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Energy metabolism, substrate utilization, metabolite and hormone levels in infants fed various parenteral solutions

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Previous observations on the effects of various types of parenteral nutrition on changes in oxygen consumption, respiratory quotient, total heat production, distribution of nutrient utilization, metabolic and hormonal levels in infants during the neonatal and postneonatal periods are reviewed.

The relevant findings obtained in fifty-two newborn infants infused with different types of metabolic solutions were as follows. Oxygen consumption increased during Aminosol-glucose and Intralipid-glucose infusion. The respiratory quotient varied according to the oxidation of the nutrients. A significant elevation was observed during Aminosol-glucose infusion, which tended to fall in response to Intralipid. Total heat production was increased during all types of parenteral nutrition, and substrate utilization depended on the quality and amount of nutrient intake. The magnitude of the changes in concentrations of metabolites (glucose, free fatty acids, alpha-amino-nitrogen) and insulin and growth hormone were smallest when the parenteral nutrition consisted of glucose, amino acids and lipid and the total caloric intake did not exceed the maintenance energy expenditure. On the basis of the results, during the neonatal period it seems advisable to administer as parenteral nutrition, about 70—75 kcal/kg/day in the form of 7.0—8.0 g/kg/day glucose, 1.7—2.0 g/kg/day amino acids and 3.0—4.0 g/kg/day lipid.

Nutrition by intravenous infusion of various nutritive mixtures appears to be of great importance for the adequate management of sick infants during the postneonatal period. Long-term parenteral nutrition by giving only an amino acid-glucose mixture or a glucose-amino acid-lipid solution can produce a gain in weight with a positive nitrogen balance [2, 8, 11, 13, 29). Some metabolic and biochemical studies, however, show that these feeding methods may cause adverse metabolic effects such as hyperammonaemia, hyperaminoacidaemia, increased osmolality, metabolic acidosis, etc. [4, 6, 7, 9, 14, 16, 20, 28, 30].

It is well-known that maintenance caloric requirement varies greatly according to gestational, postnatal age, body weight and numerous other factors [18, 19, 24, 25]. Knowledge of the caloric expenditure of newborns and the calorigenic effect of parenteral nutrition is also essential when alimentation takes place by intravenous route. In spite of many reports on the

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metabolic effects of intravenous nutrition and on the aspects of maintenance energy expenditure in the neonatal or postneonatal period, there is a dearth of data on the effect of various types of parenteral nutrition on heat production and substrate utilization. This report deals with the responses of energy metabolism and substrate utilization to various types of parenteral nutrition during the neonatal and postnatal periods. In view of the metabolic adaptation of the low-birth-weight infant it appeared important to determine the optimum amount of parenteral nutrient intakes which do not cause metabolic alterations but are still high enough to cover the maintenance energy expenditure of the newborn infant.

Methods

Clinical material. Fifty-two newborn infants divided into 5 series of 7–15 each (see Table I) were infused with five different types of nutritive solution.

The infants in the first four series (I–IV) were selected on the basis of their inability to tolerate oral or tube feeding without the danger of apnoeic spells and/or aspiration. The patients in the fifth series (V) had undergone surgery in the neonatal or postneonatal period and needed parenteral nutrition during intensive postoperative care.

The number of infants, mean $\pm$ SE body weight, gestational and postnatal age at examination are summarized in Table I.

Infusions. In the first three series (I, II, III) we investigated the acute effects of parenteral solutions using short infusion periods.

In the first series (I) Aminosol-glucose (Vitrum, Stockholm) was infused for 240 min after a 4-hour starving period. The infusion was discontinued for 2 h in order to study the metabolic response to interruption of the parenteral nutrition.

In series II the effect of a 28 hour Aminosol-glucose infusion was studied after a 12 h control period.

In series III, the infants received glucose as a basic solution infused at a steady rate throughout 42 hours. The first 12 hours, when the infants received only intravenous glucose, served as control period. Over the next 6 h, Intralipid (10%, Vitrum, Stockholm) was infused in addition to glucose. After termination of Intralipid supplementation, intravenous feeding with glucose was continued for two consecutive 12 h periods.

