STUDIES OF INFANT FEEDING. XI

HIGH PROTEIN FEEDING VERSUS HIGH CALCIUM ABSORPTION AS THE
CAUSE OF THE INCREASE IN BODY TEMPERATURE OF INFANTS *

A. W. BOSWORTH, AND H. I. BOWDITCH, M.D.
BOSTON

INTRODUCTION

We have found the excessive calcium content of cow's milk to be a disturbing factor in many of the so-called cases of malnutrition and, as any high protein food made under ordinary conditions from cow's milk will of necessity have the greater part of the protein present as calcium caseinate, it seems to us that although protein was the apparent cause of the toxic condition resulting from the feeding to infants of a high protein milk, the real cause might be due to the calcium chemically combined in the calcium caseinate.

We have also found that the feeding to infants of large amounts of pure protein (ash-free paracasin) does not produce any unfavorable symptoms even when the protein is fed with an extremely small amount of whey.¹ As this finding may seem to be contrary to the observations of others we have continued our investigation in an endeavor to find the factor responsible for this difference.

Our investigations have shown that the reduction of the intake of inorganic salts to a point at which chlorin-free urine is eliminated resulted in a febrile condition only when large amounts of calcium was fed as calcium caseinate. We explain these observations as follows:

Under normal conditions sodium can be excreted by the kidneys as chlorid, phosphate, carbonate or sulphate while calcium can be excreted only as chlorid or acid phosphate, the phosphate being only sparingly soluble. A reduction in the intake of chlorin or phosphorus, that is to say, a reduction in the intake of whey, will not interfere with the excretion of sodium because it can form a soluble carbonate, but under the same conditions the excretion of calcium is seriously

* Submitted for publication July 12, 1918.

* From the Boston Floating Hospital Laboratories.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

1. Bosworth, A. W., and Bowditch, H. I., and Ragle, B. H.: Casein in Infant Feeding, *AM. JOUR. DIS. CHILD.*, 1914, **8**, 120.

interfered with and results in an accumulation or retention of calcium until a toxic condition is finally reached which results in a febrile condition accompanied by the excretion of large amounts of calcium lactate in the urine. This excretion of calcium relieves conditions temporarily, or until the calcium retained again reaches the danger point, when there will follow another fever and an increased elimination of calcium lactate. This condition is relieved by the ingestion of whey which furnishes chlorin for the elimination of the accumulated calcium as calcium chlorid.

A careful scrutiny and analysis of the conditions surrounding the data presented by Holt, Levene, and others,² and the data secured by us in some preliminary experiments has led us to investigate the following conditions in infant feeding:

1. The reduction of the intake of inorganic salts to a point which results in the elimination of:

(a) A chlorin-free urine.

(b) A chlorin-free and phosphorus-free urine.

(c) A chlorin-free urine accompanied by the ingestion of large amounts of sodium caseinate.

(d) A chlorin-free urine accompanied by the ingestion of large amounts of available calcium as calcium caseinate.

2. The ingestion of large amounts of calcium caseinate accompanied by the ingestion of large amounts of milk salts.

In presenting the results obtained we have selected the data from one experiment under each of the headings given above.

I. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED

The investigation began with the admission of the baby to the hospital on July 9 and may be divided into six periods as follows:

First Period, 6 p. m., July 9, to 6 p. m., July 12.—From 6 p. m., July 9, until 10 a. m., July 11 (forty hours), the child received only sterile water. From 10 a. m., July 11, to 6 p. m., July 12 (thirty-two hours), the food consisted of a mixture of 840 c.c. of whey, 420 c.c. of breast-milk and 420 c.c. of water and was divided into ten feedings. The child was on the metabolism frame during all three days.

The high output of uric acid, creatinin and creatin during the fast indicates a high endogenous metabolism and is followed by a higher excretion of these substances on the administration of food; the excretion of nitrogen, however, is lowered during the first day following the fast, indicative of a replacement of the nitrogen lost during the endogenous metabolism of the fast. During the fast the chlorin excreted was very small in amount, and both indican and acetone were detected in the urine. The child also had an acetone breath.

2. Holt, L. E., Levene, P. A., and others: The Influence of High Protein Feeding on the General Metabolism, *AM. JOUR. DIS. CHILD.*, 1912, **4**, 265.

