PROTEIN REQUIREMENTS OF INFANTS

4—SERUM PROTEIN CONCENTRATIONS IN NORMAL FULL-TERM INFANTS*

BY

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A number of investigators have estimated the plasma and serum protein concentrations in newborn infants and young children (Utheim, 1920; Darrow and Cary, 1933; Rennie, 1935; Dodd and Minot, 1936; Trevorrow, Kaser, Patterson, and Hill, 1941; Bridge, Cohen, and McNair Scott, 1941; Hickmans, Finch, and Tonks, 1943; Rapoport, Rubin, and Chaffee, 1943). The differences in the results which were obtained by these workers may be partly due to the fact that they employed different methods. All agree, however, that the protein concentrations tend to be lower in newborn infants than in older children and that adult concentrations are not reached until the first year of life. Trevorrow *et al.*, who obtained data from a large series of infants, have also shown that there is a fall in the total plasma protein concentrations during the first four weeks of life followed by a gradual rise to the adult concentration, which is reached by about four years of age. These changes are due to variations with age in both the albumin and the globulin fractions, which vary independently of each other.

Studies of the protein requirements of infants at the Children's Hospital, Birmingham (Young, Bishop, Hickmans, and Williams, 1949; Young, Poyner-Wall, Humphreys, Finch, and Broadbent, 1950) stimulated interest in the serum protein concentrations of infants. The present observations on normal full-term infants were planned in order to provide a basis of comparison for values obtained from sick and premature infants.

Present Investigation

Material. Two hundred and forty-five estimations of serum protein concentrations were made on samples obtained from 225 infants whose ages ranged from thirty-six hours to one year. The newborn infants were occupants of the nurseries at the Birmingham Maternity

Hospital and at the Sorrento (one of the City of Birmingham maternity hospitals), and the infants aged two weeks to three months were attending the follow-up welfare clinics at these hospitals. The older group were healthy infants attending the out-patient department of the Children's Hospital, Birmingham, for minor surgical procedures, such as circumcision. Infants, who showed signs of malnutrition or had a history of infection during the preceding three months, were not included. Details regarding feeding and immunization were not obtained.

Blood for analysis was usually taken from a scalp vein but occasionally capillary blood obtained by heel prick was used. The results of estimations on samples collected by the two methods from one subject on the same occasion were always found to agree within the limits of experimental error, and therefore the two methods could be used indiscriminately in obtaining material for this investigation.

Method of Analysis. All of the serum protein concentrations in this and in the parallel investigations (Young *et al.*, 1949) were estimated by micro-Kjeldahl digestion followed by direct nesslerization (Hickmans, 1948). It has been shown that this method tends to give lower results (on average about 0.25 g. of protein/100 ml.) than are obtained by micro-Kjeldahl digestion followed by titration (Broadbent and Finch, 1950).

Results. The individual values, and the averages calculated from them, for total serum protein, albumin, and globulin concentrations in full-term infants from birth to one year are shown in Fig. 1. The exact data are given in Table 1.

It can be seen from Fig. 1 that there was a very wide range for the total serum protein, albumin and globulin concentrations throughout the first year of life. This finding confirms the observations made by Trevorrow *et al.* (1941), and also by Hickmans *et al.* (1943) for the total protein values in plasma.

The average concentrations of both the serum albumin and the serum globulin fractions during the first three months of life varied with age and these variations resulted in changes in the average concentration of total protein. The average value for the total protein concentration for the first fortnight of life was 5.65 g./100 ml. and it fell

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FIG. 1.—Total serum protein, albumin, and globulin (g./100 ml.) in normal infants from birth to one year. (Compare Table 1.)

