Serum Protein Values in Premature Infants in the First Three Months of Life

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The normal values for full-term infants have been dealt with in numerous studies. Less attention has been devoted to those for premature infants although the functions of the latter are in many respects different from those of normally born children. Of the numerous unelucidated problems concerning the physiology of premature infants, the behaviour of serum proteins during the first three months of extrauterine life constituted the subject of the present investigations that were designed to find an answer to the following questions.

(i) How does the amount of total serum protein change during the first three months of life?

(ii) How do the individual serum protein fractions behave?

(iii) Does the amount of ingested protein affect this proportion?

(iv) Does the amount of total serum protein depend on body weight at birth?

(v) How do infections contracted in the first three months influence the level of gamma globulin in premature babies?

The elucidation of these problems constitutes but the first step of our investigations into the physiology of prematures. Our present aim was to determine the normal values of serum protein and its fractions in premature infants, to provide a basis for further investigations. It seemed best to compare the values of one and the same premature infant recorded on different days of its extrauterine life, and this the more so as the growth of such infants in an environment of 32° C involves a high degree of insensible perspiration and its consequences, so that comparisons between the respective serum-protein levels of premature and full-term babies would lead to false results. Comparisons of this kind will be discussed in a subsequent paper dealing with the determination of absolute protein values per kg body weight.

Material and Method

Fifty-four healthy premature infants were examined at the age of 2—4, 14, 30, 60 and 90 days. Body weight at birth was between 1000 and 1500 g in 17 cases, between 1501 and 2000 g in 23 cases, between 2001 and 2500 g in 14 cases. More than half of the babies was breast-fed.

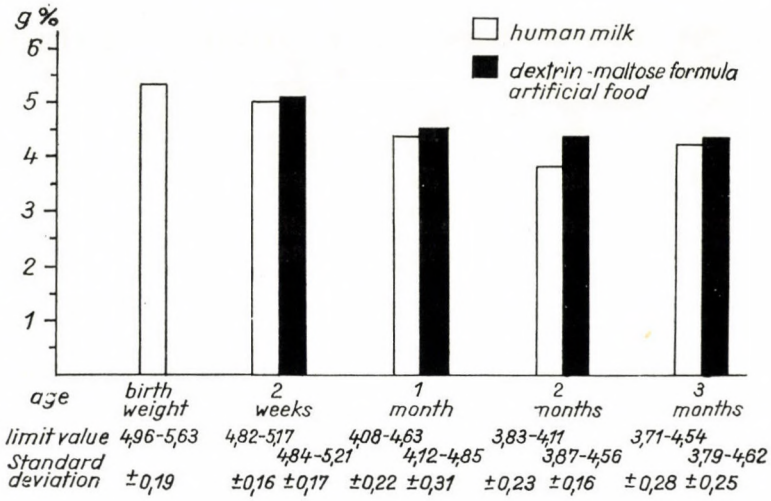

FIG. 1

The amount of total serum protein was determined with the micro-Kjeldahl method. Protein fractions were analyzed by

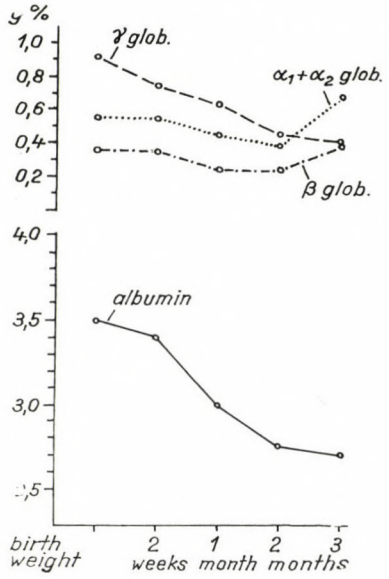

FIG. 2

paper electrophoresis on Schleicher-Schüll's paper No. 2043 b, in veronal Na-acetate buffer of 9.0 pH and 0.06 ionic strength, at room temperature, for 18 hours, at 1 mA per strip. Acid fuchsin was used for staining and 0.1 n sodium hydroxide for elution. The photometer employed was of the FEK-M type, with green filter and a cuvette of 1.0 cm.