Second Period, 6 p. m., July 12, to 6 p. m., July 22.—A period during which the food was changed several times in order to find a mixture suitable for the child. The child was not on the metabolism frame and no analytical data were secured during this period.

Third Period, 6 p. m., July 22, to 6 p. m., July 26.—The child had recovered from his intestinal trouble and was receiving the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream.....	160 c.c.
Buttermilk	800 c.c.
Sterile water.....	640 c.c.
Milk-sugar	53 gm.

Seven feedings of 210 c.c. each every twenty-four hours. Approximately 637 calories or 145 calories per kilogram body weight.

As he seemed to be in good condition and gaining in weight on this food, he was placed on the metabolism frame at 6 p. m., July 22. During this period he continued to receive the food indicated above and the urine and feces were collected and examined in order to furnish data representing his normal nitrogen metabolism. During this period the body weight increased 165 gm., an average of 41.2 gm. per twenty-four hours. He was well in every respect.

Fourth Period, 6 p. m., July 26, to 6 p. m., July 29.—The child was not on the frame during this period but received the same food given in the preceding period. No macroscopic or microscopic evidence of fat, carbohydrate or protein indigestion was found.

Fifth Period, 6 p. m., July 29, to 6 p. m., August 7.—The child was again placed on the frame and the food received was made up according to the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream.....	161 c.c.
Sterile water.....	1,439 c.c.
Lactose	89 gm.
Dry paracasein.....	25 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This mixture contained about the same amounts of fat, sugar and protein as the mixture given in the two preceding periods. The amount of protein ingested in twenty-four hours was less than in the case of the food made with buttermilk. This was due to the fact that it was almost impossible to manipulate the feeding-bottles so that all the paracasein was removed with the liquid portion of the food.

The inorganic salts were very much decreased in this mixture. In the preceding periods the mixtures fed contained the salts carried in the 160 c.c. of cream and the 800 c.c. of buttermilk. In the present case all the inorganic salts were derived from the 161 c.c. of 10 per cent. cream. The response to this decrease in the inorganic salt intake is shown in the lower figures obtained during this period for sodium chlorid, phosphates and acidity. The food contained 0.116 gm. of sodium chlorid per twenty-four-hour quantity while the amounts excreted dropped from 0.326 gm. the first day to nothing on the eighth and ninth days, chlorin again appearing on the tenth day (the first day of the sixth period) even with a reduction in the chlorin intake on that day. This small chlorin excretion, zero for two days even, was not accompanied by any signs of physical discomfort.

During this period the body weight increased 120 gm., an average of 13.3 gm. per twenty-four hours.

Sixth Period, 6 p. m., August 7, to 6 p. m., August 14.—From 6 p. m., August 7, and during this period the food given to the child was made accord-

ing to the following formula: Fat, 2 per cent.; sugar, 6 per cent.; protein, 2 per cent.

32 per cent. cream.....	54 c.c.
Sterile water.....	1,546 c.c.
Lactose	89 gm.
Dry paracasein.....	28 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This decreased the inorganic salts again and made the chlorin intake per twenty-four hours equal to 0.033 gm. of sodium chlorid, and the amounts excreted dropped from 0.148 gm. to 0 gm. on the fifth, sixth and seventh days. The child showed no particular discomfort as a result of this rather prolonged confinement on the metabolism frame, but on account of the loss of body weight it was thought best to discontinue the collection of urine and feces and remove the child from the frame at 6 p. m., August 14.

GENERAL DISCUSSION

In connection with the table which gives the result of our daily examination of the urines, we desire to call attention to the following points:

The acidity of the urines and the amounts of phosphates present decreased with the decrease in the amounts of whey ingested. This was to be expected as all the inorganic phosphates ingested were contained in the whey or cream used to make up the formulas. The amounts of organic phosphorus ingested were practically the same through all the periods.

The elimination of chlorin-free urine for two-day and three-day periods without symptoms of any nature is worthy of note.

