

American Journal of Diseases of Children

VOL. 1

MAY, 1911

No. 5

STUDIES ON INFANT NUTRITION

UNDER THE DIRECTION OF L. EMMETT HOLT, M.D., AND P. A. LEVENE, M.D.

*I. Metabolism in Chronic Malnutrition **

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Growth is the principal function of infancy, and any disturbance of it constitutes a serious condition. A state of nutrition which maintains the weight and size of the organism unchanged is desirable for the adult; it cannot be endured with impunity for any length of time by the infant.

Unfortunately disturbances of nutrition are not infrequent, principally among artificially-fed infants. The condition may follow some acute disease or may develop gradually as a result of some form of irrational feeding. It has been named differently by various writers at different times. It has been studied as atrophy, marasmus, simple wasting, decomposition, etc. But, notwithstanding the numerous investigations into its nature, and notwithstanding the many theories advanced for the explanation of the condition, the actual pathogenesis of the retarded growth of these infants still remains obscure.

In view of these considerations an attempt has been made to study the metabolism of infants in different phases of this condition. The difficulties of the undertaking were fully realized. In addition to those that are common to all metabolism work, there are additional factors arising from the technic of the investigation on infants. The position and restraint necessary in the metabolism apparatus, and even the surroundings of the hospital, affect the general health of an infant much more than the usual routine of a metabolism experiment affects the adult.

However, it was hoped that a careful study of a considerable number of patients, extended over a long period of time, would furnish information which might serve to establish a rational treatment of these disturbances. The patients on whom these studies have been made were all inmates of the Babies' Hospital, and for the most part they were admitted for disordered nutrition. The clinical details have been carried

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The present communication may be regarded as preliminary and contains a report on metabolism experiments on seven infants. The age of the patients varied from 3 to 7 months, and the duration of the observation from 3 to 106 days. The last represents the longest metabolism experiment on an infant thus far recorded. Attention has been paid to the nitrogen metabolism, fat metabolism, and to a certain extent to the mineral and water balance.

The food analysis was made in every experiment.

METHODS OF ANALYSIS

Total nitrogen in food mixture, urine, and dried feces was determined by the Kjeldahl-Gunning method.

Ammonia nitrogen was determined by the Folin method.

Sugar was determined by Pavy's method.

Starch when present was first hydrolyzed by heating with dilute sulphuric acid in an autoclave, and the sugar thus formed titrated according to Pavy.

Fat estimation: In order to determine the total fatty acids, food mixtures or feces were evaporated to dryness on a water-bath. Samples of the dry residues were thoroughly mixed with dilute phosphoric acid and the mixtures extracted in a Soxhlet apparatus with ether. In order to free the ethereal residues from moisture they were redissolved in chloroform, filtered through filter paper saturated with chloroform, and the weight of the chloroform residue determined. The neutral fat and free fatty acids were determined by extracting the dry samples of food-mixtures or feces with ether.

The total ash was obtained by igniting the dried feces and the residues from the evaporated urine with a few drops of concentrated nitric and sulphuric acid. The bases were calculated as sulphates.

Phosphoric acid was determined by titration with uranium acetate. For determination of phosphoric acid in the feces, the ash was dissolved in the smallest possible quantity of concentrated hydrochloric acid. An aliquot part of the solution was neutralized with sodium acetate and titrated with uranium acetate.

Calcium estimation was carried out in the usual manner. It was precipitated from solution by means of ammonium oxalate. The oxalate was transformed by ignition into the oxid. The calcium content of the urine was found too small to make possible an accurate determination.

The clinical histories of the patients are given at the end of the report. The results of the analyses are tabulated (Tables 1, 2 and 3).

The discussion of the results will be directed principally to the analysis of the peculiarities of nitrogen and fat metabolism. Carbohydrate, mineral and water balance will be discussed only in their effect on either protein or fat assimilation.

NITROGEN METABOLISM

A. General Considerations

Protein was regarded for a long time as the exclusive foodstuff on which depended the growth of the young. The utility of a foodstuff according to the views of those days, was determined principally by the digestibility of its protein material. These views, however, collapsed as soon as they were subjected to the experimental test. Rubner and Heubner have made it clear that fat and carbohydrates share equally with protein in their power to aid the maintenance and growth of the young as they do in maintaining the integrity of the adult. The law of the isodynamic value of these three principal sources of animal energy is applicable to all ages. Later investigations have demonstrated that in health practically every protein is equally well digested and absorbed from the intestinal tract of the infant; and further, it was established that in health, fat has an insignificant influence on the rate of absorption and assimilation of protein, while the influence in this direction of carbohydrate is very marked, exercising a protecting power over the combustion of protein and therefore increasing the degree of its assimilation.

Notwithstanding the revision in the view of the rôle of protein in the process of nutrition of the infant, it remains true that growth of tissues cannot take place without a retention of nitrogen in the organism. It is natural to find, therefore, that considerable attention was devoted to the study of nitrogen metabolism in conditions of malnutrition.

The earlier investigations into the nitrogen metabolism of atrophic children belong to Rubner and Heubner,¹ to Baginsky,² and to Bendix.³ In the patients of Rubner and Heubner and of Baginsky, protein assimilation was lowered. Baginsky reached the conclusion that infantile atrophy was caused by disturbed assimilation resulting from the atrophic changes in the gastro-intestinal tract.⁴ Also in the patient of Heubner and Rubner the absorption was apparently defective. Bendix was the first to make the observation that normal protein metabolism coexisted

1. Rubner and Heubner: *Ztschr. f. Biol.*, 1899, xxxviii, 360.

2. Baginsky: *Deutsch. med. Wchnschr.*, 1899, xviii, 281.

3. Bendix: *Arch. f. Anat. u. Physiol. Suppl. Vol.*, 1899, 206.

4. In this discussion the term "atrophic" will be abandoned, and the terms of Finkelstein—decomposition and intoxication—will not be made use of. All the various conditions that result in the retardation or the apparently complete arrest of growth will be referred to as infantile malnutrition.

