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THE FASTING METABOLISM OF INFANTS.

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THE investigation of the processes which take place in the animal or human body when the supply of energy from outside ceases and the total life functions are asserted by means of metabolism of the substances already present in the body, is from different points of view of the greatest interest.

The fasting metabolism forms the fundamental basis for the explanation of the existing conditions of the normal metabolism in different kinds of nutrition, for the investigation of the absolute amount of the metabolism, and for determining the food requirements of the organism under different physiological and abnormal conditions.

The fasting metabolism has been repeatedly investigated experimentally since the work of Lavoisier, the founder of our knowledge of metabolism. Although many and thorough investigations of this subject exist with animals and men, but little is known of the relation of the growing organism during fasting. Since the pediatrician uses the fasting as a therapeutic measure in the treatment of disturbance of digestion in early childhood, the whole question is of a great practical importance. In a small monograph Czerny weighed "pro et contra" of the fasting therapy from the clinical standpoint. He came to the conclusion that nurslings stand complete fasting as well as partial for a long time without evident harm, but he points to the dangers which might arise from the increase of acidosis on top of an acidosis which might already be present in a disturbance of digestion. Langstein and Benfey also expressed the opinion that the healing effect of fasting had been demonstrated in nurslings that have been ill because

of overfeeding, but that fasting can also result in disease.

We know very little about the metabolism of the healthy nursling during fasting.

The few investigations which until now are at hand, as those by Ludwig F. Meyer, as well as those by Ludwig F. Meyer and by Leo Langstein, treat this question from only one angle. The former studied the nitrogen elimination in the urine of three children of different ages during two fasting days. We do not find any report of the food previous to the fasting.

The investigations of Ludwig F. Meyer and Leo Langstein show only the elimination of acetone during a three days' fast.

Rietschel demonstrated in his experiments on six babies which had been taken away abruptly from the mothers' breast and put on a three days' diet of weak tea the one fact, that the urine of five of the children reduced Fehling's solution when they received nourishment again. His results lead him to the conclusion that fasting of several days leads to a disturbance of the normal utilization of the nourishment and diminishes the power of assimilation for sugar. All other investigations were done on sick children and are, therefore, not to be considered physiological. But for us the question is how infants in absolute or nearly healthy conditions react when subjected to fasting.

We do not enter into those experiments where there is no question of real fasting, as in the experiment of Rubner and Heubner, who determined the metabolism of an infant during twenty-four hours' abstinence from food, because in this instance the metabolism and the production of energy is in a great measure influenced by the food, which was previously given. By fasting metabolism we understand the combustion of the real body material. A strict line of division cannot be drawn here, but one can reckon that the beginning of the fasting period, from the physiological viewpoint, comes only after eighteen to twenty-four hours have elapsed after food has been given.

When Schlossmann and myself began the experiments of the respiratory exchange several years ago, the hope of answering the question of the fundamental and fasting metabolism of the nursling seemed to us very small. If, then, the gaseous metabolism which corresponds to the fundamental metabolism should be determined, the organism of the subject must be kept in a perfect state of rest. Therefore every factor which produces energy and which can be avoided must be excluded,—on one hand, the muscular activity, in so far as it is not absolutely necessary for vital functions; on the other hand, the work of digestion. The children, to express myself practically, must be kept in a state of starvation and must keep absolutely quiet during the respiratory experiment. It seemed to us most improbable that healthy and normal nurslings should submit to these de-

mands, which are so apparently contradictory to the character of the infant, but it soon became evident that it was possible to carry out such investigations. The exclusion of muscular activity in the ordinary sense can be attained pretty easily if we choose suitable subjects which are not too lively, and if we undertake the respiratory experiments at a time when the infants are asleep; it was obviously best during the night. On the other hand, we were surprised that very many nurslings are very indifferent to starvation. It is necessary to swindle the nursling so that it will not appreciate that it is being starved by the way that the experiment is arranged. There should, therefore, not be any change in the daily routine evident to the nursling. Above all things, water should be given at the regular intervals in the same quantity which the baby is in the habit of getting its milk. Breast-fed infants must be accustomed to the bottle before such experiments. Our nurslings took the bottle of water willingly without exception and showed no discomfort in the course of the whole fasting period. Our experience does not coincide with that of Rietschel, whose babies cried on the first fasting day and showed signs of lassitude in the following days. Rietschel's babies also eliminated, as I mentioned before, sugar in the urine, after they were given nourishment again. We could find no sugar in the urine when we gave nourishment again after the starvation. We suppose that Rietschel used for his experiment babies only a few weeks old, but we used babies of several months.

