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# GLYCEMIA IN CACHEXIA OF NURSLINGS

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Cobliner [1] found that the blood sugar was lower in malnourished infants than in normal ones. He obtained amounts as low as 0.5 mg. of dextrose per thousand cubic centimeters of blood. He made the interesting observation that as soon as the conditions of nutrition improved the blood sugar was increased.

Brown [2] discovered that the average dextrose content of the blood was 0.77 mg. per thousand cubic centimeters in hypothreptic infants whose weights were 50 per cent lower than normal. If the weight was from 50 to 80 per cent of normal, the blood sugar reached an average of 0.91. From this observation he inferred that glycemia and the degree of denutrition maintain a certain relationship.

Tisdall, Drake and Brown [3] observed that the average dextrose content of the blood in atrophic infants was 0.76 mg. per thousand cubic centimeters.

Wilson, Levine and Gottschall [4] stated that the blood sugar in athreptic infants, when fasting, was 0.59 mg. per thousand cubic centimeters. Vitetti [5] did not find that the blood sugar in thirteen hypothreptic infants, when fasting, differed from that of normal babies, the average being 0.78.

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From the service of Dr. Bravo and Dr. Muñoyerro, Provincial Institute of Puericulture.

1. Cobliner: Blutsuckeruntersuchungen bei Säuglingen, Ztschr. f. Kinderh. **1**:207, 1911.

2. Brown, M. J.: Quart. J. Med. **18**:175, 1925.

3. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of Marantic Infants, Am. J. Dis. Child. **30**:829 (Dec.) 1925.

4. Wilson, J. R.; Levine, S. Z., and Gottschall, G.: IX. The Respiratory Exchange in Marasmus: Carbohydrate Metabolism of Normal and Marasmic Infants With and Without the Administration of Insulin, Am. J. Dis. Child. **36**: 470 (Sept.) 1928.

5. Vitetti, G.: Contributo sperimentale al comportamento della curva glicemica in bambini iponutriti sottoposti alla cura insulinica, Pediatria **36**:1210, 1928.

According to the data presented by Macciotta,[6] the average blood sugar in four atrophic patients was 0.71 mg.; on recovery, this average was increased to 0.84.

Nervi [7] in a recent work gave the amount of blood sugar both in atrophic and dystrophic children as between 0.58 and 0.82 mg. per thousand cubic centimeters, the average being 0.72.

From an analysis of these figures the conclusion is drawn that the degree of glycemia in dystrophic infants is lower than in normal ones. The figures given by the authors mentioned show an average blood sugar of 0.72 mg. in dystrophic infants. Considering 0.88 as the normal average for nurslings, this average is seen to be 18.9 per cent lower.

## EXPERIMENTAL DATA

We have determined the blood sugar in fifty-four infants with various chronic disturbances who were hypothreptic or athreptic, at the Provincial Institute of Puericulture. We employed the Bang II method [8] according to the technic used in the Laboratory of General Pathology of Dr. Novoa Santos by Dr. Outeirino. We made all the determinations in infants who had had no nourishment for at least three hours (from three to four as an average). The heel was the spot selected for the taking of blood. In some cases, however, because of the serious condition of the child, it was impossible to obtain blood from this source; in these cases we resorted to puncture of the longitudinal sinus, which we did with a syringe that was carefully washed, passed through distilled water and wiped scrupulously.

Other technical details followed by us were as follows: All tests that required more than one minute for the blood-taking maneuvers and weighing of the paper containing the blood were set aside, as it is a well known fact, confirmed by experience, that speed is necessary to insure accuracy. We made three tests for every determination, computing the average amount from the figures obtained separately, and rejecting a test if its results deviated from those of the other two. The table gives the figures obtained by us.

The average of all blood sugar values found in merely nutritional (not infectious) cachexia, i. e., in the first forty observations, is 0.53 mg. per thousand cubic centimeters.

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6. Macciotta, G.: Sulla somministrazione di glucosio per via sottocutanea nella gravi intossicazione di origine alimentare e nella atrofie dei lattanti, Pediatria **37**:283, 1929.

7. Nervi, C.: La glicemia e le curve glicemiche alimentari nell'infanzia, Pediatria **38**:251, 1930.

8. Durupt: Microméthodes et semi-microméthodes appliquées aux analyses chimiques du sang et des humerus, Paris, A. Poinat, 1924, p. 78.