TABLE 1.—AVERAGE DAILY FOOD INTAKE AND WEIGHT BALANCE

Period	Dates	Composition of Food	Volume of Milk c.c.	Protein Gms.	Carbo- hydrate Gms.	Fat Gms.	Weight Balance* Gms.
I. JAMES							
1	Nov. 18-22½ milk, 5% lime-water, barley-water to volume, 3¼% milk-sugar additional	512	18.0	30.8	23.3	+36.8
2	Nov. 23-26Same, except 5 5/7% milk-sugar	525	18.1	66.2	18.1	+46.0
3	Nov. 28-Dec. 150-60% skimmed-milk, 5% lime-water, barley-water to volume, 5% milk-sugar	578	19.4	51.4	10.7	-10.6
4	Dec. 8-1665-65% skimmed-milk, 5% lime-water, concentrated barley-water to volume	651	25.0	39.3	14.9	+ 9.4
5	Dec. 18-2065% skimmed-milk, 5% lime-water, conc. barley-water to vol., 12 c.c. Mellin's Food	651	24.0	54.3	18.3	+14.2
6	Dec. 22-24Same, except no Mellin's Food	651	25.8	39.4	15.8	+18.9
7	Dec. 31-Jan. 3½ milk, 5% lime-water, water to volume	770	27.3	31.4	31.5	+60.2
8	Jan. 5-6Same, but peptonized	770	26.0	29.7	27.0	-42.5
9	Jan. 9-14¼ skimmed-milk, ¼ water, 3.08 gms. NaHCO ₃	880	28.0	33.7	12.1	+ 2.4
10	Jan. 22-24½ skimmed-milk (3 oz. off top), ½ soy bean gruel, 2 gms. NaCl, 16 c.c. beef-juice	604	26.1	26.0	16.2	+55.6
11	Jan. 26-28Same, except milk 4 oz. off top	604	26.3	27.6	7.9	-54.0
12	Feb. 19-24½ fat-free milk, ½ soy bean gruel, 2 gms. NaCl, 32 c.c. beef-juice, 1.2% olive oil	508	24.9	23.0	14.2	-25.8
13	Feb. 25-Mar. 2Same, except 1.6-2.0% olive oil	525	27.2	25.9	18.8	+ 5.2
II. DAKAR							
1	Mar. 8-11Skimmed-milk, 5% lime-water, milk-sugar to 6%, 20 c.c. malt soup extract	1050	18.1	67.9	19.7	+48.5
2	Mar. 12-14Same, except only 12 c.c. malt soup extract	641	10.8	38.2	12.3	+ 4.3
III. STOCKER							
1	Mar. 17-1840% milk, 5% lime-water, barley-water to volume, 4 1/6% milk-sugar additional	415	15.2	60.4	17.0	+68.5
2	Mar. 19-20Same, except milk-sugar only to 3%	418	15.3	38.2	18.7	+ 7.7

3	Mar. 23-24Same, except no additional milk-sugar	462	16.6	29.2	22.4	-10.0
4	Mar. 26-27Same, except 10 c.c. malted milk additional	462	16.1	32.9	16.3	+72.5
5	Mar. 28Same as in Period 3	462	14.4	29.2	19.9	- 7.0
6	Mar. 2940% milk, 5% lime-water, arrow-root gruel (2 drams to pt.) to volume	462	13.8	26.8	15.5	-12.0
7	Mar. 31-Apr. 135% fat-free milk, 5% lime-water, soy bean gruel (1 oz. to pt.) to volume	404	17.9	19.5	2.3	-80.5

IV. GUERIN

1	Apr. 13-1645% milk, 5% lime-water, barley-water to vol., 2 13/16% milk-sugar additional, 16 c.c. malt soup ext., albumin of 2 eggs	473	25.5	50.3	17.9	+ 8.5
2	Apr. 18-25Same, except 50% milk	479	27.0	51.5	22.5	+23.4
3	Apr. 27-29Same with 6 c.c. olive-oil	479	26.9	49.1	29.8	-17.0
4	May 1-240% milk, 5% lime-water, barley-water to vol., 16 c.c. malt soup ext., albumin of 2 eggs, 8 c.c. olive-oil	120	23.5	47.7	25.5	- 1.0

V. FRANCO

1	May 7-1040% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt soup extract	414	16.0	60.6	15.8	+27.8
2	May 22-27Same, with 4 gms. NaCl	420	15.5	55.0	14.0	+ 4.6
3	May 28-30Same, except 5 gms. NaCl	417	15.7	54.1	12.9	+ 1.7

VI. VOGELIN

1	May 13-1545% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt-soup extract	473	18.2	56.3	15.0	-25.0
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VII. DOLAN

1	May 18-2040% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 20 c.c. malt soup extract, 6 c.c. olive-oil	420	16.3	57.1	21.8	-18.7
	May 18-19 to 5%, 20 c.c. malt soup extract, 6 c.c. olive-oil	420	16.8	57.1	22.3	-14.5
	May 20	420	15.1	57.1	20.8	-27.0

*By weight balance is meant average gain or loss per twenty-four hours.

with the condition of chronic malnutrition. Later similar observations were recorded by many writers⁵ on protein metabolism in infants.