In our investigations with the fasting babies we determined the protein, the respiratory exchange and the elimination of acetone and B-oxybutyric acid.

The metabolism of nitrogen can be studied easiest; it is sufficient to examine only the urine, because the quantity of the hunger stool *per se* and the quantity of its nitrogen is very

small, so that it can be ignored. According to recent experiments the total nitrogen of the urine, 18 hours after the last meal, consists of the decomposed body substance.

The knowledge of the quantity of nitrogen which is eliminated enables us to draw conclusions as to the decomposition of protein. Furthermore, if we determine the O₂ consumption and the CO₂ production, and we know how much protein was decomposed, we can compute the amount of fat and glycogen of combustion. In that way we are able to show clearly both the metabolism and the transformation of energy.

In order to study the question of the metabolism of the fasting nursling, it was necessary to make the experiments as comprehensive as possible. A series of interesting experiments made previously on infants, as well as on dogs fed on a one-sided diet, led us to the conviction that the combustion of material during fasting depends greatly upon the previous food. Therefore we took into consideration in our later experiments infants who were differently brought up. Here I will give from our material only some very typical examples.

The first baby which was experimented on was breast fed, and had been kept on this food for a preliminary period of three days' duration. Then a fasting period of sixty hours followed, during which at the usual meal times the infant received only water, to which was added three-tenths per cent. of chloride of sodium, and which was sweetened with some saccharine.

The fasting period was followed by a period with human milk. The milk and urine were examined. The weight of the nursling at the beginning of the investigation (No. 1=30th of June) was 3410 grams, and two days after fasting 3600 grams.

Table 1 gives us a condensed view of the course of the exchange of nitrogen and of the waterbalance during the whole eight days' experiment.

TABLE I. (EXPERIMENT 16.)
BREASTFED INFANT.

Bodyweight at beginning = 3410 grms.
Bodyweight at end = 3600 grms.

Periods.	Per Kilo Bodyweight per Hour.		Waterbalance.		
			Amount of Fluid Taken. Ccm.	Urine.	
	N. of Food. Mg.	N. of Urine. Mg.		Ccm.	Output in % of Intake.
Preliminary					
1. day	15.7	—			
2. day	16.6	4.76	1360	782	58 %
3. day	14.3	4.99			
Fasting					
1. day	—	5.54			
2. day	—	7.87	1680	914	54.4%
3. day	—	7.42			
(12 hours)					
Recovery					
1. day	13.2	7.95	1270	900	70.9%
2. day	12.7	4.74			

The table shows that the elimination of nitrogen, the amount of which was 4.88 mg. per kilo per hour during the feeding period, was much higher during fasting and rose to 7.87 milligrams. The nursing receiving breast milk with a small amount of nitrogen saves more of his nitrogen during feeding than while fasting. In this case the subject was a thin baby, which had only a little glycogen and fat to dispose of, when the nourishment ceased. Therefore the protein was immediately used in a large amount. On the second day of the recovery period the nitrogen exchange regulated itself completely; the infant eliminates just as much as in the preliminary period. The appearance that the breast-fed baby eliminates more nitrogen during

fasting than during the period of feeding might be a general one: for in all cases examined by us we made the same observation. With regard to the waterbalance in the preliminary period the nursing eliminated 58% of the fluid taken in the urine, during fasting 54.4%, and in the recovery period 70.9%.

Hence during the fasting period there was a considerable water retention. This was observed by slight but clearly noticeable œdema. This œdema disappeared on the second day of the recovery period, in which an increased water excretion followed through the kidneys.

The following three experiments made on one and the same infant, which was bottle fed, are reproduced in Tables 2, 3 and 4. In the pre-

TABLE 11. (EXPERIMENT 17.)

BOTTLED CHILD. G.

Bodyweight at beginning = 4360 grms.

Bodyweight one day after fast = 4370 grms.