*Blood Sugar of Fifty-Four Infants with Various Chronic Disturbances*

| Number | Age, Months | Weight, Gm. | Disturbances in Nutrition | Feeding | Blood Sugar, Mg. per 1,000 Cc. | Observations |
|---|---|---|---|---|---|---|
| 1 | 4½ | 3,550 | Athrepsia | Milk and cereals | 0.73 | |
| 2 | 2 | 2,640 | Athrepsia | Breast | 0.44 | Habitual vomiting |
| 3 | 3 | 2,450 | Athrepsia | Mixed | 0.59 | |
| 4 | 2½ | 2,450 | Hypothrepsia, 2d grade | Mixed | 0.78 | |
| 5 | 2½ | 2,950 | Athrepsia | Mixed | 0.59 | |
| 6 | 2 | 3,050 | Hypothrepsia, 2d grade | Mixed | 0.65 | Habitual vomiting |
| 7 | 1 | 2,640 | Hypothrepsia, 2d grade | Breast | 0.82 | Hypo-alimentation |
| 8 | 3 | 2,850 | Athrepsia | Mixed | 0.56 | |
| 9 | 4 | 3,320 | Hypothrepsia, 2d grade | Mixed | 0.79 | |
| 10 | 7 | 3,440 | Athrepsia | Artificial | 0.30 | Agonic. B. of the sinus |
| 11 | 2 | 2,375 | Athrepsia | Mixed | 0.375 | Agonic. B. of the sinus |
| 12 | 6 | 3,790 | Athrepsia | Artificial | 0.475 | Habitual vomiting |
| 13 | 2 | 2,540 | Athrepsia | Mixed | 0.48 | Blood from the sinus |
| 14 | 4 | 3,230 | Hypothrepsia, 2d grade | Mixed | 0.435 | Habitual vomiting |
| 15 | 2 | 2,540 | Athrepsia | Mixed | 0.115 | Agonic. B. of the sinus |
| 16 | 1½ | 2,750 | Hypothrepsia, 2d grade | Breast | 0.47 | Habitual vomitiing |
| 17 | 2 | 2,440 | Athrepsia | Breast | 0.325 | Habitual vomiting |
| 18 | 2 | 2,250 | Athrepsia | Breast | 0.12 | Blood from the sinus |
| 19 | 1½ | 2,645 | Hypothrepsia, 2d grade | Maternal breast | 0.40 | |
| 20 | 6 | 5,045 | Hypothrepsia, 2d grade | Breast and cereals | 0.585 | |
| 21 | 1 | 2,640 | Hypothrepsia, 2d grade | Mixed | 0.68 | |
| 22 | 1 | 3,185 | Hypothrepsia, 2d grade | Breast | 0.69 | |
| 23 | 3 | 2,265 | Athrepsia | Breast | 0.30 | Infant weak |
| 24 | 12 | 4,265 | Hypothrepsia, 2d grade | Cereals | 0.74 | |
| 25 | 3½ | 3,950 | Hypothrepsia, 2d grade | Breast and cereals | 0.73 | |
| 26 | 4½ | 3,500 | Athrepsia | Breast and cereals | 0.103 | |
| 27 | 3½ | 2,950 | Hypothrepsia, 2d grade | Breast and cereals | 0.77 | |
| 28 | 4½ | 3,715 | Hypothrepsia, 2d grade | Mixed | 0.43 | |
| 29 | 2 | 2,570 | Hypothrepsia, 2d grade | Breast | 0.37 | |
| 30 | 2 | 3,245 | Hypothrepsia, 2d grade | Breast | 0.665 | Convalescing from toxicosis |
| 31 | 4 | ..... | Athrepsia | Mixed | 0.40 | |
| 32 | 2 | 3,180 | Hypothrepsia, 2d grade | Mixed | 0.575 | Convalescing from toxicosis |
| 33 | 7½ | 4,300 | Hypothrepsia, 2d grade | ..... | 0.44 | |
| 34 | 2 | 2,910 | Hypothrepsia, 2d grade | Breast | 0.525 | Habitual vomiting |
| 35 | 4½ | 2,930 | Athrepsia | Mixed | 0.38 | |
| 36 | 6 | 3,350 | Hypothrepsia, 2d grade | ..... | 0.45 | |
| 37 | 2 | 2,780 | Athrepsia | Breast | 0.39 | |
| 38 | 5 | 2,950 | Hypothrepsia, 2d grade | Breast and cereals | 0.635 | Infant weak |
| 39 | 5½ | 3,350 | Hypothrepsia, 2d grade | Breast and cereals | 0.605 | |
| 40 | 15½ | 4,960 | Hypothrepsia, 2d grade | Cereals | 0.875 | |
| 41 | 5 | 2,850 | Athrepsia | Breast | 1.02 | Congenital syphilis |
| 42 | 1 | 3,200 | Hypothrepsia, 2d grade | Mixed | 0.875 | Congenital syphilis |
| 43 | 11 | 4,700 | Hypothrepsia, 2d grade | Mixed | 0.885 | Congenital syphilis |
| 44 | 1½ | 2,670 | Hypothrepsia, 2d grade | Mixed | 0.77 | Congenital syphilis |
| 45 | 2 | 2,440 | Athrepsia | Mixed | 0.44 | Congenital syphilis |
| 46 | 7 | 3,520 | Athrepsia | Mixed | 1.02 | Tuberculosis |
| 47 | 3 | 3,050 | Athrepsia | Breast | 0.895 | Tuberculosis |
| 48 | 6 | 3,765 | Hypothrepsia, 2d grade | Mixed | 0.715 | Tuberculosis |
| 49 | 4 | 3,200 | Hypothrepsia, 2d grade | Mixed | 0.98 | Gained 600 Gm. in 20 days |
| 50 | 21 | 5,300 | Hypothrepsia, 2d grade | Artificial | 0.805 | Gained 450 Gm. in 28 days |
| 51 | 3½ | 2,965 | Hypothrepsia, 2d grade | Mixed | 1.085 | Gained 370 Gm. in 18 days |
| 52 | 4 | 2,750 | Hypothrepsia, 2d grade | Mixed | 0.755 | Gained 300 Gm. in 10 days |
| 53 | 7 | 4,300 | Hypothrepsia, 2d grade | Breast | 0.88 | Gained 610 Gm. in 17 days |
| 54 | 4 | 3,835 | Hypothrepsia, 2d grade | Mixed | 0.81 | Gained 315 Gm. in 15 days |