B. Protein Absorption

Protein absorption generally is measured by the difference in the values of the nitrogen intake and of the nitrogen content of the feces. However, in recent years attention has been called by Orgler⁶ to the fact that the nitrogenous portion of the feces is composed not exclusively of the unabsorbed residue of the food nitrogen, but contains the nitrogenous substances of the intestinal secretions. Orgler, in fact, regards all the nitrogen of the feces as derived from the latter source. So long, however, as the source of the feces nitrogen is not as yet fully established, it was considered more conservative to estimate the value of protein absorption by the old method, bearing in mind that the values obtained in this manner are minimal.

It has been pointed out by Orgler that the nitrogen output through feces remains approximately constant, regardless of the nitrogen intake, although the value varies for every infant. The observations on our patients (Table 2) harmonize with this view. Thus, in Janes (Case 1) the nitrogen content of the feces was for only one day 0.23 gm. and for two days about 0.35 gm. each day. In the other periods, the output was about 0.40 gm. and only once reached 0.78 gm. Thus the value was not absolutely constant, though the fluctuations were not very great. It remained practically constant when there was little variation in the nitrogen intake. Thus in the three experiments on Franco (Case 5) the intake remained 2.56, 2.47, 2.51 gm. nitrogen per day of each period, and the nitrogen output for each of the three periods was 0.49, 0.48, 0.50 gm. The proportion of absorbed nitrogen varied in Janes (Case 1) from 80 to 91.5 per cent., the average being about 87.0 per cent. of the intake. In all other patients the absorption exceeded considerably 80 per cent. of the intake, with the exception only of Stocker (Case 3). In this instance the low average of nitrogen absorption of about 78 per cent. was conditioned by higher intestinal peristalsis. Thus, from the standpoint of protein absorption our patients presented little abnormality.

C. Nitrogen Balance

The nitrogen retention reached a higher value in those of our patients who showed a very considerable gain in weight in course of the experi-

5. Orgler: *Jahrb. f. Kinderh.*, 1908, lxxvii, 383; *Monatschr. f. Kinderh.*, 1908, 135; Freund: *Jahrb. f. Kinderh.*, 1904, lix, 421; 1905, lxi, 36; Cronheim and Muller: *Biochem. Ztschr.*, 1908, ix, 76; Lange and Behrend: *Jahrb. f. Kinderh.*, 1897, xlv, 337; Philips: *Monatschr. f. Kinderh.*, 1906, 413; Meyer, L. F.: *Jahrb. f. Kinderh.*, 1910, lxxi, 379.

6. Orgler: *Ergebn. d. Inn. Med.*, 1908, ii, 464.

ment, and thus were in a state of convalescence. In Franco (Case 5), who was gaining weight continually, the nitrogen retention reached the high value of 41.8 per cent.; in Guerin (Case 4), who also showed a marked gain in weight during three experiments, the highest retention was 33.1 per cent. of the intake. On the other hand, in Janes (Case 1) no parallelism is noted between the curve indicating the gain in weight and that of nitrogen retention. Thus, during the period of the highest nitrogen retention of 1.091 gm. per day, the body weight showed no gain; and on the other hand in period 9, when the body weight reached the highest value of 4,680 gm., the nitrogen retention was only 0.552 gm. per day. However, most instructive is the consideration of the total nitrogen balance for the fifty-three days recorded in the tables. The total retention of nitrogen for the period was 34.53 gm. According to the analysis of W. Camerer,⁷ Jr., the nitrogen content of a new-born infant is 1.95 per cent. On the basis of this the nitrogen gain ought to correspond to 1.726 gm. The ultimate gain in weight was only 120.0 gm. Admitting that the value of Camerer is not absolutely correct, and that some of our values are not free from error, one nevertheless is impressed by the fact that during the time of the experiment there was undoubtedly a considerable growth of the mass of cellular material, without any marked increase in the body weight. It must be mentioned in this connection that Camerer has also noted a gain in the size of infants without a corresponding gain in weight.

FAT METABOLISM

A. General Considerations

According to the view of the majority of writers, the most striking manifestation of abnormal metabolism in infantile malnutrition is the response of the organism to the administration of fat. Fat added to the food of normal infants in quantities exceeding considerably the average requirement does not alter in any way the character of the general metabolism, may not cause any disturbance, and on the contrary may bring about a rise in the rate of daily gain in weight.

In infantile malnutrition the response is very different. The most obvious abnormality and, from the practical standpoint, the most important one is, that the increase in the fat intake causes a disturbance of digestion and a loss instead of an increase in weight. The abnormal "weight response" is associated with symptoms of general discomfort. This peculiar influence of fat in infants with chronic malnutrition has been the subject of numerous experimental investigations. Steinitz,⁸