RESULTS

Values for serum total protein are shown in Fig. 1. The mean at birth amounted to 5.32 g per 100 ml (4.96 to 5.63, $\pm$ 0.19); the babies received human or cow's milk. The lowest value was reached at 2 months; it remained at this level for some time, and began to rise slowly thereafter. The mean in the breast-fed babies was slightly lower throughout than in infants kept on artificial food richer in proteins.

It is evident from Fig. 2 that the loss of total protein during the first three months of life was mainly due to the diminution of albumin and gamma globulin. Alpha and beta globulins underwent no essential change: after a slight decrease, their amount

showed a renewed upward trend at the age of 3 months.

The level of gamma globulin presented in Fig. 3, showed a steep downward course; the fall was less pronounced in breast-fed than in artificially fed infants.

Table I assembles the further results for gamma globulin. The level not only ceased to diminish but markedly rose after the contraction of various infections (pyoderma, furunculosis, respiratory catarrh) in 7 cases.

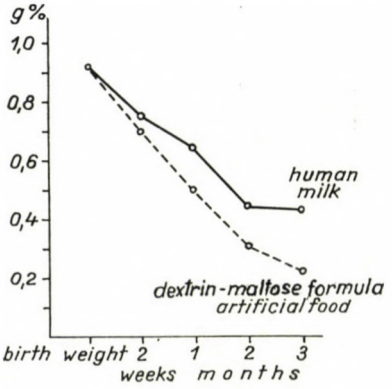

FIG. 3

On the other hand, in several infants the level continued to fall after the infection.

Fig. 4 shows the serum protein value of breast-fed infants grouped according to birth weight. The mean serum protein value was higher in the higher and lower in the lower weight groups in every examined period, but the scattering was within physiological limits throughout, although the values in the low weight group were tending towards the lower, in the high weight group towards the upper limit.

DISCUSSION

The total serum protein level was invariably lower in our premature infants than the values for healthy full-term infants reported in the literature [3, 11, 14, 16]. The difference became more and more pronounced during the months after birth; the average adult value is reached at the age of 1—2 years [12, 16]. According

TABLE I

No.	Age (days)	Body weight (g)	Food	γ globulin, g per 100 ml		
				Before infection	Immediately after the subsidence of infection	4 weeks later
1	36	2460	h	0.59	0.72	0.83
2	63	2620	h	0.40	0.94	0.87
3	34	2110	h	0.65	0.79	0.82
4	61	1980	c	0.33	0.58	0.55
5	42	1940	h	0.62	0.67	0.74
6	23	1580	h	0.71	0.65	0.76
7	40	1480	h	0.69	0.65	0.73

h = human milk
c = cow's milk

to certain authors [1], serum protein values are at the initial level at the end of the first postnatal month. The aetiology of this postnatal hypoproteinaemia is obscure. Rapid postnatal breakdown of protein, insufficient synthesis, and a sudden increase in plasma volume may contribute to it. If this is the case, the true diminution of the protein level is less than that expressed in g per 100 ml, from which it would follow that "hypoproteinaemia", as observed in the first three months of life, is a physiological condition; this assumption is substantiated by the fact that, however low their serum-protein level, prematures develop and grow normally.

A premature infant is, biologically, a different individual in each period (even as compared to its previous self), and it would be erroneous to compare its characteristic physiological features with those of adults or even with those of full-term infants. If only the normal values of the latter were accepted as physiological, all prematures would have to be regarded as hypoproteinaemic, whereas changes due to protein deficiency are fairly rare in infants born before term.