In series IV, the caloric intake was increased. Low-birth-weight infants were fed intravenously for altogether 36 hours divided into three 12 h periods. In the first 12 h 10% glucose was given; during the second 12 h period 10% glucose with 2.7% crystalline amino acids (Aminosol 2400, Vitrum, Stockholm) was infused thereafter, in addition to glucose and an amino acid mixture, 10% lipid solution (Intralipid, Vitrum, Stockholm) was infused by means of a second infusion pump. In brief, solutions containing glucose (regimen A), glucose and amino acids (regimen B), and glucose with amino acids and lipids (regimen C) were given.

In series V we compared three consecutive 24 h periods, in which the infusion contained the same caloric and volume intake, but the composition of the nutrients was changed. Regimen A contained 10% glucose, regimen B glucose-amino acids, and regimen C Intralipid and amino acids. The volume and energy content of the infusates were the same, and in the case of two mixtures care was taken to infuse identical amounts of amino acids (1.70 to 1.77 g/kg/day).

The daily caloric input and the nutrients infused are shown in Table I.

Determination of energy expenditure and substrate utilization. Oxygen consumption

TABLE I

Data of infants, amount of calories and nutrients infused

Parenteral nutrition programme	No. of infants	Gestational age, weeks	Postnatal age, h	Body weight, g	Caloric input, kcal/kg/day	Nutrients infused, g/kg/day		
						glucose	amino acids	lipid
I. Short period of Aminosol-glucose infusion	7	30.8±0.7	31.4±2.8	1570±87.8	52.6±2.3	8.6±0.3	5.6±0.2	—
II. Longer period of Aminosol-glucose infusion	15	30.1±0.9	20.9±2.1	1282±86.2	36.4±2.7	5.9±0.4	3.9±0.3	—
III. Intralipid-glucose infusion	12	33.4±0.6	11.7±1.2	1734±75.7	43.6±2.4	5.5±0.5	—	7.5±0.2
IV. Increasing caloric intake, variable composition of nutrients	8	32.0±1.0	18.2±5.9	1362±148.4				
Regimen A = glucose alone					28.7±1.2	7.1±0.3	—	—
Regimen B = glucose + amino acid					35.1±1.4	7.1±0.3	1.5±0.07	—
Regimen C = glucose + amino acid + lipid					70.3±1.4	7.1±0.3	1.5±0.07	3.1±0.2
V. Same caloric intake, variable composition of nutrients	10	38.4±0.5	19.0±7.1	3067±285.9				
Regimen A = glucose alone					56.2±2.2	14.0±0.5	—	—
Regimen B = glucose + amino acid					55.4±2.5	12.2±0.5	1.7±0.07	—
Regimen C = lipid + amino acid					56.3±1.7	—	1.7±0.06	4.1±0.1

and carbon dioxide production were measured using a Kipp diaferometer, which allowed continuous measurement of the respiratory gas exchange and the respiratory quotient. The Kcal value of oxygen used for calculation of heat production corresponded to the average RQ of the observation period. The relative values of substrate utilization were calculated from the oxygen consumption and CO_2 production after subtraction of the oxygen and carbon dioxide related to the protein metabolism, as determined by the urea nitrogen excretion [3]. For this purpose urine collections were made during the observation periods according to the infusion periods. The relative utilization of fat and carbohydrates was estimated from the non-protein RQ [22, 26].

Chemical monitoring. Before and at the end of the infusion periods, blood samples were drawn through an umbilical venous catheter in series I to IV, and from a peripheral vein in series V. The following metabolites were measured: glucose [21], free fatty acids [5, 17], alpha-amino-nitrogen [27]. Plasma insulin and growth hormone were estimated by the method of Hales and Randle [12], and Hunter and Greenwood [15].

For statistical analysis the means and standard errors were calculated; when it seemed necessary, significance was estimated by Student's t-test.

Results

Oxygen consumption and respiratory quotient

Mean oxygen consumption and respiratory quotient calculated for 30-min periods before, during and after Aminosol-glucose infusion as well as Intralipid-glucose infusion are shown in Fig. 1. The upward tendency of oxygen consumption was obvious in both cases; but owing to the great individual variation of the initial data and responses to the fat and amino-glucose mixtures, the increase turned out to be insignificant whichever period was used for comparison. It is seen from Fig. 1 that the low RQ of fasting prematures varied greatly according to the oxidation of the nutrients during the infusion periods. A significant elevation was observed during Aminosol-glucose infusion and the mean respiratory quotient tended to fall in response to Intralipid.

