Capillary Blood Sugar Values in Children During the Oral Cortisone-Primed Glucose Tolerance Test

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SUMMARY

Three-hour oral cortisone-primed glucose tolerance tests were performed on a total of 113 children in three age groups; 1½ to less than 4 yrs., 4 yrs. to less than 8 yrs., and 8 to 12 yrs. of age. All children had negative family histories for diabetes, were in good health, and had recent normal oral glucose tolerance tests. A capillary blood microtechnic for blood sugar was used. Oral glucose was administered according to age and weight. The total cortisone dosage was 280 mg. per M^2 given in two equally divided doses eight-and-one-half and two hours before the testing.

It is suggested that the blood sugar values for the 1½ to less than 4 yrs. age group be considered separately because of significant differences from the other age groups. The values for the ± 2 standard deviation range for boys and girls from 4 to 12 yrs. of age were: fasting (54.4-114.0 mg./100 ml.); 30 min. (96.1-202.9 mg./100 ml.); 60 min. (74.7-202.3 mg./100 ml.); 90 min. (72.5-169.3 mg./100 ml.); 120 min. (65.8-157.4 mg./100 ml.); 180 min. (49.6-122.4 mg./100 ml.). DIABETES *20*:615-21, September, 1971.

The thrust of much present day research is to identify those individuals predisposed to diabetes mellitus[1] and to evaluate the effectiveness of early therapy.[2,3] The evidence for the importance of genetic factors in diabetes[4] has resulted in an increasingly large number of children being examined for the presence of the disease.

Probably the most widely used test in studies of the prevalence of diabetes has been the oral glucose tolerance test (OGTT). However, the modification of the glucose tolerance test with cortisone is also being utilized with increased frequency as an additional approach to the prediction of diabetes.[5-11]

Previous standards for evaluating the cortisone glucose tolerance test (CGTT) have been derived from studies performed on adult subjects. It is the purpose of this study to establish standards for capillary blood sugar values in children during the CGTT.

MATERIAL AND METHODS

Three groups of children, 1½ yrs. to less than 4, 4 yrs. to less than 8 yrs. and 8 to 12 yrs. were studied. Not included were subjects with a family history of diabetes in grandparents, parents, aunts, uncles, siblings or first cousins. The children were in good health and all were between the 25th and 75th percentiles for weight.[12] They were selected from the local community; none had been recently hospitalized. They were ambulatory at the time of testing. The composition of the groups relative to age, sex and race is shown in table 1.

All the children in the study had been examined one to two weeks previously by OGTT's and the results conformed to the standard values previously established.[13]

For three days prior to testing, the children were maintained on a diet consisting of approximately 50 per cent of the calories as carbohydrate. No patients were over or underfed relative to reasonable calorie requirements. All children were fasted for twelve hours. The total dosage of cortisone acetate was calculated as recommended by Wajchenberg, Pupo, Quintao, Leon and Saldanha[5]—280 mg. per M^2. This was given in two equally divided doses eight-and-one-half and two hours before the CGTT as suggested by Fajans and Conn[6] and Conn.[7]

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TABLE 1

Distribution of subjects used in this study, according to age, sex, and race

Ages	Puerto Rican		Negro		White		Total
	Males	Females	Males	Females	Males	Females	
1½<4 years	17	7		1	1		26
4<8 years	14	24		2	1	2	43
8-12 years	13	23	3	2	2	1	44
Total	44	54	3	5	4	3	113

The dose of oral glucose was given according to the recommendations of Traisman and Newcomb,[14] and Nelson.[15]

Age	Amount of glucose
1½-3 yrs.	2.0 gm./kg. body weight
3-12 yrs.	1.75 gm./kg. body weight

Glucose was administered as the commercial preparation Koladex.* This preparation contains 1 gm. of glucose per 3 ml. of a pleasant cola-flavored drink. It was administered chilled and was readily accepted by almost all of the children. All drank the required amount within five minutes.

Capillary blood, 0.02 ml., was collected in a Unopette† as previously described.[13] Single blood specimens were obtained prior to administration of the oral glucose and at 30, 60, 90, 120, and 180 min. following its ingestion. All specimens were refrigerated and analyzed for blood sugar the same day with the Technicon AutoAnalyzer following the method of Gray, Stowe, and Holden.[16] The reliability of the method has been previously confirmed.[13]

RESULTS

The total number of children in all three groups tested was 113. The mean blood sugar values of each of the three age groups of boys were compared with one another (figure 1), and also with the over-all mean for boys for each time period.