A very marked increase in the ammonia output during the sixth period of the experiment is noticeable. During the fifth period the whey in the 161 c.c. of 10 per cent. cream furnished considerable neutral salts of organic acids (citrates, albuminates, etc.), the bases of which could be used to neutralize the acid bodies eliminated in the urine. During the sixth period, however, the intake of such base-carrying substances was much reduced, and sufficient bases were not ingested to neutralize the acid bodies eliminated in the urine. This resulted in an immediate increase in the amount of ammonia in the urine with a corresponding decrease in the urea. For the twenty-four hours ending at 6 p. m., August 7, the urine contained 0.261 gm. of nitrogen present as ammonia, and for the twenty-four-hour period ending at 6 p. m., August 8, the first day of the reduction of the intake of the salts to the lowest figure, the urine contained 0.522 gm. of nitrogen in the form of ammonia, an increase of 100 per cent. in one day.

It will be noticed that only a small part of the ammonia is necessary to neutralize the phosphates. Just what the nature of the acid bodies is we are not able to state. We did not detect the presence of acetone bodies in the urine at any time during this period.

TABLE 1.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS

Date*	Body Weight, Gm.	Urine											Average N. in Feeces, Gm.
		Volume, C.c.	Specific Gravity	Total Acid, N/10, C.c.	P ₂ O ₅ , Gm.	Cl as NaCl, Gm.	Total N, Gm.	N as NH ₃ , Gm.	N as Urea, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	
7/10†	4,500	505	1.007	82.8	0.577	0.024	1.513	0.161	1.111	0.107	0.030	0.041	
7/11†		630	1.005	54.2	0.534	0.048	1.658	0.247	1.094	0.131	0.028	0.068	
7/12†	4,540	670	1.005	144.7	0.574	0.206	1.294	0.110	0.884	0.243	0.037	0.065	
7/12-22													
7/23	4,480	700	1.006	127.4	0.610	0.913	1.372	0.319	0.896	0.065	0.020	0.026	0.365
7/24	..	660	1.006	97.7	0.918	0.500	1.774	0.292	1.279	0.057	0.019	0.024	0.365
7/25		980	1.006	156.8	1.129	1.180	2.387	0.274	1.949	0.084	0.021	0.030	0.365
7/26	4,645	990	1.007	134.6	1.161	1.509	2.550	0.360	2.051	0.084	0.021	0.034	0.365
7/26-29													
7/30	4,730	1,200	1.004	98.4	0.760	0.326	1.747	0.175		0.053	0.022	0.020	0.173
7/31		1,220	1.003	41.5	0.386	0.332	1.264	0.164	0.929	0.078	0.022	0.030	0.173
8/ 1		1,300	1.002	41.6	0.398	0.140	1.092	0.175	0.845	0.053	0.023	0.020	0.173
8/ 2		1,240	1.002	39.7	0.379	0.298	1.146	0.208	0.724	0.066	0.021	0.025	0.173
8/ 3		1,070	1.003	42.8	0.317	0.223	1.079	0.216	0.713	0.057	0.019	0.022	
8/ 4		670	1.003	24.1	0.233	0.115	0.925	0.173	0.522	0.045	0.018	0.021	
8/ 5		1,170	1.003	56.2	0.370	0.047	1.409	0.216	0.963	0.081	0.020	0.028	
8/ 6		1,060	1.003	33.9	0.357	0.000	1.676	0.261		0.072	0.020	0.029	
8/ 7	4,850	1,060	1.003	33.9	0.357	0.000	1.676	0.261		0.072	0.020	0.029	
8/ 8		1,060	1.002	38.2	0.232	0.148	1.089	0.522	0.284	0.072	0.020	0.037	
8/ 9		850	1.003	47.6	0.390	0.065	1.275	0.509		0.084	0.020	0.015	
8/10		970	1.003	26.6	0.317	0.067	1.249	0.494		0.082	0.022	0.019	
8/11		1,060	1.003	27.6	0.378	0.015	1.276	0.392	0.613	0.086	0.020	0.020	
8/12		1,000	1.003	32.0	0.275	0.000	1.036	0.476		0.087	0.017	0.015	
8/13		900	1.005	23.8	0.303	0.000	1.411	0.731		0.075	0.017	0.019	
8/14	4,510	760	1.003	33.4	0.357	0.000	1.105	0.655	0.378	0.092	0.020	0.017	

* Twenty-four-hour period ending 6 p. m.