Food: Cow's milk 2 Water 1 + Sugar 5% Per day = 600 calories (800 ccm.)				Protein = 2.06% Carbohydrate = 8% Fat = 2%		
				Waterbalance.		
Periods.	Duration	Per Kilo Bodyweight per Hour.		Amount of Fluid Taken. Ccm.	Urine.	
		N. of Food. Mg.	N. of Urine. Mg.		Ccm.	Output in % of Intake.
Preliminary	36	27.05	17.3	1280	835	67.7
Fasting						
1. day	24	—	14.3	1600	1007	62.9
2. day	24	—	13.1			
Recovery						
1. day	24	25.3	14.8	1920	1367	71.2
2. day	24	25.3	13.1			
3. day (12 hours)	12	20.3	12.0			

liminary period of the first fasting experiment this infant was fed on a mixture of two-thirds milk and one-third water with 5% sugar.

From that mixture the infant received 800 ccm. per day, corresponding to 490 calories per day or 112 calories per kilo and 24 hours. The amount of calories was too small to cause an increase in the weight of the infant.

The preliminary period lasted 36 hours, the fasting period 48 hours, the recovery period 60 hours. The infant endured the fasting splendidly. There was no œdema, but in this case there was also some retention of water during fasting, as is to be seen from Table 2. From that water retention we can explain the fact that there was no loss of weight during fasting; neither did the body weight increase some days later, after the infant had taken food again. During these days there was evidently a compensation between water and body material. The amount of nitrogen in the urine decreases from 17 mg. of the preliminary period to 14 mg. on the first fasting day, and 13 mg. on the second day. During the whole recovery period it is low, a sign of a large retention of nitrogen.

After the end of this experiment we put the infant on food rich in calories, consisting of buttermilk, cream, flour and sugar. The infant received 800 ccm. of this mixture per day, corresponding to 640 calories, or 140 calories per kilo. After having been fed on this food for ten days, the weight of the infant rose to 4270 grms. In this state a new investigation began which was introduced by a forty-eight hour preliminary period with this food. The fasting period lasted sixty hours; the recovery period, with the same food as that of the preliminary period, forty-eight hours. At the end of the fast the child weighed 4,800 grams. The nitrogen and waterbalance are given in Table 3. In spite of the fact that the water elimination during this fast was much higher than during the former (80.3%), nevertheless there was a certain retention which caused the appearance of œdema. On the second day of the recovery period the water elimination shows the same value as in the preliminary period and the œdema disappeared. In this case the appearance of œdema may be explained by diminished elimination of water in another way. As a matter of fact, in

TABLE III. (EXPERIMENT 18.)

BOTTLEFED CHILD. G.

Bodyweight at beginning = 4720 grms.
Bodyweight at end of fasting = 4800 grms.

Food: Buttermilk + cream + flour + sugar. Per day 800 ccm. = 640 calories Per kilo = 140 calories			Protein = 3 % Carbohydrate = 9.5 % Fat = 3 %		Waterbalance.					
Periods.	Duration Hours.	Per Kilo Bodyweight per Hour.		Amount of Fluid Taken. Ccm.	Urine.			Output in % of Intake.		
		N. of Food. Mg.	N. of Urine. Mg.		Ccm.					
Preliminary	48	37.7	24.9	1600	463 462	925	58.1 58.0	58		
Fasting										
1. day	24	—	21.6	1760	477	1412	59.6	80.3		
2. day	24	—	12.9		935		97.2			
3. day	12	—	15.4							
Recovery										
1. day	24	38.0	18.0	1600	643	1141	80.4	71.3		
2. day	24	31.9	21.6		498		62.2			

this case the amount of fasting stool was very small and therefore there was no elimination of water from the intestine.

The combustion of protein in this experiment was different from the previous one mentioned.

With the poor nourishment, *i.e.* two-third milk in the previous experiment, the nitrogen elimination was 17.3 mgs; now, with abundant nourishment, 25 mgs. With the larger amount of nitrogen in the food there was a greater elimination of nitrogen in the urine. During fast the elimination drops and amounts on the second fasting day only to about half of the preliminary period. The small nitrogen elimination during the recovery period shows again that after fast-

ing, the body strives towards compensating the loss of nitrogen.