Figure 2 similarly compares the three age groups of girls, and figure 3 compares the three age groups of boys and girls combined.

Tables 2-8 respectively show the mean blood sugar values during the CGTT, the two standard deviation ranges and the third and 97th percentile ranges for:

Boys (3 age groups)	table 2
Girls (3 age groups)	table 3
Boys and Girls (3 age groups)	table 4
Boys (all ages combined)	table 5
Girls (all ages combined)	table 6
All ages and sexes combined	table 7
Boys and Girls (two age groups, 4-12 yrs. combined)	table 8

Ninety-six tests for significance were performed in

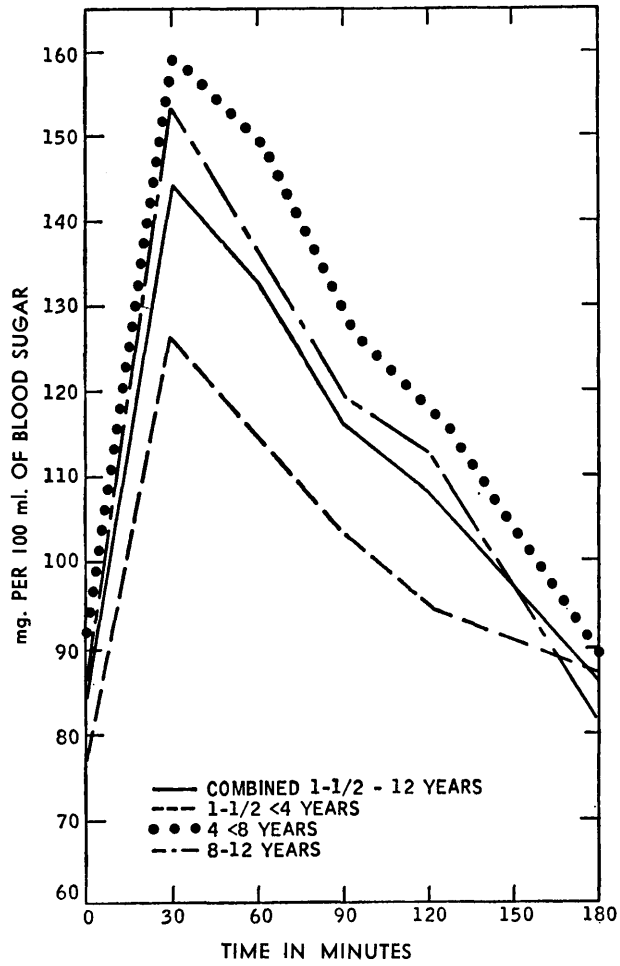

FIG. 1. Mean blood sugar values for boys in the 1½ to less than 4 yrs., the 4 to less than 8 years and the 8 to 12-year age group and the over-all mean values of all three groups combined.

*Koladex was supplied by Custom Laboratories Inc., Baltimore, Maryland 21223.

†Kindly supplied by Dr. Horace Gerarde of Becton-Dickinson and Company, Rutherford, New Jersey 07070.