7. Camerer, W., Jr.: *Ztschr. f. Biol.*, 1900, xxxix, 182; and *Ztschr. f. Biol.*, 1900, xl, 531.

8. Steinitz: *Jahrb. f. Kinderh.*, 1905, lvii, 689.

3	Mar. 23-24	2.65	1.86	.34	18.2†	.69	1.96	73.9	.10	3.7	5.0
4	Mar. 26-27	2.59	1.83	.36	19.9†	.56	2.03	78.2	.20	7.7	9.9
5	Mar. 28	2.30	1.71	.32	18.9†	.47	1.83	79.7	.13	5.4	6.8
6	Mar. 29	2.20	1.58	.33	20.7†	.68	1.52	69.0	— .07
7	Mar. 31-Apr. 1	2.86	1.92	.30	15.6†	.65	2.21	77.6	.29	10.3	13.2
IV. GUERIN											
1	Apr. 13-16	4.08	2.22	.14	6.2	.68	3.40	83.5	1.18	29.1	34.8
2	Apr. 18-25	4.32	2.36	.15	6.3	.62	3.71	85.8	1.34	31.1	36.2
3	Apr. 27-29	4.31	2.11	.18	8.3	.77	3.53	82.2	1.43	33.1	40.3
4	May 1-2	3.76	2.12	.18	8.7	.68	3.08	81.8	.96	25.4	31.1
V. FRANCO											
1	May 7-10	2.56	1.00	.09	9.3	.49	2.07	81.1	1.07	41.8	51.6
2	May 22-27	2.48	1.36	.11	7.9	.48	1.99	80.7	.63	25.5	31.7
3	May 28-30	2.51	1.52	.12	7.9	.50	2.01	80.2	.49	19.7	24.6
VI. VOGELIN											
1	May 13-15	2.91	1.44	.16	11.2	.60	2.31	79.5	.86	29.7	37.4
VII. DOLAN											
..	[May 18-19]	2.69	1.59	.07	4.3	.31	2.29	88.2	.72	27.6	31.3
..	[May 20]	2.41	1.56	.08	4.8	.26	2.43	90.3	.85	31.4	34.8
1	May 18-20	2.60	1.58	.07	4.4	.40	2.01	83.7	.46	18.9	22.6

*Figures represent average values for twenty-four hours.

†Urine alkaline.

‡Urine acid.

Keller,⁹ Freund,¹⁰ Birk,¹¹ Rothberg,¹² and L. F. Meyer¹³ have furnished most valuable contributions in this connection. Special attention was paid by these authors to the mineral metabolism. But even after these recent contributions, the number of thoroughly described cases is not sufficient to permit establishing a clear causative relationship between the various symptoms observed in the course of this diseased condition. *A priori*, the ill effects of fat intake may be attributed to either one of the following assumptions:

1. Lack of absorption.
2. The effect of the fatty acids on the mineral metabolism. The presence in the intestinal wall of considerable quantities of soaps may lead to a deficient supply of mineral elements to the tissues.

B. Fat Absorption

In health comparatively little fat is removed by the feces, over 95 per cent. being absorbed from the intestinal tract. On this point most observers are in harmony. Less accord exists regarding the view on fat absorption in the various conditions of infantile malnutrition. According to Freund, even under abnormal conditions of nutrition, the fat absorption may remain perfectly normal, and he records instances in which with "soap stools" the fat absorption reached as high a value as 97 per cent. of the intake. On the other hand, Bahrddt,¹⁴ Birk,¹⁵ M. Chatruet,¹⁶ Hecht,¹⁷ and L. F. Meyer¹³ record in conditions of malnutrition with "soap stools" a fall in the fat absorption averaging about 80 per cent.

In all patients under our observation the fat absorption was considerably below normal (Table 3). The lowest percentage noted in Janes (Case 1) was 52.3 per cent.; the highest, 95.8 per cent., the average varying between 70 and 80 per cent. The greatest loss of fat was undoubtedly caused by diarrhea, and the most complete absorption can be explained by the addition of olive-oil to the diet of that period. The other fluctuations were conditioned by the quantity of the fat intake. On the day of the highest intake 78.6 per cent. was absorbed. In the other patients the absorption fluctuated within the same limits, namely between 70 and 85 per cent. The only exception with a considerably lower fat absorption is presented by Stocker (Case 3), in whom the lowest rate of absorption fell to 34.2 per cent. and the highest did not reach above 71.5

9. Keller: Arch. f. Kinderh., 1900, xxix, 1.

10. Freund: Jahrb. f. Kinderh., 1905, lxi, 36.

11. Birk: Jahrb. f. Kinderh., 1907, lxvi, 300.

12. Rothberg: Jahrb. f. Kinderh., 1907, lxvi, 69.

13. Meyer, L. F.: Jahrb. f. Kinderh., 1910, lxxi, 379.

14. Bahrddt: Jahrb. f. Kinderh., 1910, lxxi, 249.

15. Birk: Jahrb. f. Kinderh., 1907, lxvi, 69.

16. Chatruet, M.: Thèse de Paris, 1904.

17. Hecht: Jahrb. f. Kinderh., 1905, lxii, 613.

per cent. Again in this instance the low absorption was caused by increased peristalsis. On the other hand, the patient who showed the highest average fat absorption—Dolan (Case 7)—was receiving olive-oil. The beneficial effect of olive-oil on fat absorption had been noted already by Freund.¹⁸

According to his experiments the comparative degree of fat absorption on a diet containing no olive-oil, and one containing the oil (the total amount of fat intake being equal) varied as follows:

Cases	Diet	Per cent of Soap
A.	Meal	46.7
	Oil	7.9
	Malt	5.9
B.	Meal	57.0
	Oil	6.2
	Malt	5.0

In reviewing these observations on the fat absorption one is impressed by the fact that in all patients (with the exception of Dolan, Case 7), the loss of fat through the feces was not sufficient to cause in itself any perceptible deviation in the general nutrition.

C. Soap Content of the Feces

In health, according to Freund,¹⁹ the average proportion of insoluble soaps in feces is 18.3 per cent. of the total fat in the feces, the lowest figure being 4.9 per cent. and the highest 35.9 per cent. In conditions of malnutrition the average reaches 48.0 per cent., the lowest being 42.1 per cent. and the highest 57.0 per cent.

In the patients under our observation the soap content of the feces varied considerably. The percentage of soap in the stools of Janes (Case 1) was as a rule very high, 83.5 per cent. in one period, and gave an average of 46.3 per cent. for the thirteen periods. The low content of soap of 11.0 per cent. was conditioned by diarrhea and on two other occasions the low percentage of soap in the feces was caused by the addition to the diet of olive-oil.

Of the other patients a high percentage of soap in the feces was noted only in Dakak (Case 2), the average being 66.7 per cent. and, as can be seen from the following table, the soap content of the remaining patients did not exceed the normal value.