† Traces of indican appeared in the urine on these days.

‡ Traces of acetone on these days.

The amounts of creatinin and creatin excreted during the fasting period were much above the normal as would be expected. During the other three periods the creatinin figures are strikingly uniform.

During the third period, when the food contained an excess of all constituents, the child increased in body weight an average of 41.2 gm. per twenty-four hours and the creatin output averaged 0.028 gm. per day. In the fifth period when the whey had been reduced to the amount carried in 161 c.c. of 10 per cent. cream, the average daily increase in body weight was reduced to 13.3 gm. and the average daily creatin excretion was 0.025 gm. In the sixth period there was an average daily decrease in body weight of 48.6 gm., and the average daily excretion of creatin was 0.015 gm. with a daily fluctuation giving figures between 0.027 and 0.015 gm.

No symptoms of any nature developed during the fifth and sixth periods.

II. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUOUS EXCRETION OF CHLORIN-FREE AND PHOSPHORUS-FREE URINE IS PRODUCED

We have shown in a previous paper how the feeding of an excessive amount of calcium may result in the precipitation within the intestines of all the ingested phosphorus as insoluble calcium phosphate and thus reduce the phosphorus metabolism to such a low level that the urine becomes phosphorus-free and contains a large amount of carbon dioxid.³

We have been able to take advantage of this fact and, by the feeding of a synthetic food containing no inorganic salts but considerable soluble calcium, we have reduced the chlorin intake and output to nil and brought about the excretion of a phosphorus-free urine.

This investigation began when the child was placed on the metabolism frame, July 13, 1915, and may be divided into two periods.

First Period, 9 a. m., July 13, to 9 a. m., July 14.—During this first twenty-four hours the child received 1,260 c.c. of a modified milk containing 2 per cent. of fat, 6 per cent. of lactose and 2 per cent. of protein.

Second Period, 9 a. m., July 14, to 9 a. m., July 22.—During the next eight days the child received a chlorin-free synthetic⁴ milk containing pure butter fat, 2 per cent.; lactose, 6 per cent.; sodium caseinate, 2 per cent., and calcium acetate $[(CH_3COO)_2Ca.H_2O]$ 0.167 per cent. The only phosphorus present in this food was that contained within the casein molecule. The child received 1,260 c.c. of this food every twenty-four hours.

3. Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, **177**, 864.

4. Bowditch, H. I., and Bosworth, A. W.: Studies of Infant Feeding, Tr. Am. Ped. Soc., 1916, **28**, 114.

The data secured will be found in Table 2. By consulting the table it will be noticed that the urine became alkaline on the first day of the second period and remained so while the child received the synthetic milk. All the urines during this period were heavily charged with carbon dioxide, the addition of a drop of hydrochloric acid causing a marked effervescence.

The urine became chlorin-free on the first day of the second period and phosphorus-free on the fourth day. A marked increase in the ammonia excretion is noticed during the time the child received the food containing no milk salts. Most of the phosphoric acid resulting from the digestion of the casein was precipitated in the intestines as insoluble calcium phosphate and appeared as such in the feces. The remainder must have been assimilated and retained, for the urine soon became phosphorus-free.

No symptoms of any kind developed during this experiment.

III. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT WHERE A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF SODIUM CASEINATE

The child selected for this experiment was 11 months old, weighed 7,129 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 9:30 a. m., July 26. The investigation may be divided into two periods.

First Period, July 26, to July 27.—During the first twenty-four hours the child received a food made up as follows:

Whole milk.....	75 c.c.
Dextri-maltose to make total sugar.....	5%
Boiled water to make.....	100 c.c.
Five feedings, 227 c.c. each.	

This food contained fat, 3 per cent.; sugar, 5 per cent., and protein 2.4 per cent.

Second Period, July 27 to August 7.—At 9:30 a. m., July 27, the food was changed to a synthetic milk containing fat, 2 per cent.; sugar, 6 per cent., and sodium caseinate, 6.5 per cent. He received five feedings of 227 c.c. each per day. The feces was so small in amount that no work was done on it. (In this connection see a previous paper by us.⁵)

The data secured will be found in Table 3. Here we again have an alkaline urine containing large amounts of carbonate and ammonia. The uric acid, creatinin and creatin outputs show no marked variations from day to day. No symptoms of any nature developed.

5. Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, 177, 864.

TABLE 2.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS TO A POINT WHICH RESULTS IN THE EXCRETION OF A CHLORIN- AND PHOSPHORUS-FREE URINE

24-Hour Period Ending 1915	Body Weight, Gm.	Urine						Feces						
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	P ₂ O ₅ , Gm.	Chlorin, Gm.	Total N Gm.	N as NH ₃ , Gm.	Calcium Oxid., Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Fat, Gm.	Calcium Oxid., Gm.	Phosphoric Oxid., Gm.
8/14	5,336	510	1.009	113.2	0.316	0.707	1.948	0.251	0.067	None	12.15	5.01	0.937	0.363
8/15		260	1.014	Alk.	0.286	None	1.877	0.497	0.068	None	7.67	3.03	0.571	0.186
8/16		530	1.008	Alk.	0.133	None	1.677	0.502	0.062	None	7.06	1.88	0.660	0.131
8/17		410	1.009	Alk.	0.062	None	1.484	0.786	0.048	None	7.47	3.07	0.573	0.126
8/18		300	1.012	Alk.	0.064	None	1.490	0.572	0.045	None	9.28	3.04	0.504	0.213
8/19		300	1.011	Alk.	None	None	1.374	0.539	0.030	None	3.58	0.87	0.243	0.084
8/20		240	1.010	Alk.	None	None	1.291	0.304	0.040	None	6.68	2.55	0.565	0.175
8/21		490	1.007	Alk.	None	None	1.032	0.454	0.046	None	6.50	2.41	0.612	0.150
8/22	4,768	420	1.006	Alk.	None	None	0.997	0.316	0.041	None	5.27	2.46	0.457	0.128

TABLE 3.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS AND FEEDING LARGE AMOUNTS OF SODIUM CASEINATE

24-Hour Period Ending	Body Weight, Gm.	Urine											
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	Phosphori- Oxid, Gm.	Total N, Gm.	N as NH ₃ Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.
7/27	7,129	640	1.008	83.2	0.672	0.826	2.87	0.39	0.147	0.078	0.089	0.029	None
7/28		760	1.010	Alk.	0.359	0.456	4.36	0.85	0.120	0.074	0.075	0.056	None
7/29		780	1.011	Alk.	0.187	0.741	5.13	2.88	0.110	0.078	0.020	0.055	None
7/30	...	880	1.011	Alk.	0.145	0.315	6.51	0.49	0.089	0.072	0.050	0.076	None
7/31		810	1.011	Alk.	0.062	0.194	5.90	0.41	0.092	0.071	0.050	0.060	None
8 / 1	...	840	1.013	Alk.	0.047	0.378	6.88	0.85	0.120	0.080	0.065	0.077	None
8 / 2	...	840	1.010	Alk.	0.082	0.294	8.47	0.86	0.073	0.074	0.074	0.097	None
8 / 3		1,020	1.010	Alk.	0.062	0.306	7.14	1.26	0.119	0.077	0.072	0.135	None
8 / 4		840	1.010	Alk.	0.000	0.327	8.88	2.42	0.092	0.069	0.060	0.068	None
8 / 5		760	1.013	Alk.	0.000	0.800	7.02	3.02	0.076	0.066	0.048	0.041	None
8 / 6		570	1.013	Alk.	0.000	0.500	8.06	3.17	0.064	0.072	0.050	0.031	None
8 / 7	7,013	680	1.011	Alk.	0.000	0.200	8.85	2.53	0.107	0.081	0.070	0.064	None

IV. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT
AT WHICH CHLORIN-FREE URINE IS EXCRETED, ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS
OF CALCIUM CASEINATE

The child selected was 10 months old, weighed 5,477 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Fat-free milk.....	75 c.c.
Dextri-maltose	5 gm.
Boiled water to make.....	100 c.c.

Six feedings, 170 c.c. each.

This food contained fat, a trace; sugar, 8 per cent., and protein 2.4 per cent.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream.....	65 c.c.
20 per cent. lactose solution.....	377 c.c.
Calcium caseinate.....	87 gm.
Sodium citrate.....	80 grains
Water to make.....	1,392 c.c.