Between this and the following experiment, which began after eleven days, the infant was fed on the same nourishment with the same amount of calories. At the beginning of the experiment the infant weighed 5220 grms. After a preliminary period of 48 hours, the fast began and lasted this time 72 hours. After fasting there was a loss of 140 grams in weight, and three days later after feeding this was regained. During this time the water and solids balance each other and the body weight rises again.

TABLE IV. (EXPERIMENT 19.)

BOTTLEFED CHILD. G.

Bodyweight at beginning = 5520 grms.
Bodyweight at end of fasting = 5380 grms.

Food: Buttermilk + cream + flour + sugar. Per day 800 ccm. = 640 calories Per kilo = 140 calories			Protein = 3 % Carbohydrate = 9.5% Fat = 3 %		Waterbalance.		
Periods.	Duration Hours.	Per Kilo Bodyweight per Hour.		Amount of Fluid Taken. Ccm.	Urine.		
		N. of Food. Mg.	N. of Urine. Mg.		Ccm.	Output in % of Intake.	
Preliminary	48	32.7	22.7	1600	716	44.8	
Fasting							
1 to 36 hours	36	—	17.6	2400	1984	82.8	
37 to 76 hours	40	—	12.9				
Recovery	140	29.0	18.3	4800	2835	59.0	
1 to 70 hours			18.7				
21 to 44 hours			8.5				
45 to 140 hours			20.9				

Table 4 shows the relations of the nitrogen and waterbalance. The proportion of food volume and urine volume in the preliminary period, compared with the previous experiment, is diminished; during fast it rises to 83%, and falls in the recovery period to 59%.

The nitrogen combustion shows about the same values as in the previous experiment. The

general aspect of the nitrogen balance of the investigations mentioned shows to us that during fasting the combustion of protein depends in a great measure upon the previous nourishment. The more nitrogen the nourishment contains the more protein of the body material is decomposed, both on the second and third fasting day. So we see that generally during fasting of the

valuable body protein the organism decomposes less than it does during the time in which it receives protein from outside. An essential difference exists between the naturally or breast-fed infant and the bottle fed or unnaturally fed. The breast fed has an increase of nitrogen elimination during fasting, consequently there is a larger combustion of protein. This fact was already observed by Amberg and Morrill and led them to the conclusion that at a suitable composition of food the amount of the necessary protein minimum is lower for the nursing than the quantity of protein decomposed by the organism during fasting.

FIG. I.
Elimination of Nitrogen in Urine.