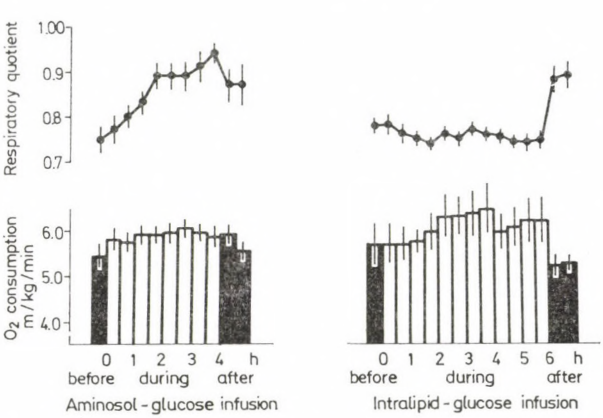

FIG. 1. Oxygen consumption and respiratory quotient during short periods of Aminosol-glucose and Intralipid-glucose infusion

Total heat production in response to various types of parenteral nutrition

Mean total heat production per kg body weight per day is shown in Fig. 2. During all types of parenteral nutrition there was a rise in total heat production, which reached the level of significance only in the case of the short Aminosol-glucose infusion period (I) when the amino acid input (see Table I) was the highest in the investigated series. Total metabolism during the longer Aminosol-glucose infusion (II), the Intralipid-glucose infusion (III), and in series V where caloric input and volume input were the same, did not appreciably exceed that obtained in the control periods.

Distribution of the chief nutrients in total heat production

To quantitate the nutrients utilized' the amount of protein was calculated from urinary nitrogen, and the amounts of carbohydrates and lipids were obtained from the non-protein respiratory quotient. The mean relative distribution of calories produced in series I, III and V is presented in Table II. Three individual examples of nutrient utilization during the longer Aminosol-glucose infusion are shown in Fig. 3.

It can be seen from Table II that the catabolism of amino acids had doubled, the amount of metabolized fat was still not negligible, and the amount of carbohydrates utilized was higher during the second half of the Aminosol-glucose infusion period (series I). When the Aminosol-glucose infusion was contained for a longer period of time (Fig. 3) the participation of carbohydrates increased, while fat metabolism became the smallest energy component, and the proportion of amino acid oxidation reached a high value, 60, 32 and 28% of total heat production during the 16–28 h of infusion. The effect of Intralipid on the distribution of the calories produced is also shown in Table II. It is seen (series III) that before Intralipid supplementation the metabolic state was dominated by fat utilization. The metabolic pattern during Intralipid-glucose infusion was characterized by an increase in fat

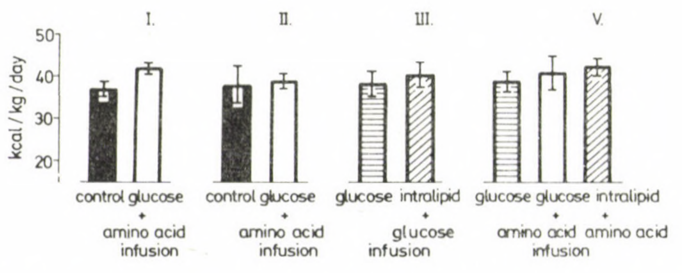

FIG. 2. Total heat production during various types of parenteral nutrition. I = short period of Aminosol-glucose; II = longer period of Aminosol-glucose; III = short period of Intralipid-glucose infusion; V = same caloric intake of different nutrients

TABLE II

Relative distribution of calories produced by fat, carbohydrate and protein during various types of parenteral nutrition

Parenteral nutrition programme	Periods of investigation	Relative distribution of calories produced by		
		Fat, per cent	Carbohydrate, per cent	Protein, per cent
Series I	0–120 min	48.96±6.43	44.96±6.57	6.07±0.68
	121–240 min	29.04±7.14	58.35±8.02	12.59±1.48
Series III	Glucose period	70.42±3.86	25.35±3.84	4.22±0.92
	Intralipid+glucose period	76.34±3.92	14.87±3.91	8.77±1.73
	Glucose period	38.49±7.62	53.06±8.80	8.44±1.98
	Glucose period	34.96±9.71	56.58±10.45	8.45±1.78
Series V	Glucose period	33.31±6.06	58.53±5.84	8.19±1.43
	Glucose+amino acid period	29.90±5.81	63.55±5.85	6.53±1.52
	Amino acid+lipid period	77.24±6.16	17.38±5.44	5.37±1.20

and protein oxidation. After termination of the infusion of fat, continuation of glucose infusion at the same rate markedly changed the distribution pattern of energy metabolism; the contribution of carbohydrate oxidation increased while that of fat decreased. Table II also shows the effect of parenteral nutrition on substrate utilization when caloric input and volume input were the same and the composition of the nutritive mixture was changed. It can be seen from the results of series V, that energy metabolism was dominated by carbohydrate utilization during the glucose infusion period and the addition of amino acids to glucose did not appreciably alter the distribution of substrate utilization. The distribution