For a more detailed study of the subject, I shall set apart the cases of both tuberculous and syphilitic cachexia and the cases progressing toward recovery, and I shall divide the cases left into groups according to the intensity of the disturbance in nutrition. This intensity is determined (coefficient C) by dividing the present weight of the child by the difference between this and the normal weight. For instance, a hypothreptic infant 4 months old, weighing 3,700 Gm., who at birth weighed 3,000 Gm., when the normal weight is computed according to the previous observations of Nobécourt,[9] should weigh 6,000 Gm.; the present weight, then, is 2,250 Gm. less than normal. Therefore, $C = \frac{3,750}{2,250} = 1.66$. As is clearly understood, the coefficient C represents the intensity of denutrition in relation to the present weight.

But if, above all, a division is made with reference to nutritional factors, one sees the outstanding fact in the different behavior of the dextrose content of the blood in infants that were given cereals and in those that were not. Thus, the group of the first forty cases is divided into two others: (1) infants whose diet contained cereals (observations 1, 20, 24, 25, 26, 27, 38, 39 and 40), and (2) infants whose diets did not include cereals. In the first group, the average blood sugar value was 0.741 mg. per thousand cubic centimeters; in the second it was 0.493.

It follows clearly, therefore, that the addition of cereals to the diet of the hypothreptic infant prevents the fall in blood sugar, which remains close to the normal average, while infants who were not given cereals show accentuated hypoglycemia, the intensity of which is related, as will be seen, to the condition that produces the nutritional trouble.

The dystrophic infants in whose feeding cereals are not included were classified according to the values of coefficient C, and the results of this grouping are as follows:

| Coefficient Value | Number of Cases | Average Blood Sugar, Mg. |
|---|---|---|
| (1)....less than 1.5 | 18 | 0.448 |
| (2)....from 1.5 to 2 | 5 | 0.541 |
| (3)....greater than 2 | 8 | 0.625 |

The conclusion drawn from these figures is that the lower the blood sugar, the more accentuated the nutritional disturbance will be.