TABLE 1

AVERAGE TOTAL SERUM PROTEIN, ALBUMIN, AND GLOBULIN CONCENTRATIONS FOR INFANTS FROM BIRTH TO ONE YEAR

No. of Cases	Age	Total (g./100 ml.)	Albumin (g./100 ml.)	Globulin (g./100 ml.)
46	Birth to 2 weeks	5.65	3.26	2.41
30	2 to 4 weeks	5.48	3.57	1.92
15	4 to 6 weeks	5.40	3.72	1.68
34	6 to 13 weeks	5.66	3.94	1.73
63	3 weeks to 6 months	5.66	3.69	1.95
40	6 to 9 months	5.70	3.66	2.02
17	9 months to 1 year	5.87	3.83	2.05

to 5.40 g./100 ml. between the second and sixth week, after which there was a gradual rise to the original level by the third month of life. The average value remained at this level (5.70 g./100 ml.) during the following nine months with a slight rise as the age approached one year. The average value for the albumin fraction was relatively low (3.26 g./100 ml.) during the first fortnight of life, but by the sixth week it had risen to 3.72 g./100 ml.,

and it remained at this level until one year of age. The average value for the globulin fraction was correspondingly high during the neonatal period (2.43 g./100 ml.), and fell to 1.68 g./100 ml. between the second and sixth week of life. It was maintained at this level until the age of three months after which there was a gradual rise to an average value of 2.00 g./100 ml. This was reached between the fourth and sixth months of life. The high average globulin and low average albumin concentrations which have been found during the first two weeks of life were partly due to a small number (nine) of very high values for the globulin fraction with correspondingly low values for the albumin fraction in most cases. These exceptional levels may have been 'true values' or they may have been due to some factor or factors in the serum of certain infants which affected the salting out procedure.

The results of plasma and serum protein concentrations in full-term infants obtained by other workers who used the micro-Kjeldahl method, and those obtained in the present investigation, have been tabulated (Table 2). Some of the data from this table have also been graphed (Fig. 2); 0.2 g. (an allowance for fibrinogen) has been deducted from the plasma values which were obtained by Trevorrow *et al.* in order to make the levels directly comparable with the other serum protein levels shown in Fig. 2. The average total serum protein concentrations of the infants in the present series compared with those

TABLE 2

PLASMA AND SERUM PROTEIN CONCENTRATIONS OF FULL-TERM INFANTS DETERMINED BY MICRO-KJELDAHL METHOD

Author		No. of Cases	Age	Total (g./100 ml.)*	Albumin (g./100 ml.)*	Globulin (g./100 ml.)*
Darrow and Cary (1933)	Serum	20	Newborn (3-10 days)	5.52 (±0.58)	3.73 (±0.38)	1.78 (±0.45)
		14	150-180 days	6.29 (±0.33)	4.28 (±0.38)	2.01 (±0.34)
Rennie (1935)	Serum	4	3-6 months	7.09	4.75	2.34
		7	6-12 months	7.11	4.81	2.30
Dodd and Minot (1936)	Serum	16	Birth-3 months	5.44	3.66	1.78
		34	3 months-2 years	6.19	4.28	1.91
Trevorrow, Kaser, Patterson, and Hill (1941)	Plasma		Birth	5.70 (±0.45)	3.79 (±0.33)	1.66 (±0.29)
			4 weeks	5.33 (±0.37)	3.79 (±0.33)	1.31 (±0.25)
			6 months	(6.00)		
			1 year	(6.20)	4.70 (±0.73)	1.38 (±0.68)
Hickmans, Finch, and Tonks (1943)	Plasma	180	Birth	4.00-7.00		
			3-12 weeks	4.70-7.40		
			Over 3 months	6.00-7.40		
Rapoport, Rubin, and Chaffee (1943)	Serum	17	Newborn (First 48 hours)	5.11 (±0.76)	3.76 (±0.43)	1.34 (±0.41)
		16	2-11 months	6.10 (±0.29)	4.97 (±0.73)	1.38 (±0.68)
Present investigation	Serum	46	Birth-2 weeks	5.65 (±0.51)	3.26 (±0.47)	2.41 (±0.69)
		30	2-4 weeks	5.48 (±0.64)	3.57 (±0.48)	1.92 (±0.41)
		15	4-6 weeks	5.40 (±0.65)	3.72 (±0.39)	1.68 (±0.55)
		34	6-13 weeks	5.66 (±0.63)	3.94 (±0.55)	1.73 (±0.77)
		120	3 months-1 year	5.70 (±0.62)	3.70 (±0.41)	2.00 (±0.38)