Patients	Per cent. of Soap in Feces	Patients	Per cent. of Soap in Feces
Janes	46.3	Franco	11.66
Dakak	66.7	Vogelin	13.8
Stocker	20.3	Dolan	34.
Guerin	20.9		

18. Freund: *Biochem. Ztschr.*, 1909, xvi, 453.

19. Freund: *Ergebn. d. inn. Med.*, 1909, iii, 163.

TABLE 3.—ANALYSIS OF FAT AND ASH

Period	Date	Fat				Water		Feces				Urine				Balance	
		Total	Neutral	Soap	Percent.	in	Feces	Total	Ca as	P ₂ O ₅	Total	P ₂ O ₅	Total	P ₂ O ₅	Approx.	Out-	Re-
		Gms.	fat and	Gms.	of			as Sul-	Sul-	Gms.							
			Fatty		Percent. In-		c.c.	phates	phates								
			Acids		of Total take			Gms.	Gms.								
				 Ab-												
				sorbed												
I. JAMES																	
1	Nov. 18-22	3.87	.82	3.05	78.9	83.4	29.8	2.94	2.69	.64	3.26	.47	4.07	2.63	1.44		
2	Nov. 23-26	5.78	4.56	1.22	21.1	68.1	155.4	2.70	1.92	.60	2.64	.39	4.47	2.27	2.20		
3	Nov. 28-Dec. 1	3.05	1.80	1.25	41.0	71.5	83.9	3.25	2.55	.73	3.98	.38	4.87	3.07	1.80		
4	Dec. 8-16	2.28	.38	1.90	83.5	84.7	40.2	4.63	4.49	.68	3.92	.52	5.41	3.63	1.78		
5	Dec. 18-20	4.01	2.00	2.01	50.2	78.1	74.6	4.40	2.12	1.12	3.79	.45	5.42	3.47	1.95		
6	Dec. 22-24	3.35	1.33	2.02	60.3	78.8	109.8	3.98	2.88	.81	2.90	.53	5.42	2.92	2.50		
7	Dec. 31-Jan. 3	6.75	3.42	3.33	49.3	78.6	64.8	4.38	3.74	1.16	2.16	.52	5.84	2.77	3.07		
8	Jan. 5-6	7.57	4.49	3.08	40.8	72.0	89.8	4.67	3.83	.59	3.19	.48	5.84	3.33	2.51		
9	Jan. 9-14	5.77	5.13	.64	11.1	52.3	139.0	5.15	3.35	.55	5.06	.43	7.74	4.33	3.41		
10	Jan. 22-24	2.41	.71	1.70	70.6	85.1	56.1	5.21	3.82	1.48	4.16	.45	5.59	3.97	1.62		
11	Jan. 26-28	1.69	.47	1.22	72.2	78.6	39.5	3.69	2.83	.48	4.24	.05	5.59	3.36	2.23		
12	Feb. 19-24	.60	.54	.06	10.0	95.8	44.4	2.92	2.16	.74	4.63	.53	4.87	3.20	1.67		
13	Feb. 25-Mar. 2	2.67	2.34	.33	12.4	85.8	131.5	3.93	2.24	1.12	3.49	.38	5.00	3.15	1.85		
II. DAKAK																	
1	Mar. 8-11	6.04	2.73	3.31	54.8	69.2	68.9	3.4645	2.90	.59	7.93	2.70	5.23		
2	Mar. 12-14	2.63	.56	2.07	78.7	78.6	23.0	1.7031	2.71	.18	4.84	1.87	2.97		

III. STOCKER																
1	Mar. 17-18	8.61	7.87	.74	8.6	49.4	355.0	4.0357	1.00	.06	3.64	2.13	1.51
2	Mar. 19-21	7.74	5.15	2.59	33.5	58.6	148.6	3.2182	1.63	.34	3.67	2.05	1.62
3	Mar. 23-24	8.11	5.98	2.13	26.3	63.9	246.2	4.1567	2.19	.23	4.01	2.69	1.32
4	Mar. 26-27	7.06	5.88	1.18	16.8	56.7	222.4	4.0867	2.17	.15	4.01	2.65	1.36
5	Mar. 28	5.67	3.83	1.84	32.5	71.5	239.2	3.56	2.19	...	4.01	2.44	1.57
6	Mar. 29	10.18	10.18	34.2	279.4	4.6560	2.84	.11	4.01	3.18	.83
7	Mar. 31-Apr. 1.	1.39	1.05	1.05	.34	24.5	40.0	225.8	3.5667	.71	.13	3.57	1.81	1.76
IV. GUEBIN																
1	Apr. 13-16	2.04	1.41	.63	30.8	88.6	71.7	2.0524	3.77	.17	4.07	2.47	1.60
2	Apr. 18-25	2.85	1.85	1.00	35.1	87.3	68.0	2.0423	3.06	.33	4.12	2.16	1.96
3	Apr. 27-29	4.32	3.27	1.05	24.3	85.5	80.7	2.5138	2.57	.12	4.12	2.15	1.97
4	May 1-2	6.10	5.03	1.07	17.6	76.1	80.3	2.0023	3.82	.15	3.68	2.47	1.21
V. FRANCO																
1	May 7-10	3.07	2.62	.45	14.7	80.5	141.4	2.7730	2.65	.13	3.64	2.30	1.34
2	May 22-27	3.23	2.84	.39	12.1	76.8	129.6	2.6917	5.24	.12	5.80	3.36	2.44
3	May 28-30	2.93	2.69	.24	8.2	77.3	95.2	2.7323	6.99	.12	6.31	4.12	2.19
VI. VOGELIN																
1	May 13-15	4.42	3.81	.61	13.8	70.6	160.2	2.9532	1.78	.26	4.08	2.01	2.07
VII. DOLAN																
1	May 18-20	3.09	1.95	1.14	36.9	85.9	31.8	2.0426	2.54	.17	3.68	1.94	1.74
..	[May 18-19]	2.76	1.32	1.44	52.2	87.7	17.3
..	[May 20]	3.76	3.20	.56	14.9	81.9	60.9