The last fourteen observations are cachexias of specific syphilitic or tuberculous origin, and cases of hypothreptic infants who were recovering. The average amount of blood sugar in the cases of congenital syphilis investigated is 0.798 mg. per thousand cubic centimeters, and in the cases of tuberculosis, 0.876 mg. The values, as is seen, are

9. Nobécourt, P.: Conférence pratiques sur l'alimentation des nourrissons, ed. 3, Paris, Masson & Cie, 1922, p. 7.

normal. In the case of congenital syphilitic infants fed by breast, it is understood that syphilitic nurses gave them the breast or that they were fed with milk pumped from it.

It is conspicuous that, with very low values for coefficient C, the dextrose content of the blood remains close to the normal value; thus, in the forty-first observation in which coefficient C was 0.72, the blood sugar was 1.02 mg. per thousand cubic centimeters; the diet consisted only of human milk. If one keeps in mind that for values of C lower than 1.5 the average blood sugar value obtained in cases of nutritional dystrophy was 0.448, one must infer that the process leading to athrepsia in the two groups of cases is absolutely different, since in dystrophies resulting from chronic infection, the carbohydrates do not seem to be affected. In six hypothreptic infants on the way to recovery (the last six observations), the average amount of blood sugar was 0.885 mg. per thousand cubic centimeters.

## COMMENT

According to our own data, the average dextrose content of the blood in the nutritional cachexias is 0.53 mg. per thousand cubic centimeters. As was noted, my associates and I obtained a figure distinctly lower than the averages given by several investigators. But that is because we considered merely nutritional dystrophies, excluding those of specific origin (syphilitic or tuberculous) in which I have shown that the hypoglycemia characteristic of the former group does not occur; neither does this average include the cases of hypothrepsia in which the patients were on the way to recovery, as these patients present also, as was shown, high normal values for blood sugar. If all these groups should be included in the computation, an average of 0.624 mg. per thousand cubic centimeters is obtained. But our figure is, even then, lower than those of other authors (with the exception of Wilson and his co-workers), and this may, in part, be due to the inclusion of some particularly low figure obtained before and at the agonal stage. When these factors—the cases of cachexia of nonnutritive origin and the unusually low figures—are excluded, an average is finally obtained that is comparable to those obtained by the authors mentioned previously, which reaches 0.656 mg. per thousand cubic centimeters, i. e., a figure 25 per cent lower than the normal average.

If, however, as was done, the complex group of cases of hypothrepsia is dismembered in order to consider only those with a nutritional cause and if these are further subdivided into those with a high blood sugar content, it will be observed that, save for a few exceptions, these high values are found (in the absence of severe complaints) in subjects fed cereals or in hypothreptic infants progressing toward recovery. When these cases are eliminated, there is a group left that

includes extremely hypothreptic babies in whose diet cereals were not included; in this group the blood sugar reaches, according to our own data, an average of 0.493 mg. per thousand cubic centimeters, i. e., a figure 43.9 per cent lower than the normal one.

It is also deduced from our experimental researches that the fall in blood sugar is in relation, to a certain extent, to the intensity of denutrition, which is considered in some degree as an index of the gravity of the dystrophy. Thus, the nearer to the time of death that the determination was made, the lower, in general, was the figure for the blood sugar. In the ten days preceding death, the blood sugar was 0.32 mg. on an average; between ten and twenty days prior to death, it reached an average of 0.47 mg., and more than 30 days before death, the average was 0.57 mg.

The interest of these data is greater because the only alteration clearly confirmed in the carbohydrate metabolism in the dystrophies is the hypoglycemia. In fact, Talbot and Hill [10] and Utheim [11] observed that the absorption of carbohydrates is perfectly achieved by athreptic infants, since they can be administered in large proportions without increasing the amount in the feces. One might well think of an excess of carbohydrate ferments in the intestine; this is true, however, only in cases followed by diarrhea.

Moreover, the organism of the athreptic infant not only absorbs regularly the dextrose that is ingested, but allows it to pass into the blood stream and removes it therefrom in the same time and proportion as does that of healthy infants, as was shown by the blood sugar curves in the experimental work of Brown and Tisdall and their assistants. Brown verified the observation that the highest blood sugar value for athreptic infants does not reach that of normal children, and Tisdall and Brown found, besides, that injected dextrose disappears from the blood stream of athreptic infants quicker than from that of healthy nurslings.

The tolerance of hypothreptic infants for dextrose seems to be even greater than that of healthy infants. Thus, Nobécourt [12] confirmed that the former can ingest at once from 4 to 5 Gm. of dextrose per kilogram of weight without showing higher glycemia, while normal infants cannot ingest more than 3 Gm. per kilogram.