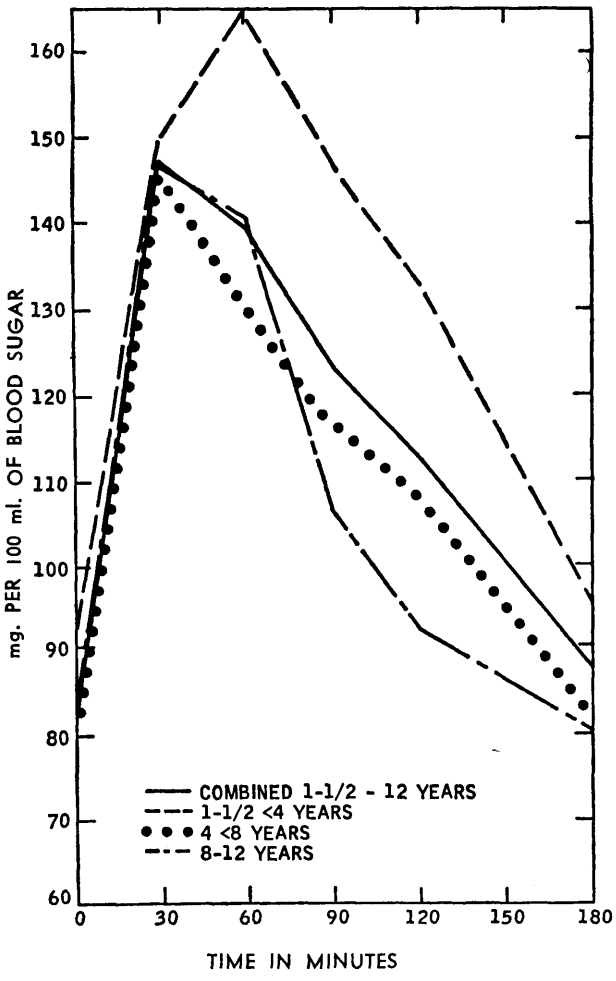

FIG. 2. Mean blood sugar values for girls in the 1½ to less than 4 yrs., the 4 to less than 8 yrs., and the 8 to 12-year age group and the over-all mean values of all three groups combined.

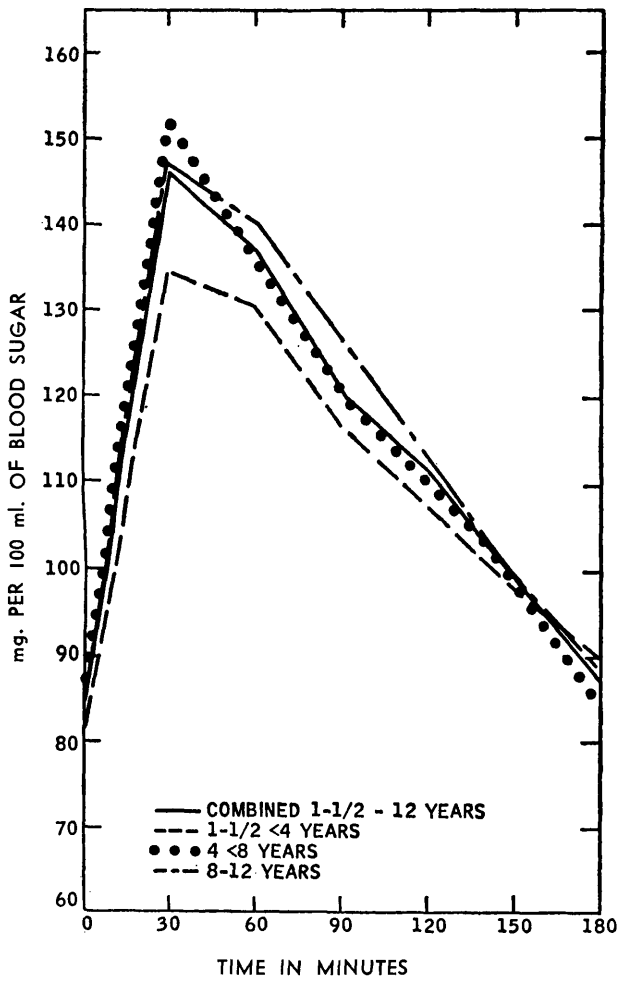

FIG. 3. Mean blood sugar values for boys and girls in the 1½ to less than 4 yrs., the 4 to less than 8 yrs., and the 8 to 12-year age group and the over-all mean values of all three groups combined.

an attempt to compare the subjects with respect to age and sex. The results are shown in table 9.

DISCUSSION

Conn,[8] and Conn and Fajans[9] performed OGTT's on 553 "nondiabetic" close relatives of diabetic patients. Eighteen per cent were revealed as diabetics. A CGTT performed on 393 subjects of this same group who had demonstrated a normal response to glucose alone revealed an additional 16 per cent with an abnormal response. The CGTT showed no superiority over the OGTT in producing abnormal responses in individuals with negative family histories of diabetes.

Questions have been raised regarding the effectiveness of the CGTT as a useful instrument in the prediction of diabetes. Klimt, Wolff, Silverman and Conant[10] tested 116 nondiabetic adults with a single dose of cortisone, 50 mg. per M^2, administered one-and-one-half hours before glucose loading. They found no evidence of bimodality, so that with the numbers tested there was no objective dividing line between the abnormal and the normal. They did find, however, that the test was reproducible with a highly significant correlation between tests in the same person at one, two and three hours after glucose.

Jackson[17] questioned whether two doses of cortisone were sufficient to produce a definite diabetic curve in prediabetics. However, he considered the test to be possibly useful in people over forty-five years of age or when performed during pregnancy.