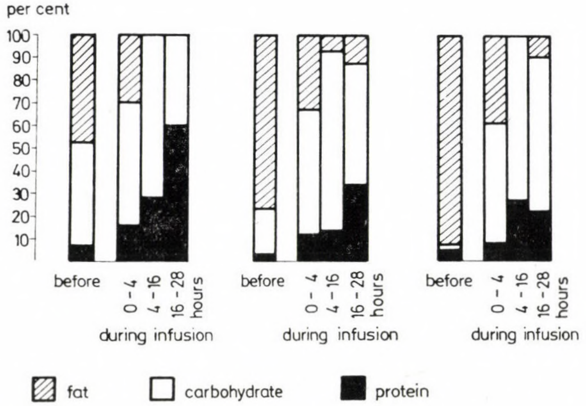

FIG. 3. Relative distribution of calories produced by fat, carbohydrate and protein in three preterm infants receiving Aminosol-glucose infusion for longer period

pattern of energy metabolism changed markedly when lipid was administered together with an amino acid solution; then heat production was dominated by fat utilization.

Metabolic and hormonal responses to infused calories not exceeding maintenance energy expenditure

The changes in total heat production and substrate utilization showed that the former parameter slightly increased and the latter depended on the quality and amount of nutrient intake. In order to investigate what kind of metabolic and hormonal changes were caused by a type of parenteral nutrition which covered the maintenance energy expenditure but, at the same time did not exceed the intravenously infused calories, three consecutive 12 h periods (infusion of glucose, glucose + amino acid, glucose + amino acid + lipid) were investigated.

Metabolic responses. Figure 4 shows that the concentration of glucose at the end of the three infusion periods was higher than the control level ($p < 0.01$ and <0.05). The greatest rise was seen during the glucose period (A), thereafter the addition of an amino acid mixture to glucose resulted in a fall (regimen B), and supplementation with lipid (regimen C) did not greatly influence the blood glucose level. The mean concentration of plasma free fatty acids fell in response to glucose, the infusion of

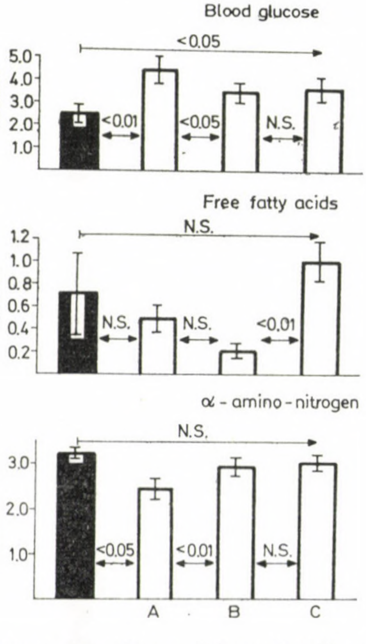

FIG. 4. Response of blood glucose, free fatty acids and alpha-amino-nitrogen to infusions of (A) 10% glucose, (B) 10% glucose + 2.7% amino acid, and (C) 10% glucose + 2.7% amino acid + 10% lipid

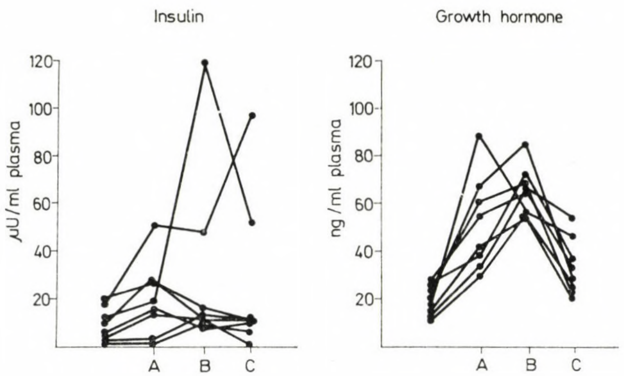

FIG. 5. Individual changes of plasma insulin and growth hormone during 10% glucose (A), 10% glucose + 2.7% amino acid (B), and 10% glucose + 2.7% amino acid + 10% lipid (C) infusion