The lowest percentage of soap was noted in Franco (Case 5), who at the time of the metabolism experiment was in a condition of convalescence. Vogelín (Case 6) also was in a condition of convalescence, gaining weight at the beginning of the experiment, although his condition became aggravated during the experiment. On the other hand, Dakak (Case 2) was apparently in a comparatively good condition, showing a gain in weight during the time of the metabolism experiment, and yet the percentage of soap in his feces was very high.

It must, however, be borne in mind that all other observations with the exception of the one on Janes (Case 1) were of comparatively short duration, and therefore are less instructive. But, even in the case of Janes, it is as yet difficult to determine the factors which control the soap formation. Comparing three periods, the fourth, fifth and sixth, which differ principally in the carbohydrate intake, one notes that the lowest percentage of soap formation coincides with the period of the highest carbohydrate intake. Also very instructive are the last three periods. They all differ principally in their fat intake. The highest content of soap in the feces coincides with the lowest fat intake. At first glance, the result seems very paradoxical. However, it is possible that the addition of olive-oil to the diet of the last two periods conditioned the improvement in the fat absorption and the fall in the ratio of soap formation.

Thus the analysis of the composition of the fat of the feces in infantile malnutrition leads to the conclusion that in this condition the fat absorption from the small intestines is diminished. The unabsorbed fat, fatty acid and alkaline soaps, therefore, reach the colon. There the fat, fatty acids and the alkaline soaps are transformed into insoluble calcium soaps.

D. Salt Content of the Feces

The abnormal soap formation may lead to a fundamental change in the character of the general composition of the feces, which in its turn may affect the general health and the growth of an infant. Thus, *a priori*, by the formation of calcium soaps, the insoluble phosphates may be transformed into soluble salts, and in this manner may suffer absorption. The theoretical considerations were corroborated by experiment. In healthy infants with a normal fat absorption, high fat intake remains without influence on the mineral composition of the feces. In chronic malnutrition the salt output through the feces is considerably raised by the fat of the diet. This was demonstrated by Steinitz,⁸ Freund,¹⁰ Rothberg,¹² Birk,¹¹ and L. F. Meyer.¹³ Experimentally the same effect of high fat intake was observed by Schlesinger¹⁹ on dogs after the removal of the pancreas. The loss of mineral bases after high fat intake may reach

19. Naunyn's Festschrift: Ztschr. f. klin. Med., 1904, Iv, 214.

a degree sufficient to produce a negative salt balance, which alone may arrest further growth. This consideration perhaps more than anything else, led Czerny and Keller to the assumption that loss of mineral bases and the following acidosis are the prime factors in the pathogenesis of infantile malnutrition.

In the patients under our observation there was noted a considerable content of mineral bases of the feces. The fluctuations in the absolute quantities of mineral constituents removed by the feces did not follow the rise or fall in the percentage of the soap content of the feces. In Stocker (Case 3), with an average soap content of 20.3 per cent., the average ash content of the feces (weighed as sulphates) was 3.89 gm. per day, while in Janes (Case 1), with an average of 46.3 per cent., the daily output of ash (as sulphates) in the feces was 3.91 gm. per day. The absolute quantity of ash in the feces did not follow closely even the curve of the absolute quantities of soap removed through the feces; thus, in Janes (Case 1), with an average daily output of soap of below 2.0 gm., the ash output through the feces was 3.98 gm. per day, and in Dakak (Case 2) the daily output of soap was 2.7 gm. with a corresponding ash output of 2.78 gm. per day. Further, in Stocker (Case 3) a daily output of 1.41 gm. soap corresponded to 3.80 gm. of ash. This apparent paradoxical phenomenon is readily interpreted by the consideration of phosphoric acid output. A comparison of the phosphoric acid output through the feces of Janes, Dakak and Stocker (Cases 1, 2 and 3) reveals the fact that its value rises with the fall of the proportion of soap to ash. This observation is of great importance, for the reason that it demonstrates that in the chronic forms of infantile malnutrition the formation of fatty acids in the intestines does not reach the degree at which the ash content of the intestinal tract is insufficient to neutralize them. In such forms, the pathogenesis of the disease cannot be interpreted either in the light of insufficient fat absorption, or in the light of excessive loss of mineral bases, owing to the presence of unabsorbed fatty acids in the colon. The theory connecting the pathogenesis of infantile malnutrition with the phenomenon of the formation of soap stools is not applicable to conditions similar to those in our observations. Also Bahr²⁰ reached the conclusion that the quantity of fatty acids found in the patients under his observation was insufficient to neutralize all the mineral bases found in the feces. And yet in his observation the ratio of fatty acids to ash was much higher than in our patients.

MINERAL BALANCE AND ACIDOSIS

Thus the behavior of fat in the intestinal tract in chronic infantile malnutrition is insufficient to disturb markedly the salt output through

20. Bahr²⁰: *Jahrb. f. Kinderh.*, 1910, lxxi, 267.

the feces and, therefore, there is little reason to expect a pronounced disturbing effect of the fat intake on the general salt balance. The analysis of the tables (Table 3) shows that in all our patients the salt balance was positive. In Janes (Case 1), who was under observation for the longest period of time, the curve of the salt balance does not follow the one of fat intake, nor that of fat absorption, nor the curve of the soap content of the feces. Thus, the behavior of fat in the intestinal tract of our patient gave no cause for creating a want of mineral bases in the tissues, nor for creating the acidosis in the organism. This hypothesis is substantiated by the analysis of the curve of the ammonia-nitrogen elimination. Only in one patient, Stocker (Case 3) the ammonia output reached the value that indicates a condition of acidosis (average = 21.3 per cent.); in all other patients, as can be seen from the tabulation below, the average ammonia output is approximately normal.