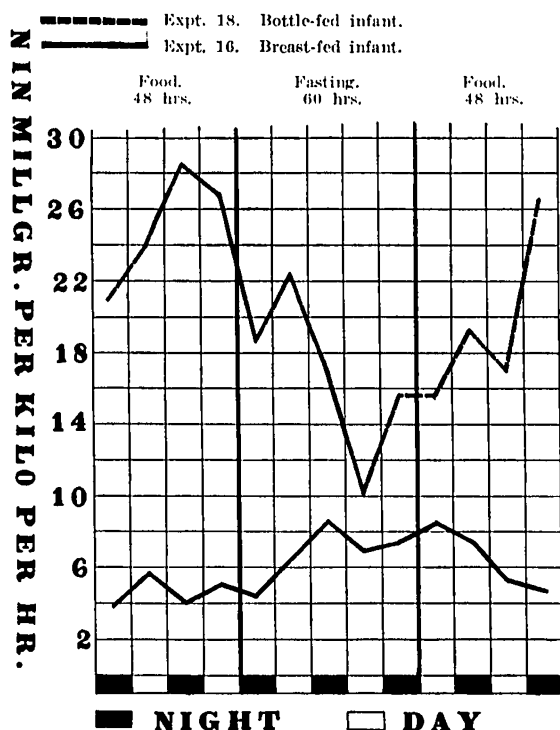


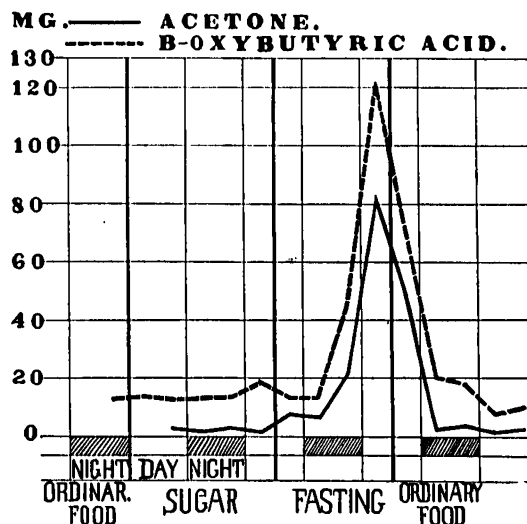
Figure I shows the difference of the nitrogen elimination between the breast-fed and the bottle fed infant during the feeding and fasting periods. The lower curve represents that of the breast fed, the upper that of the unnatural fed one. Therefore when breast fed there is less protein decomposition than when fasting. The quantity of protein which a fasting breast baby takes from his body material in order to cover its expenditures is still considerably less than the quantity of protein which an unnatural fed infant uses. Therefore, the breast-fed baby will decompose during fasting less of its body protein than the baby which has been brought up in an unnatural way. If for any reasons a breast-fed baby has to fast, it will stand this fasting with much less loss than the one which has been brought up unnaturally.

Now we enter into the second part of our in-

vestigations, into the question of acetone and B-oxybutyric acid excretion. The quantity of acetone which is excreted in the urine in an ordinary diet of an adult amounts to about 0.01 mgr. per kilo of body weight per hour. The elimination through the lungs is said to amount from two to three fold. During fast of an adult the acetone excretion rises considerably in the urine as well as from the lungs. For the nursing Ludwig F. Meyer and Leo Langstein brought figures which showed a great increase of acetone during fasting. Our experiments show that on the usual diet the nursing excretes in the urine only traces of acetone, but about 12 hours after the last meal the quantity of acetone rises first slowly and then rapidly. Quantities of acetone were excreted by our infants, which essentially exceed those in adults, on the fourth and fifth day of fast. So we found in the last mentioned experiment (No. 19) between the nineteenth and thirty-sixth hours, almost two milligrams per kilo per hour, from the sixteenth to the seventy-sixth hour 1.2 mg. In general the maximum quantities move about in the same height, as was found in Cetti and Breithaupt during fast. We also can show a considerable difference between breast-fed and unnatural fed infants. In general the breast-fed child excretes during fasting less acetone than the bottle fed child. In the breast-fed child shown above, the quantity of acetone amounted per kilo body weight per hour on the first fasting day to 0.12 mg., on the second fasting day to 0.421 mg., and on the third fasting day to 0.292 mg. With the unnatural fed child, from the 19th to the 36th hour of fast, 1.98 mg.; from the 37th to the 60th hour of fast, 0.93 mg.; from the 61st to the 76th hour of fast, 1.20 mg. Furthermore, we could state, that if one puts an infant on protein and fat fast, but gives to him carbohydrate, the acetoneuria ceases. This is to be seen from Figure II.

FIG. II.

Total Elimination of Acetone, B-oxybutyric Acid in Urine during Feeding Milk, Milsugar and Absolute Fasting.



In this experiment, after a preliminary period with the usual food, the infant received 1000 cm. of a 7% milk sugar solution. In this period the acetone secretion was scarcely higher than in the preliminary period. But when the sugar was left out, with one below the acetone contents rose. Hence there is no doubt that the deficiency of carbohydrate represents the causal factor in the origin of acetone, both for the nursing and for the adult. The excretion of β -oxybutyric acid runs pretty parallel to the excretion, as seen from Figure II. Its quantity is a little higher than that of acetone.

In order to complete the picture of fasting metabolism we also determined the respiratory

exchange of the nursing. Therefore we have inserted in the last two experiments mentioned above, investigations of the gaseous metabolism of three hours' duration. In experiment No. 18 the respiratory exchange of the infant was determined 48 hours after the last feeding; in experiment No. 19, 48 and 72 hours after the last meal. The infant had behaved very well during the respiratory experiments, so that the figures recorded by us must be considered as resting figures during fast. We can compute the material combustion of the body by means of the figures recorded in the respiratory experiments, and knowing the nitrogen elimination.