amino acids in addition to glucose caused a further decrease in plasma FFA, and supplementation with lipid was, as expected, followed by a rise in FFA concentration. The changes in alpha-amino-nitrogen are shown in Fig. 4. The mean level of alpha-amino-nitrogen fell significantly in response to glucose ($p < 0.05$), but returned to the fasting level when an amino acid mixture was added to the glucose. The supplementation with lipid solution did not affect this level.

Insulin and growth hormone response. It is seen from Fig. 5 that the magnitude and time course of the individual changes in plasma insulin were varied. The changes in growth hormone were uniform: the definite increase elicited by glucose was followed by a further pronounced increase in response to the combined infusion of glucose and amino acids, and the addition of lipid was associated with a pronounced fall.

Discussion and Conclusions

Earlier investigations on the maintenance energy expenditure of low-birth-weight infants kept at neutral temperature had pointed to the need of an individual approach to the estimation of calorie requirement [18, 24], but it was obvious that total heat production was low during the neonatal period. By direct measurements of the components of total heat production (basal metabolic rate, specific dynamic action, activity, thermoregulatory heat production) it was found [18, 19] that the energy need of very low-birth-weight infants was about 50–65 kcal/kg/day.

These observations are of great importance for the parenteral alimentation of newborn infants since by using the conventional estimates of maintenance energy expenditure, an excessive caloric load may be imposed, leading to dangerous complications such as hyperammonaemia, hyperaminoacidaemia and metabolic acidosis [4, 9, 23]. Besides, the specific dynamic action of a protein-rich formula greatly contributes to the extra calories produced above the basal requirement [19], and non-protein energy sources such as glucose or fat [10] may improve the nitrogen balance. Still, even an energy input exceeding energy expenditure cannot maintain nitrogen equilibrium in the absence of nitrogen input [1, 26].

In the present study, heat production increased in every case of parenteral nutrition, but was significant only during series I, when amino acid input was highest (5.69 g/kg/day). Protein breakdown was also important when only the glucose-amino acid mixture was given over a longer period in series II with a higher amino acid input (3.95 g/kg/day) and a lower glucose input (5.94 g/kg/day). When fat or glucose were given as non-protein energy source with lower nitrogen input (1.70 – 1.77 g/kg/day as amino acid), the proportion of protein in the total heat production decreased as compared with the glucose period (series V).

The changes in the concentration of metabolites (glucose, free fatty acids and alpha-amino-nitrogen) and hormones (insulin and growth hormone) were smallest in the last infusion period of series IV, when parenteral nutrition consisted of glucose, amino acids and lipid, but the total caloric input did not exceed the maintenance energy expenditure.

On the basis of the results it seems advisable during the neonatal period to administer about 70–75 kcal/kg/day in the form of 7.0–8.0 g/kg/day glucose, 1.7–2.0 g/kg/day amino acids and 3.0–4.0 g/kg/day lipid as parenteral nutrition. In view of the usual absence of growth in low-birth-weight neonates during the first 10 days of life, it appears unnecessary to increase the caloric input above the maintenance requirement, otherwise most of the extra calories and substrates would probably be rapidly oxidized rather than incorporated in the body tissues.

References

1. Anderson TL, Muttart CR, Bieber MA, Nicholson JF, Heird WC: A controlled trial of glucose versus glucose and amino acids in premature infants. J Pediatr 94:947, 1979
2. Boeckmann CR, Krill CE: Bacterial and fungal infection complicating parenteral alimentation in infants and children. J Pediatr Surg 5:117, 1970
3. Ceriotti G: Ultramicro determination of plasma urea by reaction with diacetylmonoxide-antipyrine without deproteinization. Clin Chem 17:400, 1971
4. Chan JCM, Ash MJ, Lin St, Hays DM: Hyperalimentation with amino acid and casein hydrolysate solutions. Mechanisms of acidosis. JAMA 220:1700, 1972
5. Dalton C, Kowalski C: Automated colorimetric determination of free fatty acids in biologic fluids. Clin Chem 13: 741, 1967
6. Das JB, Filler RM, Rubin VG, Eraklis AJ: Intravenous dextrose-amino acid feeding: the metabolic response in the surgical neonate. J Pediatr Surg 5:127, 1970
7. Driscoll JM, Heird WC, Schullinger JN, Gongaware RD, Winters RW: Total intravenous alimentation in low-birth-weight infants. A preliminary report. J Pediatr 81:145, 1972