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10. Talbot, F. B., and Hill, L. W.: The Influence of Lactose on the Metabolism of an Infant, with Special Reference to Fat, Nitrogen and Ash, Am. J. Dis. Child. **8**:218 (Sept.) 1914.

11. Utheim, Kirsten: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**:329 (Oct.) 1921.

12. Nobécourt, P.: La tolérance des nourrissons pour le sucre: Les hautes doses de saccharose chez les bébés cachectiques, Arch. de méd. d. enf. **30**:313, 1927.

Similar, though of greater precision, were the experiments of Matill, Meyer and Sauer,[13] who found increased tolerance for dextrose in the athreptic infant. The average tolerance in seven athreptic infants was from 1.4 to 1.5 Gm. per kilogram per hour (normal, from 0.8 to 0.9 Gm.). Helmholz and Sauer,[14] using Woodyatt's method, found that in six athreptic infants the tolerance for dextrose varied between 1.4 and 1.8 Gm.

However, the seeming increase in tolerance for dextrose in athreptic infants does not really exist, as when calculations are made, not according to the present weight, but according to the metabolically active tissue (as was the method of Tisdall and his co-workers) identical values result for both normal and athreptic babies.

In an interesting work, Wilson, Levine and Gottschall [4] investigated the metabolic capacity of the organism of the athreptic infant for dextrose, determining the increase in the respiratory coefficient after the ingestion of a known amount of carbohydrate. They have discovered that, on the basis of the present weight, athreptic infants burn a greater proportion of dextrose than sound nurslings (0.7 Gm. per kilogram an hour). But when computations are made according to the amount of metabolically active tissue, identical results are obtained in both normal and athreptic infants (0.5 Gm. per kilogram an hour). These authors assume that in normal infants 30 per cent of the body weight is made up of fat tissue, metabolically inactive, and that by multiplying the athreptic baby's weight by $\frac{100}{70}$, one obtains the weight that would have resulted had the body contained the proportional amount of fat. These authors conclude, like those already mentioned, that athreptic infants absorb carbohydrates and metabolize them in the same way as do normal infants.

There remains, then, as the only positive datum on the blood sugar the fact that it is low, having been found to average 0.493 mg. per thousand cubic centimeters.

The similarity of these data to those obtained by Tosi [15] for infants on a fasting stomach is surprising. Determining the dextrose content of the blood in ten children from 1 to 5 years of age during twelve, twenty-four, twenty-eight and fifty-four hours during which they were given only sweetened water, this author showed that in the first thirty-six hours (twenty-four for nurslings) the blood sugar descends to a minimum of from 0.3 to 0.4 mg. per thousand cubic centimeters; after-

13. Matill, P. M.; Mayer, K. M., and Sauer, L. W.: Dextrose Tolerance in Atrophic Infants, Am. J. Dis. Child. **19**:42 (Jan.) 1920.

14. Helmholz and Sauer: Dextrose Tolerance in Atrophic Infants, Tr. Am. Pediat. Soc., 1919.

15. Tosi, G.: Il comportamento della curva glicemia nel bambino, durante il digiuno prolungato, Clin. pediat. **8**:577, 1926.

ward, it ascends a little, reaching about 0.5 mg., at which level it remains. The author attributes this elevation to the fact that the hepatic supply of glycogen has been exhausted and a demand is made on the extrahepatic supply (muscular, etc.) to keep up the minimum threshold. He suggests also the possibility of an excitation of the suprarenal glands through long fasting.

In athrepsia, both the physiopathologic and anatomic data have demonstrated their similarity with the findings in simple starvation of young animals. By this similarity, the decrease in blood sugar parallel with the intensity of the nutritional disturbance may find an explanation. In less marked cases (coefficient C higher than 2) the available supply of hepatic glycogen has not yet been exhausted and the blood sugar remains relatively high (0.625 mg. per thousand cubic centimeters); with the progress of the denutrition, the hepatic supply is exhausted, the organism then making use of the extrahepatic glycogen in order to keep the glycemic index, already so low (C, 1.5 to 2; blood sugar, 0.54 mg.), as high as possible. At last, the process of autophagia, which has already consumed 90 per cent of the fat of the body, destroys the muscular masses (final hyperazotemia [Nobécourt [16]]) and exhausts its supply of glycogen, following which the dextrose content of the blood falls again (C, lower than 1.5; blood sugar, 0.448 mg.). In the final stages the organism of the athreptic infant is unable to maintain even the smallest blood sugar value found in cases of long fasting (from 0.3 to 0.4 mg.), and these patients during their last moments consume hepatic dextrose that is not replaced, so that the blood sugar descends rapidly to an incredibly low value, such as 0.1 mg. per thousand cubic centimeters.