Six feedings, 170 c.c. each.

This food contained fat, 1.50 per cent.; sugar, 5.63 per cent.; protein, 6.25 per cent., and calcium oxid, 0.1575 per cent. The data secured during this experiment will be found in Table 4 and Chart 1. The food used for this investigation had a low chlorin and high calcium content.

The most striking point brought out by the data in Table 4 is the appearance of lactic acid in the urine on the 15th, followed by a toxic condition which manifested itself during the night of the 16th. The appearance of the lactic acid is accompanied by a greatly increased elimination of calcium. It will be noticed that the temperature of 102.4 F. recorded on the morning of the 17th is reduced during the day and seemed to be directly associated with the ingestion of the early morning feeding. Possibly the lactose in the food had some influence in reducing the temperature.

The lactic acid was determined by extracting the acidulated urine with ether, distilling off the ether, dissolving the residue in water, evaporating to a thick syrup, taking up with water, converting the lactic acid to the zinc salt by the addition of zinc oxid, boiling, filtering, evaporating the filtrate to dryness, drying in the oven for two hours and weighing. The weights were checked by burning the zinc lactate and weighing the residual zinc oxid. The lactic acid was identified by the crystals of zinc lactate.

Owing to the uncomfortable condition of the child, he was removed from the metabolism frame on the 18th, but continued to receive the

Chart 1.—Record of the temperature, pulse and respiration as observed in connection with the tests outlined in Table 4.

same food until the morning of the 21st. During the night of the 19th another temperature was noticed which also seemed to be lowered by the ingestion of food.

The greatly increased elimination of uric acid, creatinin and creatin during this experiment is to be expected as a result of the fever. It is worthy of note that none of the urines in this set showed the presence of carbonates.

The toxic condition produced during this experiment we believe to be due to the following circumstances. The digestion of fat and protein within the intestine results in the production of acids, fatty acids from fat and amino-acids or polypeptic acids from the proteins. These acids do not remain as free acids but immediately unite with the bases present in the intestines to form salts, the soluble salts being absorbed, the insoluble salts being eliminated in the feces. In the presence of the large amount of calcium carried into the intestines in combination with the casein many more of these acids form calcium salts than would be the condition under more normal circumstances. The soluble organic salts are carried to the tissues and the organic part used for vital activities leaving as refuse the base calcium which has acted simply as a conveyor and neutralizer. Under normal conditions this calcium would form chlorid or phosphate and be eliminated in the urine immediately. Under the conditions of this experiment there was no chlorin available for such purpose and very little phosphorus. The result is an accumulation of calcium until a toxic condition is reached and then, during the fever, an abundant elimination of soluble calcium lactate.

V. THE FEEDING OF LARGE AMOUNTS OF CALCIUM CASEINATE WHEN ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF INORGANIC SALTS (WHEY)

The child selected was 5 months old, weighed 5,371 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Whole milk.....	60 c.c.
Boiled water.....	40 c.c.
Maltose to make sugar.....	6%
Six feedings, 170 c.c. each.	

This food contained, fat, 2.4 per cent.; sugar, 6 per cent., and protein 1.9 per cent.

TABLE 4.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS AND FEEDING LARGE AMOUNTS OF CALCIUM CASEINATE

24-Hour Period Ending at 8 p. m., 1914	Urine								Feces							
	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	P ₂ O ₅ , Gm.	Total Nitrogen, Gm.	Nitrogen, as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Total N, Gm.	P ₂ O ₅ , Gm.	Calcium Oxid, Gm.
7/12	660	1.010	59.4	0.809	0.53	3.53	0.340	0.145	0.086	0.084	0.0462	0.0000	10.1	0.606	0.170	1.075
7/13	720	1.009	13.0	0.655	0.36	4.29	0.363	0.092	0.060	0.049	0.0432	0.0000	9.1	0.528	0.122	0.901
7/14	750	1.010	123.0*	0.394	0.34	4.83	0.522	0.085	0.072	0.023	0.0825	0.0000	9.0	0.653	0.109	0.603
7/15	626	1.011	82.2*	0.031	0.95	4.62	1.403	0.186	0.097	0.052	0.1640	0.5799	13.0	0.808	0.222	0.902
7/16	680	1.013	21.8*	0.000	0.20	5.21	0.823	0.336	0.113	0.127	0.1537	0.5208	14.0	0.963	0.252	1.244
7/17	650	1.016	27.3	0.073	0.31	6.64	0.454	0.325	0.100	0.100	0.1274	0.3608	14.5	0.931	0.246	0.940
7/18	730	1.015	2.9	0.000	0.22	6.95	1.083	0.380	0.123	0.083	0.2015	0.9075				

* Alkalinity.