West performed the CGTT in twenty-six persons with both parents diabetic. All had normal OGTT's. Their

TABLE 2

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for boys in three age groups, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
1½ < 4 yrs.	(18)	(18)	(17)	(18)	(18)	(18)
Mean value ± S.E.M.	75.2±3.50	127.9±8.40	114.5±7.20	103.2±5.00	94.6±5.70	86.8±5.50
1 standard deviation	±14.6	±35.5	±30.0	±21.2	±24.4	±23.5
2 standard deviation range	46.0-104.4	56.9-198.9	54.5-174.5	60.8-145.6	45.8-143.4	39.8-133.8
3rd and 97th percentile range	47.8-102.7	61.2-194.6	58.1-170.9	63.3-143.1	48.7-140.5	42.6-131.0
4 <8 yrs.	(15)	(15)	(15)	(15)	(15)	(15)
Mean value ± S.E.M.	91.0±2.70	159.5±7.40	149.1±7.20	127.9±5.10	118.0±5.60	89.1±3.50
1 standard deviation	±10.4	±28.8	±27.9	±19.6	±21.7	±13.7
2 standard deviation range	70.2-111.8	101.9-217.1	93.3-204.9	98.7-167.1	74.6-162.1	61.7-116.5
3rd and 97th percentile range	71.5-110.6	105.4-213.6	96.6-201.6	91.1-164.8	77.2-158.8	63.3-114.9
8-12 yrs.	(17)	(16)	(17)	(17)	(17)	(17)
Mean value ± S.E.M.	84.8±3.80	153.3±9.50	136.7±8.00	119.4±5.51	112.9±3.60	81.4±5.00
1 standard deviation	±15.5	±39.3	±32.8	±22.7	±14.7	±20.7
2 standard deviation range	53.8-115.8	74.7-231.9	71.1-202.3	74.0-164.8	83.5-142.3	40.0-122.8
3rd and 97th percentile range	55.9-113.8	79.4-227.2	75.0-198.4	76.7-162.7	85.3-140.5	42.3-120.3

( ) = number of subjects tested

responses to cortisone administered by the Fajans and Conn technic were not significantly different from those of a control group with a normal OGTT and a negative family history of diabetes.

Fajans and Conn[19] do indeed stress that the CGTT is primarily a research tool. They concluded that it offered promise in the search for earlier detection of diabetes by separating the nondiabetic relatives of diabetics from people with no known family history of diabetes.

The cortisone dosage utilized in previous studies[6,7,10,11,18,20] were all primarily for adult subjects. In the present study the recommendation of Wajchenberg et al.[5] was followed. These authors performed CGTT's with progressively increasing doses of cortisone in control children and children with one or both parents diabetic. They concluded that the cortisone dosage of 280 mg. per M^2 given in two equally divided doses prior to the oral glucose load might be critical in detecting those predisposed to diabetes. This dosage corresponds to the pharmacologic dose of 75 to 300 mg. per M^2 per twenty-four hours recommended by Nelson.[21]

Wajchenberg et al.[5] administered a glucose load of 1.75 gm./kg. ideal body weight. A test giving a two-hour blood glucose level of 140 mg./100 ml. or above by the Somogyi-Nelson method was considered a "posi-

TABLE 3

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for girls in three age groups, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
1½ <4 yrs.	(8)	(8)	(8)	(8)	(8)	(8)
Mean value ± S.E.M.	91.9±8.20	149.3±14.90	164.3±11.00	146.9±14.70	133.4±12.80	95.5±9.40
1 standard deviation	±23.2	±42.1	±31.2	±41.7	±36.3	±26.7
2 standard deviation range	45.5-138.3	65.1-233.5	101.9-226.7	63.5-230.3	60.8-206.0	42.1-148.9
3rd and 97th percentile range	48.3-135.5	70.2-228.4	105.6-223.0	68.5-225.3	65.2-201.6	45.3-145.7
4 < 8 yrs.	(28)	(28)	(28)	(28)	(28)	(28)
Mean value ± S.E.M.	79.8±3.40	146.5±4.30	129.9±6.20	116.4±5.00	107.6±5.50	81.8±3.10
1 standard deviation	±18.0	±23.0	±32.6	±26.5	±29.3	±16.4
2 standard deviation range	43.8-115.8	100.5-192.5	64.7-195.1	63.4-169.4	49.0-166.2	49.0-114.6
3rd and 97th percentile range	45.0-113.6	103.3-189.7	68.3-189.7	66.6-166.2	52.5-162.7	51.0-112.6
8-12 yrs.	(27)	(26)	(26)	(26)	(26)	(26)
Mean value ± S.E.M.	84.3±2.30	144.8±4.50	140.3±5.90	106.8±5.00	92.2±2.90	80.5±3.50
1 standard deviation	±11.9	±22.7	±29.6	±25.8	±15.0	±18.1
2 standard deviation range	60.5-108.1	99.4-190.2	81.1-199.5	55.2-158.4	62.2-122.2	44.3-116.7
3rd and 97th percentile range	61.9-106.7	102.1-187.5	84.7-195.9	58.3-155.3	64.0-120.4	46.5-114.5