But if one considers a hypothreptic infant without diarrhea, in whom, therefore, the functions of digestion and absorption are performed perfectly, it is necessary to assume, since metabolism of the administered carbohydrates is normal, a primary cause for the decrease in his supply of glycogen leading to hypoglycemia, which is the only demonstrable anomaly in the carbohydrate metabolism.

The study of lesions of the endocrine glands in athrepsia may throw some light on the nature of the primum movens of the hypoglycemia in dystrophic children. In the pancreas in athreptic infants Mattei [17] (quoted by Nobécourt) found an increase in the islands of Langerhans and signs of hyperactivity.

In the suprarenal glands "the lesions plainly prevail in the medullary substance"; the volume and weight of the whole gland are diminished,

16. Nobécourt, P.: Des hypotrophies et des cachexies des nourrissons, Arch. de méd. d. enf. **19**:195, 1916.

17. Mattei, quoted by Nobécourt (footnote 16).

so that it weighs scarcely 1/2,000 instead of the normal 1/750 of the weight of the body.

Mattei has found in the thyroid glands of athreptic infants, atrophy, degenerative and parenchymatous lesions and invading sclerosis, severe enough to indicate that there is a striking functional insufficiency.

It is surprising that there is pronounced atrophy of the thymus, accompanied by marked sclerosis, with regression of the parenchyma. The Hassall corpuscles show cystic degeneration.

In short, there are degenerative lesions of the suprarenal glands, thyroid and thymus and signs of hyperactivity of the incretory pancreatic gland.

We know that, schematically, the metabolism of saccharin is submitted to endocrine antagonistic regulative actions represented by the islands of Langerhans and their incretion insulin, which (1) blocks the beginning formation of dextrose from proteins and fats, (2) in a first period, increases the glycogen synthesis in liver and muscles and causes hypoglycemia by the association of both mechanisms and (3) finally (if the nutritious amount of carbohydrates is not sufficient) impoverishes the liver and muscles in glycogen, as with the extraglycogenic source (fats and proteins) cut off glycogen alone must provide for the organic requirements of dextrose.

The suprarenal glands act in an antagonistic way through the medium of epinephrine, which produces hyperglycemia, stimulating the formation of dextrose from hepatic glycogen.

Excision of the thyroid gland increases the sensibility of animals to the action of insulin.[18]

Removal of the thymus of young animals, carried out by Piana,[19] led to a notable decrease in blood sugar. This author inferred that the thymus exercises an action antagonistic to that of insulin in young animals.

From a survey, then, of the facts concerning the lesions of the endocrine glands in athrepsia, it is plainly seen that the logical consequence should be hypoglycemia, as the result of hyperinsulinemia not corrected by the hyperglycemic reflex due to the discharge of epinephrine (because of the deficit of the medullary substance of the suprarenal glands). Besides, functional insufficiency of the thyroid gland sensitizes the organism of the atrophic infant to the action of the excess of insulin. On the other hand, the thymic hypofunction should make the hypoglycemia more marked. Brown [2] has shown that when lesions of the endocrine glands are present, glycogenesis from proteins and fats being barred, hypoglycemia occurs. He has also shown that the addi-

18. Evans, C. L.: Recientes adquisiciones en fisiologia, 1929, p. 344. (Recent Researches in Physiology, Philadelphia, P. Blakiston's Son & Co., 1928.)

19. Piana, G.: Modificazioni della curva glicemica in raporto all'azione del timo, Pediatria **37**:1013, 1929.

tion of 8 per cent of fat to the diet does not affect restriction in the production of blood sugar in the dystrophic infant. Tosi [15] obtained the same results in fasting children. He found that in order to keep the hepatic and extrahepatic supplies of glycogen (and the dextrose content of the blood in consequence) within normal limits, a greater amount of carbohydrates must be included in the diet of the athreptic than of the normal infant. My associates and I confirmed this result by showing conservation of the blood sugar within normal limits in the athreptic infant in whose diet cereals were included.