The opinion regarding the effect of ingested protein on the serum protein

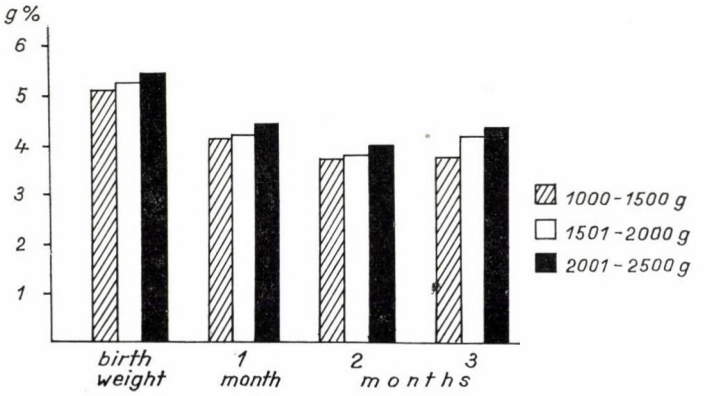

FIG. 4

level is not uniform [4, 8, 13, 15]. It would seem that the rate at which the level falls is somewhat slower if the food is rich in protein. It has, however, been proved that the elevation of the protein level by means of protein-rich food is strictly limited since the increasing excretion of nitrogen prevents any considerable rise [13]. Therefore, human milk, which has ideal colloidal-chemical properties, is perfectly digestible and contains the optimum amount and the best proportion of essential amino acids required by the baby [2], is still much the best food for premature infants. This is borne out by the response of the prematures to infections; besides, the comparatively high amount of waste matter resulting from the con-

sumption of cow's milk means a significant stress for the kidneys.

The behaviour of serum protein and its fractions in premature infants does not seem to be essentially influenced by the body weight at birth [7]. KNAPP and ROUTH [6] showed a considerable difference in the gamma globulin level between newborns and adults. It was presumed that the postnatal decrease of this fraction was due to a depletion of the reserves collected *in utero*, as also to a delay in the beginning of protein synthesis in the newborn. TREVORROW [14] has, however, proved that the circulating amount of gamma globulin did not essentially diminish during the first three months, and that the percentual loss was due to an increase in the volume of plasma and not to a lack of protein synthesis.

Our present observations are in good agreement with the findings of SEVERI and MATTEIS [10] in that, in certain cases, the gamma globulin level ceases to fall and even rises after infections, a phenomenon which shows that even young prematures are able to synthesize this fraction. Babies born with a high body weight and fed on human milk have been found to be in a better position in this respect. The postnatal diminution of the gamma globulin level is more pronounced in prematures kept on cow's milk (Fig. 3) and, moreover, in these the synthesis of globulins starts later than in breastfed infants. No case of agamma-globulinaemia has been observed in the present material.

Considering that non-specific humoral and cellular factors are also involved in the protection of the organism against infections, it seems improbable that the lack of gamma-globulin synthesis is the sole factor responsible for the susceptibility to infections of premature infants. Since, however, prematures are incapable of producing beta$_2$-immune globulins, the fall in the gamma globulin level must nevertheless play a certain role in this respect.

When studying the high susceptibility to infection of prematures, one has to pay especial attention to the difference between the intrauterine and the extrauterine environment. After birth, the young organism is exposed to numerous new environmental influences. If these are not too intensive, the prematurely born infant will be able to react to them in an adequate manner and gradually adapt itself to the external world. If the new influences are too strong or too numerous, the biologically immature organism will not be able to fulfil the required task. It is for this reason that we have to keep premature infants in an environment where they are protected from undesirable influences.

It should once more be emphasized that the "hypoproteinaemia" and — within it — the "hypogamma-globulinaemia" of premature infants is by no means a pathological sign.

SUMMARY

The level of serum protein and its fractions have been studied in 54

healthy premature infants aged 2 to 4, 14, 30, 60 and 90 days.

(i) The total serum protein level diminished after birth irrespectively of whether the babies were fed human or cow's milk. The rate of decrease was more rapid in breast-fed infants.

(ii) Birth weight did not seem to influence the total protein level to any significant extent. Values measured in babies of different birth weights but belonging to the same age group and kept on the same diet were within the limits of standard deviation.

(iii) The diminution of the total serum protein level in the first three months of life was almost exclusively due to a decrease in the amount of albumin and gamma globulin. This phenomenon was more marked in babies fed on cow's milk. The alpha and beta globulin fractions remained practically unchanged.

(iv) The diminution of the gamma-globulin level ceased and was even reversed by infections in certain cases, especially in heavier breast-fed prematurely born infants.

"Hypoproteinaemia" and "hypogammaglobulinaemia" are physiological phenomena in prematures; these conditions follow from the biological properties of their immature organism.

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