* Shows standard deviation.

of the infants in the series of Trevorrow *et al.* show (1) a slightly higher level during the neonatal period, (2) an initial fall which is similar in degree, (3) an earlier rise, and (4) good agreement with the levels from four months to one year. Darrow and Cary obtained similar, and Rapoport *et al.* somewhat lower, average values for the newborn infants, and both groups of workers found higher average values during the later months of infancy. The present series shows uniformly lower albumin and higher globulin levels than were obtained by Trevorrow *et al.* The results obtained by Rapoport *et al.* for both fractions are similar to those obtained by Trevorrow *et al.*, but Darrow and Cary found higher globulin levels, the average of which was almost the same as that obtained from our series. The method of separation of the protein fractions seems the most probable explanations for these differences.

Discussion

The observations which have been made in the present and in previous investigations may be used as a guide to the value of serum protein determinations in young infants. It has been found that the range and distribution of the serum protein concentrations of normal infants is very wide and that a proportion of infants have values which would be regarded as evidence of a severe degree of hypoproteinaemia in older children or adults. Serum protein levels, therefore, cannot be used to assess nutritional status in individual infants during the first year of life. The range, distribution, and average levels of a series of normal infants may, however, be used as a basis of comparison for the

FIG. 2.—Average serum protein levels in present series compared with the levels obtained by Trevorrow *et al.* (1941), Darrow and Cary (1933), and Rapoport *et al.* (1943).

levels of a particular group of infants, in order to determine whether hypoproteinaemia has occurred more frequently amongst them (see Parts 2 and 3 of this paper).

The serum protein concentrations which are presented in this report should not be regarded as 'standard' absolute values for normal infants, since the results obtained by the method used have been found to differ from those obtained by micro-Kjeldahl digestion followed by titration, and the difference is not a consistent one. Furthermore, a survey of a much larger number of levels would be required to obtain standards of statistical value for infants during the early months of life, because the range and distribution of the levels is so wide at this age.

Summary

Total protein, albumin, and globulin concentrations have been estimated in the serum of a series of normal full-term infants whose ages ranged from thirty-six hours to one year. The levels were estimated by micro-Kjeldahl digestion followed by direct nesslerization, a method which tends to give lower results than those obtained by micro-Kjeldahl digestion followed by titration.

A very wide scatter for all three concentrations was found throughout this period of infancy. The average total serum protein levels showed a slight initial fall during the first few weeks of life followed by a rise to the original level by three months of age

and a further slight rise as the age approached one year. These changes were due to variations in both the albumin and the globulin fractions.

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REFERENCES

- Bridge, E. M., Cohen, M. I., and McNair Scott, T. F. (1941). *J. Pediat.*, **18**, 709.
- Broadbent, I., and Finch, E. (1950). *Arch. Dis. Childh.*, **25**, 134.
- Darrow, D. C., and Cary, M. K. (1933). *J. Pediat.*, **3**, 573.
- Dodd, K., and Minot, A. S. (1936). *J. Pediat.*, **8**, 452.
- Hickmans, E. M. (1948). *Pediat. Int.*, **1**, 331.
- , Finch, E., and Tonks, E. (1943). *Arch. Dis. Childh.*, **18**, 96.
- Rapoport, M., Rubin, M. I., and Chaffee, D. (1943). *J. clin. Invest.*, **22**, 487.
- Rennie, J. B. (1935). *Arch. Dis. Childh.*, **10**, 415.
- Trevorrow, V., Kaser, M., Patterson, J. P., and Hill R. M. (1941). *J. Lab. clin. Med.*, **27**, 471.
- Utheim, K. (1920). *Amer. J. Dis. Child.*, **20**, 366.
- Young, W. F., Bishop, E. A., Hickmans, E. M., and Williams, Y. J. (1949). *Arch. Dis. Childh.*, **24**, 250.
- , Poyner-Wall, P., Humphreys, H. C., Finch, E., and Broadbent, I. (1950). *Arch. Dis. Childh.*, **25**, 31.