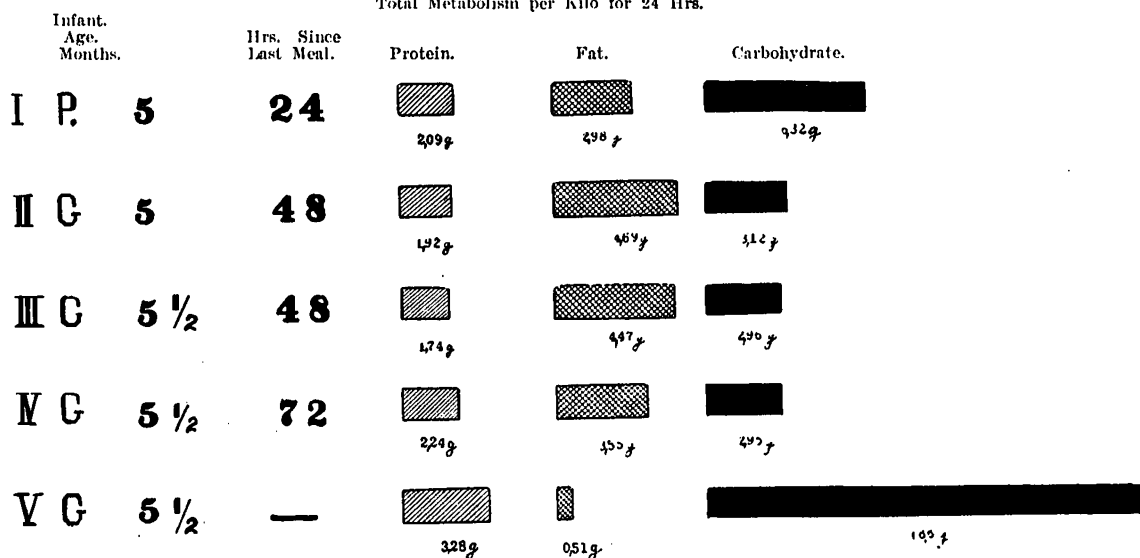
TABLE V.

THE RESPIRATORY EXCHANGE, THE COMBUSTION OF PROTEIN, FAT AND CARBOHYDRATE DURING FASTING.

Experiment.	Duration of Fasting Hours.	Per Square Meter per Hour.		R. Q.	Per Kilo Bodyweight for 24 Hours.			
		CO ₂ gr.	O ₂ gr.		Protein.	Fat.	Carbohydrate.	Calories.
18	48	12.278	11.49	0.779	1.92	4.69	3.12	62.2
19	48	12.04	11.28	0.778	1.74	4.47	2.95	61
19	72	10.94	10.09	0.790	2.24	3.55	2.95	54

Table 5 shows the production of CO₂ and the consumption of O₂ per square meter of body surface. We see that there is a very good agreement between the two experiments 48 hours after the last meal. Then we see that after 72 hours of fast the production of CO₂ and the consumption of O₂ are decreased. The respiratory quotient is pretty constant. Furthermore, the table gives us the quantities of protein, fat and carbohydrate which 1 kg. of infant decomposes, 24 and 72 hours after the last meal, computed for 24 hours. It is a striking fact that the amount of glycogen was so abundant on the third day of fast that as much could be utilized

as on the second fasting day. An explanation of this fact is to be found that our baby took very abundant nourishment for a long time previous to the experiments, and so had a considerable storage of glycogen. Therefore the diminution of metabolism and energy transformation in this case is to be attributed to the lower fat combustion. In an earlier experiment we have determined the fundamental metabolism of another baby (P.) 24 hours after the last feeding. Contrary to the infant G., in this case the subject was a very fat baby. With this baby (P.) per kilo of body weight per 24 hours were decomposed: protein 2.09 gr., fat

FIG. III.
Total Metabolism per Kilo for 24 Hrs.

2.89 gr., glycogen 6.32 gr., corresponding to 63 calories. The comparison demonstrates that 24 hours after taking the last meal the glycogen combustion is essentially higher, and the fat combustion lower than 48 hours after feeding. Finally, in order to show the difference of metabolism between the fasting-sleeping state and the state immediately after feeding and while awake, I add the results of another respiratory experiment, which was carried on at the end of our last experiment, No. 19, after the infant had received its known abundant food for six days. In this case the infant was put in the respiratory apparatus directly after taking the bottle, and was kept there for four hours until the following meal. During this experiment the infant slept only about $1\frac{1}{2}$ hours, the rest of the time it was awake but mostly quiet or played with its fingers.