( ) = number of subjects tested

TABLE 4

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for boys and girls in three age groups, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
1½ <4 yrs.	(26)	(26)	(25)	(26)	(26)	(26)
Mean value ± S.E.M.	80.3±3.71	134.5±7.47	130.4±7.60	116.6±6.84	106.5±6.53	89.5±4.77
1 standard deviation	±18.9	±38.1	±38.0	±34.9	±33.3	±24.3
2 standard deviation range	42.5-118.1	58.3-210.7	54.4-206.4	46.8-186.4	39.9-173.1	40.9-138.1
3rd and 97th percentile range	44.8-115.8	62.9-206.1	59.0-201.8	51.0-182.2	43.9-169.1	43.8-135.2
4 <8 yrs.	(43)	(43)	(43)	(43)	(43)	(43)
Mean value ± S.E.M.	83.7±2.53	152.1±3.88	136.6±4.89	120.5±3.76	111.3±4.14	84.3±2.41
1 standard deviation	±16.6	±25.4	±32.1	±24.7	±27.1	±15.8
2 standard deviation range	50.5-116.9	101.3-202.9	72.4-200.8	71.1-169.9	57.1-165.5	52.7-115.9
3rd and 97th percentile range	52.5-114.9	104.3-199.9	76.3-196.9	74.1-166.9	60.3-162.3	54.6-114.0
8-12 yrs.	(44)	(42)	(43)	(43)	(43)	(43)
Mean value ± S.E.M.	84.8±1.99	146.9±4.32	140.4±4.88	121.5±3.67	112.0±2.76	87.7±3.11
1 standard deviation	±13.2	±28.0	±32.0	±24.0	±18.1	±20.4
2 standard deviation range	58.4-111.2	90.9-202.9	76.4-204.4	73.5-169.5	75.8-148.2	46.9-128.5
3rd and 97th percentile range	60.0-109.6	94.3-199.5	80.2-200.6	76.4-166.6	78.0-146.0	49.3-126.1

( ) = number of subjects tested

tive response." They concluded that age had a marked influence upon responses of subjects to the cortisone and that the younger group responded much less uniformly to the different doses of cortisone.

Jackson, Guthrie, Murthy, Womack and McCann[22] performed triamcinolone oral glucose tolerance tests on eighty-seven normal children from six to eighteen years of age. Triamcinolone was given in a dose of 8 mg. per M^2 in two equal doses ten hours and one hour preceding an oral glucose load of 1.75 gm./kg. Their 97th percentile results were higher for both insulin and glucose than control children who received only glucose at all time periods studied; fasting, ½ hr., 1 hr., 2 hrs. and 3 hrs.

Higher values of blood sugar obtained with the CGTT as compared to the OGTT are most likely due to increased gluconeogenesis. Decreased utilization of glucose may be an additional factor due to antagonism

TABLE 5

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for boys all ages combined, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
Boys (all ages combined)	(50)	(49)	(49)	(50)	(50)	(50)
Mean value ± S.E.M.	83.2±2.13	144.4±5.07	132.8±4.72	116.2±3.29	107.8±3.21	85.6±2.81
1 standard deviation	±15.1	±35.5	±33.1	±23.3	±22.7	±19.9
2 standard deviation range	53.0-113.4	73.4-215.4	65.9-198.3	69.5-162.7	62.4-153.2	45.8-125.4
3rd and 97th percentile range	54.8-111.6	77.7-211.1	70.6-195.0	72.3-159.9	65.1-150.5	48.2-123.0

( ) = number of subjects tested

TABLE 6

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for girls all ages combined, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
Girls (all ages combined)	(63)	(62)	(62)	(62)	(62)	(62)
Mean value ± S.E.M.	83.5±2.10	147.3±3.25	139.8±4.26	123.1±3.73	112.5±3.52	87.8±2.50
1 standard deviation	±16.7	±25.6	±33.6	±29.4	±27.7	±19.7
2 standard deviation range	50.1-116.9	96.1-198.5	72.6-207.0	64.3-181.9	57.1-167.9	48.4-127.2
3rd and 97th percentile range	52.1-114.9	99.2-195.4	76.6-203.0	67.8-178.4	60.4-164.6	50.8-124.8

