them (table 5).

As in the nonoverweight younger group with reactive hypoglycemia, fasting blood glucose levels were lower in those in Group C who developed reactive hypoglycemia, i.e. 76.3 mg. per 100 ml. in those with and 85.0 mg. per 100 ml. in those without reactive hypoglycemia. Also, the oral glucose load evoked the same degree of hyperglycemia, i.e. the increments in blood glucose (ΔBl.S.) were the same, in those with and those without reactive hypoglycemia (table 5).

Similarly, the fasting levels of insulin were not significantly different in those members of Group C who did and in those who did not develop reactive hypoglycemia as herein defined. Also, the ingestion of glucose evoked insulinemia of the same order of magnitude (ΔI) in these two groups (table 5).

There is a suggestion that the mean growth hormone sum recorded during the glucose tolerance test was lower in those in Groups C and D with reactive hypoglycemia, 32.2 compared to a value of 45.1, but the difference is not statistically significant.

DISCUSSION

There is a need for standards of reference for the evaluation and interpretation of borderline instances of reactive hypoglycemia, i.e. hypoglycemia following upon glucose loading or a high intake of carbohydrate. It is not difficult to make a diagnosis of clinically significant hypoglycemia in patients who experience specific neurologic symptoms following a carbohydrate load and in

whom the blood glucose drops to 20 mg. per 100 ml. But difficulties in diagnosis often arise when persons give a history of nervousness, palpitations, hunger, etc. several hours after a meal and report relief with food, orange juice, etc. Though these may be manifestations of hypoglycemia, they can also be, and frequently are, expressions of anxiety.

If, for example, an oral carbohydrate load produces a fourth-hour blood glucose level of 49 mg. per 100 ml., does this establish a diagnosis of clinically meaningful reactive hypoglycemia? The present data suggest that this may not be so, simply because such degrees of reactive hypoglycemia are such a relatively frequent occurrence in a control population. Thus, in this series of 285 women who were participants in a health survey rather than patients, reactive hypoglycemia (defined for purposes of this study as blood glucose levels of 59 mg. per 100 ml. or lower at the second, third, fourth and/or fifth hours of an oral glucose tolerance test) occurred in 17 per cent. However, when the subjects are subdivided into four groups on the basis of age and body weight, the frequency of this degree of reactive hypoglycemia among younger nonoverweight and younger overweight individuals is 19 and 31 per cent, respectively. It is lower in the nonoverweight older group, 2.2 per cent, and only 11 per cent among the overweight older persons.

The present findings suggest that the reactive hypoglycemia which was observed in our younger nonobese and obese population was attributable to lower zero-hour blood glucose values without significant differences in the increments in glucose or in insulin, or in the ratio of the two, following the ingestion of glucose. The lesser frequency of such reactive hypoglycemia in the older nonobese and older obese populations as a whole could have been attributable not only to higher zero-hour blood glucose levels in the older group but also to greater increments in blood sugar following oral carbohydrate. Again, there is no evidence that decreases in the insulin responses of the older subjects had protected them against reactive hypoglycemia.

The probability that such reactive hypoglycemia is or is not a variant of normal can be partially defined on the basis of the patients' age and body weight. Thus, reactive hypoglycemia developed in 19 per cent of the females under forty-six years of age and under 146 lbs in weight whereas it occurred in only 2 per cent of those who were in the same body weight range but in the later decades of life. Hence, one would be more inclined to dismiss this degree of reactive hypoglycemia in a young thin person as a variant of normal and look with greater suspicion upon an equivalent degree of hypoglycemia in an older thin person. Similarly, reactive hypoglycemia was so frequent in our overweight younger females, occurring in 31 per cent, that the possibility that this is a variant of normal in obesity is high. On the other hand, a similar degree of reactive hypoglycemia in an older overweight person should be considered more carefully as a possible pathologic finding. In that age and weight group of women, reactive hypoglycemia as herein defined developed infrequently, i.e. in only seven out of sixty-two individuals.

This scrutiny of reactive hypoglycemia in a control population of women does not of course resolve the dilemmas of the more or less nondescript functional hypoglycemia syndrome viewed by physicians, but it does provide a working hypothesis for interpreting low blood glucose levels in the latter part of a tolerance. Thus, it quantitates to some degree the concept of a limited degree of asymptomatic reactive hypoglycemia as a variant of normal and identifies susceptible groups of persons.

Reactive hypoglycemia has been stated to be uncommon in obese persons.[10] Though this may well be true in the very obese, especially if they are in the later decades of life and have glucose intolerance, the findings of the present study indicate that reactive hypoglycemia by the criteria cited is common in young overweight persons.

Our findings appear to be in keeping with conclusions reached by Groen[11] and by Sussman and their colleagues.[12] Groen et al.[11] concluded from bioassays of serum that the insulin responses of persons with reactive hypoglycemia to glucose were within the normal range. Sussman et al. described fourteen adults with blood glucose levels of 45 mg. per 100 ml. or less in the later hours of a prolonged oral glucose tolerance test. Their studies enabled them to categorize these patients into three subgroups: a) individuals with a normal tolerance and normal insulin responses; b) individuals with a normal tolerance and high insulin levels; and c) individuals with diabetic glucose tolerances and what seemed to be high insulin responses. Our subjects resemble their subgroup with normal glucose tolerances and normal insulin responses.

We did not perform tolbutamide tolerance tests on our subjects. However, Steinke and Soeldner[13] have suggested that the serum insulin responses to intravenous tolbutamide are less when reactive hypoglycemia is present, irrespective of whether or not the earlier part of the glucose tolerance curve is diabetic or nondiabetic.

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