The practical conclusion drawn from this consideration is that the treatment of athreptic infants with injections of insulin is illogical and not without danger. In fact, with this method one can expect only a more intense depletion of the supply of glycogen, if a sufficient amount of carbohydrates is not given at the same time. Moreover, in infants whose blood sugar is already so low, a little mistake in dosage immediately leads to accidents of hypoglycemia, as has often been noted in athreptic infants, in whom pallor, perspiration and convulsions have been observed when from 1 to 2 units of insulin have been given, notwithstanding a previous administration of 20 per cent (from 40 to 60 Gm.) saccharose solution. The success attributed to insulin is due exclusively, I think, to the administration of carbohydrates that necessarily follows it.

Finally, I think it of interest to call attention to the absence of the classic phenomenon of hypoglycemia in the infants investigated in spite of the fact that the nematic dextrose values were below 0.5 mg. per thousand cubic centimeters and in many cases 0.13 mg.

In his researches, Tosi [15] also did not observe symptoms of hypoglycemia after long fasting, notwithstanding the finding of blood sugar values from 0.3 to 0.35 mg. per thousand cubic centimeters. Ferri [20] obtained in his turn, by ten minutes' irradiation with quartz lamps, a fall in blood sugar to about 0.5 mg. without noticing any symptoms of hypoglycemia. Vitetti,[5] on giving insulin to undernourished infants (followed by dextrose), obtained blood sugar values as low as 0.36 mg. per thousand cubic centimeters without apparent hypoglycemic accidents. Tisdall, Brown, Drake and Cody [21] also called attention to the fact that they did not observe clinical signs of hypoglycemia in infants in whom the administration of insulin (plus dextrose) had caused the blood sugar to fall as low as 0.33 mg. and even to 0.25 mg.

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20. Ferri, U.: L'azione dei raggi ultravioletti sull'apparato glicoregolator dei bambini, Riv. di clin. pediat. **25**:217, 1927.

21. Tisdall, Brown, Drake and Cody: Insulin in the Treatment of Malnourished Infants, Am. J. Dis. Child. **30**:10 (July) 1925; also in Selected Articles from the Department of Paediatrics, University of Toronto, 1929, p. 199.

If one keeps in mind that when the blood sugar of adults falls to 0.7 mg. per thousand cubic centimeters, hypoglycemic accidents due to insulin begin; that when it reaches 0.5 mg., tremor and incontinence of feces are noticed and that when it falls to 0.35 mg., coma occurs, it should be admitted that infants show a remarkable difference from adults in this respect.

It may be granted, then, on the basis of the data cited from various investigators as well as from our own observations, that the blood sugar in infants can reach 0.3 mg. per thousand cubic centimeters without the accidents of hypoglycemia.

The absence of hypoglycemia in athrepsia due to infectious diseases (syphilis, tuberculosis) distinguishes it pathogenically from the merely nutritional form. Baratta,[22] in determining the blood sugar of forty-two children of different ages with tuberculosis in various localizations, found it to be within normal limits. One could infer from this that athrepsia of infectious cause expresses a deficiency in the tissues and the latter a deficiency in the feeding. This belief is confirmed by the failure of treatment with dextrose solutions (Macciotta[6]) for syphilitic or tuberculous athrepsia in contrast to the success that such a method affords in the treatment for merely nutritional athrepsia (Macciotta,[6] Matill, Mayer and Sauer,[13] Helmholz and Sauer,[14] Tisdall, Drake and Brown,[3] Nobécourt[12] and others).

## CONCLUSIONS

1. The existence of a blood sugar value that is, on an average, 43 per cent lower than normal is confirmed in simple nutritional cachexias.

2. The intensity of hypoglycemia is in proportion to the denutrition.

3. The presence of hypoglycemia has not been confirmed in dystrophies of specific cause (syphilis, tuberculosis).

4. The blood sugar remains within normal limits in hypothreptic infants in whose diet cereals are included.

5. The blood sugar returns to its normal value when the patient with athrepsia is progressing toward recovery.

6. The blood sugar of nurslings can fall as low as 0.3 mg. per thousand cubic centimeters without clinical signs of hypoglycemia.

22. Baratta, A.: Ricerche sulla glicemia nell'infezione tuberculare dell'infanzia, Pediatria **36**:806, 1928.