( ) = number of subjects tested

TABLE 7

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for all ages and sexes combined, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
All ages and sexes combined	(113)	(111)	(111)	(112)	(112)	(112)
Mean value ± S.E.M.	83.3±1.50	146.0±2.87	136.7±3.17	120.0±2.55	110.4±2.42	86.8±1.86
1 standard deviation	±15.9	±30.3	±33.4	±27.0	±25.6	±19.7
2 standard deviation range	42.5-118.1	58.3-210.7	54.4-206.4	46.8-186.4	39.9-173.1	40.9-138.1
3rd and 97th percentile range	44.8-115.8	62.9-206.1	59.0-201.8	51.0-182.2	43.9-169.1	43.8-135.2

( ) = number of subjects tested

TABLE 8

Values in mg./100 ml. of capillary blood sugar during the cortisone glucose tolerance test for boys and girls in the two age groups 4 < 8 and 8-12 yrs. combined, 1 S.D., 2 S.D. range, and the 3rd and 97th percentiles for each of the testing periods

	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
	(87)	(85)	(86)	(86)	(86)	(86)
Mean value ± S.E.M.	84.2±1.60	149.5±2.90	138.5±3.44	120.9±2.61	111.6±2.47	86.0±1.96
1 standard deviation	±14.9	±26.7	±31.9	±24.2	±22.9	±18.2
2 standard deviation range	54.4-114.0	96.1-202.9	74.7-202.3	72.5-169.3	65.8-157.4	49.6-122.4
3rd and 97th percentile range	56.2-112.2	99.3-199.7	78.5-198.5	75.4-166.4	68.5-154.7	51.8-120.2

( ) = number of subjects tested

to insulin activity at the cellular level or to decreased sensitivity to endogenous insulin.

The numerous tests for significance apparently isolated the 1½ to less than 4-year age group from the others. This might have been because of the relatively small size of the group which contained only eighteen males and eight females. The high values obtained in these younger girls might also be accounted for by only eight

TABLE 9

Tests for significance*
(Cortisone Glucose Tolerance Tests)

	Comparisons	Fasting	30 Min.	60 Min.	90 Min.	120 Min.	180 Min.
Boys and Girls	Over-all mean vs. 1½ < 4 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all mean vs. 4 < 8 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all mean vs. 8-12 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	1½ <4 yrs. vs. 4 <8 yrs.	N.S.	$p<0.05$	N.S.	N.S.	N.S.	N.S.
	4 <8 yrs. vs. 8-12 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	1½ <4 yrs. vs. 8-12 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all vs. boys 1½ <4 yrs.	$p<0.05$	$p<0.025$	N.S.	$p<0.025$	$p<0.02$	N.S.
	Over-all vs. boys 4 <8 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all vs. boys 8-12 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all vs. girls 1½ <4 yrs.	N.S.	N.S.	$p<0.05$	$p<0.02$	$p<0.025$	N.S.
	Over-all vs. girls 4 <8 yrs.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Over-all vs. girls 8-12 yrs.	N.S.	N.S.	N.S.	$p<0.05$	$p<0.001$	N.S.
Boys vs. Girls	Boys vs. girls (All ages combined)	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
	Boys vs. girls (1½ <4 yrs.)	$p<0.05$	N.S.	N.S.	$p<0.005$	$p<0.01$	N.S.
	Boys vs. girls (4 <8 yrs.)	$p<0.05$	N.S.	N.S.	N.S.	N.S.	N.S.
	Boys vs. girls (8-12 yrs.)	N.S.	N.S.	N.S.	N.S.	$p<0.001$	N.S.

* = Student's *t* test
N.S. = Not Significant

being included in the study. We would suggest that the blood sugar values for this group be considered separately. The values for boys plus girls in the two age groups 4<8 and 8-12 yrs. combined (table 8) could be used for children in these ages. The total number of boys from four to twelve years of age was thirty-three. There were fifty-four girls from four to twelve years subdivided as follows: 4<10 yrs.—thirty-four girls, and 10-12 yrs.—twenty girls. This subdivision was made because many girls begin their prepubertal growth at ten years.

It is hoped that the data obtained in this study might prove useful in the early identification of children with diabetes mellitus long before the onset of clinical symptoms. This might provide ample time for the institution of prophylactic procedures: diet, oral hypoglycemic agents and/or insulin, in an attempt to delay or prevent the progression of the disease.[2,3]

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