AVERAGE AMMONIA NITROGEN OUTPUT

Patient	Per cent.	Patient	Per cent.
Janes	5.6	Franco	8.3
Dakak	9.1	Vogelin	11.2
Stocker	21.3	Dolan	4.4
Guerin	6.9		

In Janes (Case 1) the fluctuations in the ammonia output do coincide with the fluctuations of the fat intake, and thus they are in harmony with the observations of Czerny and Keller,²¹ Steinitz,²² on infants, and of Schittenhelm²³ on adults.

However, similar fluctuations under the influence of alteration in the diet may occur also in health. Thus, there is no evidence that the character of the intermediary fat combustion in our patients was disturbed in a manner to cause the condition of acidosis. The exception of Stocker (Case 3) was probably conditioned by an abnormally high intestinal fermentation.

SUMMARY OF THE ANALYSIS OF THE BEHAVIOR OF FAT IN THE PATIENTS UNDER OBSERVATION

This summary brings to light the following peculiarities in the effect produced by fat intake in the seven patients under our observation:

1. In all patients it undoubtedly produced an increased peristalsis of the small intestines. Whether this effect was produced by the fat independently, or whether the fat facilitated the similar action of the carbohydrates can for the present not be stated with a degree of certainty.
2. The increased peristalsis results in a fall of fat absorption and,

21. Czerny and Keller: *Jahrb. f. Kinderh.*, 1897, xliv, 25; 1897, xlv, 274.

22. Steinitz: *Monatschr. f. Kinderh.*, 1902, i, 4, 225; *Centralbl. f. inn. Med.*, 1904, xxv, 81.

23. Schittenhelm: *Deutsch. Arch. f. klin. Med.*, 1903, lxxvii, 517.

3. In an abnormal composition of the feces, which expresses itself in a high content of insoluble soap.

However, the lack of fat absorption and the withdrawal of mineral bases by the unabsorbed fat did not reach a sufficient degree of intensity to be regarded as very important factors in causing the defective nutrition in our patients.

On the other hand, the fat of the food failed to produce the principal effect that it invariably causes in health. Namely, it failed to bring about in connection with the carbohydrate of the food the normal gain in weight in the patients, who did not suffer from any difficulty in nitrogen assimilation, and whose diet contained a sufficient amount of calories for normal growth.

In this peculiarity of fat metabolism undoubtedly is contained the principal difference of metabolism in infant malnutrition as compared with that in health. The primary cause of this abnormal form of metabolism is difficult to detect. It is conceivable that in the chronic forms of infantile malnutrition a certain vicious cycle is established. In the loss of adipose tissue caused by some disease, or by some temporary condition, the organism sustains a very grave damage of its heat regulating factors. Under these conditions a higher energy value is required for normal growth, while the average normal diet is insufficient to enable the emaciated organism to continue its growth at the normal rate. It is conceivable that the organism may grow at the expense not only of the food but also of the fat and of the carbohydrates of the reserve material within the tissues. This may last so long as the glycogen and fat from the tissues is not completely removed; after this, normal growth could be made possible only by an excessively high diet, rich in fat. Unfortunately in all of the patients under our observation, and in those recorded by other authors, there was noted a marked intolerance of the intestines for both fat and carbohydrates, which expressed itself in the appearance of increased intestinal peristalsis following a high intake of fat or carbohydrate. Therefore, in order to avoid diarrhea, both the carbohydrate and fat intake need to be limited. Under these conditions the moderate food intake can suffice for only one of the functions, either for growth or for storing up reserve material in the form of fat and carbohydrate. The tendency of the infantile organism for growth is more intense than that for storing up reserve material, and thus the organism continues to perform the function of growth under most uneconomical conditions. The continuous nitrogen retention without increase in body weight may be the expression of the condition in which growth was proceeding at the expense of the fat and carbohydrate depots. The analytical data on the composition of the tissues in infantile malnutrition furnished by

Steinitz and Weigert²⁴ may be regarded as supporting the view just expressed. The findings of these authors reveal a very low fat content of the tissues in this pathologic condition. The tissues of the child with infantile malnutrition contained only 2.31 per cent. fat, while according to Camerer, Jr.,²⁵ the normal tissues of infants of the first year contain 12.3 per cent.

It is, however, noteworthy that the deviation in the utilization of fat in infantile malnutrition is principally of a quantitative nature. The analysis of the curve representing the fluctuations in weight in Janes, indicates a certain correlation between rise in weight and increase in fat intake. It should be mentioned in this place that the possibility of nitrogen retention without a corresponding increase in the storing up of fat and carbohydrate has already been pointed out by Rubner,²⁶ who designated the condition by the term "*selectiver Ansatz*."

In conclusion we wish to remark that in course of the work the impression was gained that the addition of olive-oil to the usual diet in proportion of 1 to 2 per cent. of the volume of the total intake improved the utilization of the total fat. The feces returned to a composition approaching that of the normal feces, the salt balance also approached nearer the normal, and gain in weight increased in intensity. From the appended histories it can be seen that it had been employed in several cases with some promise of success.