TABLE 5.—SHOWING COMPOSITION OF THE URINE WHEN LARGE AMOUNTS OF CALCIUM CASEINATE IS INGESTED ACCOMPANIED BY LARGE AMOUNTS OF INORGANIC SALTS (WHEY)

24-Hour Period Ending at 8 p. m., 1914	Urine						Feces					
	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	P ₂ O ₅ , Gm.	Total Nitrogen, Gm.	Nitrogen, as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.
7/12	600	1.010	30.0	0.714	0.68	2.50	0.285	0.107	0.071	0.042	0.0132	0
7/13	620	1.010	20.0*	0.608	0.59	2.97	0.576	0.069	0.071	0.045	0.0872	0
7/14	580	1.013	93.0*	0.304	0.33	4.93	0.601	0.085	0.070	0.054	0.0152	0
7/15	670	1.014	60.0*	0.304	0.37	5.07	0.657	0.107	0.070	0.065	0.0938	0
7/16	740	1.013	59.0*	0.622	0.31	8.88	0.315	0.096	0.072	0.073	0.1154	0
7/17	670	1.014	36.0*	0.530	0.35	8.85	0.555	0.103	0.074	0.052	0.1072	0
7/18	730	1.015	48.0*	1.613	0.45	8.47	0.220	0.100	0.073	0.050	0.0847	0

* Alkalinity.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream.....	65 c.c.
20 per cent. lactose solution.....	331 c.c.
Calcium caseinate.....	87 gm.
Sodium citrate.....	80 grains
Whey	580 c.c.
Water to make.....	1,392 c.c.
Six feedings, 170 c.c. each.	

This food contained, fat, 1.50 per cent.; sugar, 6.4 per cent., and calcium oxid, 0.1575 per cent.

The data secured will be found in Table 5. In this case sufficient chlorin and phosphorus had been ingested to permit the elimination of all the calcium as soluble chlorid or phosphate, and our data shows nothing worthy of note, the ingestion of the large amount of calcium causing no upset in the condition of the child.

CONCLUSIONS

We have shown that the ingestion of large amounts of calcium and the absorption of this calcium as organic salts, if not accompanied by the ingestion of sufficient chlorin or phosphorus to permit of the formation of soluble salts will result in an accumulation of calcium in the tissues which is followed by a toxic condition and the elimination of calcium lactate in the urine.

The toxic condition noticed by others when a high protein synthetic food was fed was probably the result of the high calcium content of the food, as our work reported in this and previous papers seems to indicate, and not the result of the high protein content, the protein being responsible only to the extent that it is the carrier of the calcium in the form of calcium caseinate.

Whether the toxic condition noticed is the result of the accumulated calcium itself or to a calcium salt, possibly calcium oxalate, we are not prepared to state.

C. Bruger⁶ has recorded the fact that the injection of neutral or alkaline phosphates of sodium resulted in a diminution in the calcium content of the serum and a condition of tetany. In view of the fact that the overloading of the serum with neutral or alkaline phosphates would favor the precipitation of calcium salts we are inclined to believe our results and his to be manifestations of the same phenomenon.

We also believe the observations of Marriott and Howland,⁷ in which they noticed a diminution in the calcium content of the serum and a marked phosphorus retention, to have some bearing on the same phenomenon.

6. Bruger, C.: Toxicity of Phosphates in Relation to Blood Calcium and Tetany, *Jour. Pharmacol.*, 1917, **10**, 105.

7. Marriott, W. McK., and Howland, John: Phosphate Retention as a Factor in the Production of Acidosis in Nephritis, *Arch. Int. Med.*, 1916, **18**, 108.