8. Filler RM, Eraklis AJ, Rubin VG, Das JB: Long term parenteral nutrition in infants. N Engl J Med 281:589, 1971
9. Ghadimi H, Abaci F, Kumar S, Rathi M: Biochemical aspects of intravenous alimentation. Pediatrics 48:955, 1971
10. Greenberg GR, Marliss EB, Anderson HG, Langer B, Spence W, Tovee EB, Jeejeebhoy KN: Protein-sparing therapy in postoperative patients. Effects of added hypocaloric glucose or lipid. N Engl J Med 294:1411, 1976
11. Gustafson A, Kjellmer J, Olegard R, Victorin L: Prolonged intravenous fat administration in low birth weight infants and the effect of heparin. Pediatr Res 6:61, 1972
12. Hales CN, Randle PJ: Immunoassay of insulin with insulin-antibody precipitate. Biochem J 88:137, 1963
13. Heird WC, Driscoll JM, Schullinger JN, Grebin B, Winters RW: Intravenous alimentation in pediatric patients. J Pediatr 80:351, 1972
14. Helmuth WV, Adam PAJ, Sweet AY: The effects of protein hydrolysate-monosaccharide infusion on low-birth-weight infants. J Pediatr 81:129, 1972
15. Hunter WM, Greenwood FC: A radio-immunoelectrophoretic assay for human growth hormone. Biochem J 85:39, 1962
16. Johnson JD, Albritton WL, Sunshine P: Hyperammonemia accompanying parenteral nutrition in newborn infants. J Pediatr 81:154 (1972)
17. Laurell S, Tibbling G: Colorimetric microdetermination of free fatty acids in plasma. Clin Chim Acta 16:57, 1967
18. Mestyán J, Járai I, Fekete M: The total energy expenditure and its components in premature infants maintained under different nursing and enviromental conditions. Pediatr Res 2:161, 1968
19. Mestyán J, Járai I, Fekete M, Soltész Gy: Specific dynamic action in premature infants kept at and below the neutral temperature. Pediatr Res 3:41, 1969
20. Peden VH, Karpel JT: Total parenteral nutrition in premature infants. J Pediatr 81:137, 1972
21. Pryce JD: A simple rapid method for determining glucose in blood or plasma. Analyst 92:198, 1968
22. Rubecz I, Mestyán J: Energy metabolism and intravenous nutrition of premature infants. I. The responses of oxygen consumption, respiratory quotient and substrate utilization to infusion of Aminosol-glucose. Biol Neonate 23:45, 1973
23. Rubecz I, Mestyán J: The effect of infusion of Aminosol-glucose on the acid-base balance of low-birth-weight infants. Acta Paediatr Acad Sci Hung 14:309, 1973
24. Rubecz I, Mestyán J: The partition of maintenance energy expenditure and the pattern of substrate utilization in intrauterine malnourished newborn infants before and during recovery. Acta Paediatr Acad Sci Hung 16:335, 1975
25. Rubecz I, Mestyán J: Activity, energy metabolism and postnatal age relationship in low-birth-weight infants. Acta Paediatr Acad Sci Hung 16:351, 1975
26. Rubecz I, Mestyán J, Varga P, Klujber L: Energy metabolism, substrate utilization and nitrogen balance in parenterally fed postoperative neonates and infants. J Pediatr 98:42, 1981
27. Rubinstein HM, Pryce JD: The colorimetric estimation of amino nitrogen in tissue fluids. J Clin Path 12:80, 1959
28. Stegink LD, Baker GL: Infusion of protein hydrolysate in the newborn infants: Plasma amino acid concentrations. J Pediatr 75:595, 1971
29. Victorin L, Gustafson A, Kjellmer J, Olegard R: Intravenous administration of fat to premature infants. Acta Paediatr Scand 60:102, 1971
30. Wretling A: Complete intravenous nutrition. Theoretical and experimental background. Nutr Metab 14: Suppl 1, 1972

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