In this experiment the infant decomposed per kilo body weight for 24 hours computed protein 3.28, fat 0.51, carbohydrate 16.6, corresponding to 86.1 calories. The difference of the combustion of the single foodstuffs in the five mentioned experiments can be shown clearer by a graphical presentation which is shown in Figure III.

This figure shows the grams of protein, fat and carbohydrate which were decomposed by an infant computed per kilo for 24 hours.

Table 1 gives the amount of nitrogen in grams 24 hours after the last food. Tables 2 and 3, 48 hours after the last feeding. Table 4, 72 hours after the last feeding. Table 5 shows the relations of combustion in the first four hours after feeding. From this table we can see that in the first hours after feeding the metabolism is increased and is supplied principally by carbohydrate; during this time the fat combustion is very small. Twenty-eight hours after the last food the combustion of carbohydrate is greatly diminished; now the fat is drawn upon in large measure. This diminution of carbohydrate combustion and the increase of fat combustion becomes still more evident in prolonged fasting. Of course these figures are only suggestive of what may develop in the future. As valuable as they are, they represent only some stones of the foundation on which the building of the metabolism of babies shall be erected.

over her husband's condition. There have been no miscarriages. The child of a previous pregnancy is healthy. The previous history of the mother is negative. The child, male, was born normally April 3, 1910. Fetal movements were felt during pregnancy and were quite as lively as those of the normal baby of the previous pregnancy. When the baby was three weeks old, the mother noticed that he seemed unusually limp, but was reassured by the obstetric nurse in charge. When six weeks old, the mother noticed a dropping of one hand and that the hands seemed weak and limp and were not moved as freely as they ought to be. At this time she consulted a physician, who said the condition was due to weakness, that the breast milk was probably not agreeing with the baby, and advised that it be taken off the breast. When the baby was two months old he was seen by Dr. Howland of New York, who noted a marked atrophy of the muscles of the trunk and extremities, and deformity of the chest. The baby seemed to improve somewhat, at one time being able to move his arms, but later this power disappeared. He has never been able to move his legs at the hips, knees or ankles, but could make slight movements of the toes and fingers. He has never been able to sit up or to hold up his head. The mental development is normal. The breathing has been labored since the baby was three weeks old and this has grown progressively worse. On Sept. 3 the baby caught cold and since then the trouble in breathing became worse, with choking spells from mucous accumulation. To give relief the adenoids were removed on Sept. 24. The breathing was somewhat improved by the operation, but has lately become as bad as before. The weakness increased until he could no longer nurse from the breast or bottle and had to be fed with a spoon. The baby gained weight up to the time of the adenoid operation, but since then has lost.

Physical Examination. Oct. 3. Poorly developed and poorly nourished baby. The cranium was square, the forehead prominent; the fontanelles depressed but of normal size; the mouth, tongue and throat were normal. There were no teeth. The pupils were equal and reacted normally. The respiration was irregular, labored and wholly diaphragmatic, but not notably accelerated. The chest showed marked increase in anteroposterior diameter, with marked lateral flattening and prominent sternum. The heart, lungs and abdomen were normal. The baby was entirely unable to hold up his head and there seemed to be a complete flaccid paralysis of the trapezius muscle. The upper extremities were not moved at all from the shoulder and very feebly at the elbow and wrist. The hands hung over in flexion when the arm was held upright. There appeared to be a flaccid paralysis of the shoulder girdle muscles with marked atrophy, particularly of the pectoralis. There was slight atrophy of the muscles of the extremities. The knee-jerk was absent.

From this time until death, Oct. 23, the condition gradually became worse, although there were temporary ameliorations. There was increase in the mucus accumulations and in the fits of choking, and the child died in one of these attacks.

CASE 2. History. E. S., aged 5 months. Seen July 28, 1912. The father and mother are both well. One other child five years old is well. No other pregnancies. The mother had a very trouble-

MYATONIA CONGENITA, WITH REPORT OF CASES.

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CASE 1. History. M. G., aged 6 months. The father was addicted to alcohol and was intoxicated at the time of conception and at intervals during the mother's pregnancy. During pregnancy the mother was well, but much worried and distracted