CLINICAL HISTORIES

CASE 1.—Janes, 5 months old, was admitted to the Hospital Nov. 9, 1909. There was a history of continued loss in weight since his first month, occasional vomiting and several attacks of diarrhea during the summer. For one month before admission there was constipation and vomiting after every feeding. On admission the child was poorly nourished and had a greatly distended abdomen; weight, 4,176 grams. By November 13, the general condition had somewhat improved, digestion was better and the stools were normal.

The metabolism experiment was continued from November 17 till March 3, with interruptions, viz.: December 10 to 13; December 25 to 31; January 29 to February 14.

The weight at the beginning of the experiment was 4,134 grams. At first he appeared bright and happy. The best weight was on January 14, 4,672 grams. From January 21 to 31 there was fever, cough and a double otitis media. On this account the observations were interrupted.

On March 3, when the experiment ended, the weight was 4,261 grams, the stools thin and green, and the child did not look well. He was discharged March 7, weight 4,153 grams. Subsequent to discharge his condition improved and he gained in weight on a diet including much carbohydrate.

CASE 2.—Dakak, 7 months old, was admitted Jan. 22, 1910, with broncho-pneumonia. From Sept. 14, 1909, to Jan. 20, 1910, the child had been in the hospital as a feeding case and was discharged in good condition. On readmission

24. Steinitz and Weigert: *Monatsschr. f. Kinderh.*, 1905-6, iv, 6, p. 301.

25. Camerer, Jr.: *Pfaundler-Schlossman, Handbuch der Kinderheilkunde*, 1. Aufl., Leipzig, 1906.

26. Rubner: *Das Problem der Lebensdauer*, München and Berlin, 1908, p. 110.

he was small and poorly nourished, with signs of moderate rachitis. By February 12, the symptoms of pneumonia had disappeared; he had gained in weight and looked well.

When the metabolism experiment was begun March 8, he weighed 4,179 grams. The stools were large and good. On March 15, the metabolism experiment was discontinued, as the child again developed a pneumonia. The weight was then 4,386 grams. He grew rapidly worse and died March 21.

CASE 3.—Stocker, 3½ months old, entered the Hospital March 2, 1910. There was a history of vomiting and diarrhea for three days before admission. He was moderately well nourished; not acutely ill; abdomen distended; stools thin and yellow; weight, 4,700 grams.

The metabolism experiment lasted from March 17 through April 2. The weight fell to 4,554 grams but his general condition appeared to be better at first. The experiment was stopped April 2 because the child became weak, with loss of appetite, and the weight had fallen to 4,322 grams.

His lowest weight was 4,204 grams on April 30. The albumin of two eggs was added to his daily food. Breast feeding was attempted but he refused to take the breast. By May 27, the child appeared greatly improved; the stools were normal; weight, 4,700 grams. On June 13, olive-oil, 2 grams three times a day, was added to his food. He continued to gain in weight and was discharged June 22 in good condition.

CASE 4.—Guerin, 3 months old, was admitted Dec. 11, 1909, with symptoms of an acute gastro-enteritis. He looked acutely ill. The stools were green and thin; the weight, 4,120 grams. He improved with the addition of breast feeding.

The metabolism experiment was begun April 13 and continued until May 3. Weight at the beginning was 4,320 grams and he gained to 4,451 grams. From April 26, olive-oil was given, at first 2 grams three times, later increased to four times a day. In spite of a cervical abscess and double otitis media the child continued to gain slowly and on June 14 weighed 4,643 grams, when he was discharged.

CASE 5.—Franco, 3 months old, was admitted to the Hospital April 19, 1910, with an acute bronchitis. He was small but fairly nourished. The stools were soft and contained some mucus and often soft lumps.

The metabolism experiment was started May 7 and continued to May 31 with an interruption from May 11 to 22.

At the beginning of the experiment the child was gaining and weighed 3,593 grams. On May 11 the weight was 3,704 grams and increased to 4,002 grams by May 22. During this time four grams of salt per diem were added to the food. This was increased to five grams, but he refused the food with this added quantity of salt. At the end of the experiment the weight was 4,074 grams. On June 4, olive-oil was added, 2 grams, increased to 4 grams three times a day. The child was discharged June 17, gaining in weight and in good condition.

CASE 6.—Vogelin, 4½ months old, was admitted to the Hospital April 13, 1910. For the month before admission the stools had been green and thin and there had been constant loss in weight. On examination the child was found to be greatly emaciated, with a distended abdomen and moderate degree of rachitis. Weight, 3,794 grams. He gained steadily in weight and strength and the stools became normal.

The metabolism experiment was begun May 13 and continued only to May 16. He was very restless, cried continuously, slept very little. There was some vomiting and the stools were soft and yellow. The weight was 4,115 grams at the beginning, but in the three days had dropped to 4,040 grams. The condition became gradually worse; the stools, thin and green; there was a low fever, and a general edema; and he died on May 29.

CASE 7.—Dolan, 2 months old, first entered the Hospital Oct. 19, 1909, with pyloric stenosis. His weight was 3,058 grams. He was readmitted for several short periods until March 8, when, at the age of 7 months, the mother consented

to leave him in the hospital. At this time the weight was 3,624 grams. He was extremely emaciated, and looked acutely ill. There had been daily lavage for some time and the vomiting had practically ceased. The condition then was one of marasmus. He gradually improved during the next two months.

On April 8, olive-oil was given, 2 grams three times a day. From 3,709 grams the weight increased gradually but steadily to 4,077 grams by May 5. May 18, weight was 4,139 grams.

The metabolism experiment was then begun but he was restless and fretful and in the three days of the experiment he lost from 4,139 to 4,083 grams. During the following week, however, he gained 75 grams. On June 6, olive-oil was increased to four grams three times daily. The stools were good and the child continued to gain, weighing 4,494 grams when discharged June 21. Four months later he was still gaining.