THE INFLUENCE OF THE HIGH-CALORY DIET ON THE RESPIRATORY EXCHANGES IN TYPHOID FEVER *

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The influence of a diet rich in carbohydrate on the protein metabolism in typhoid fever[1] and the extent of its absorption[2] have already been studied in detail. The striking clinical effect of the diet in a large number of cases has also been reported.[3] It has seemed desirable, therefore, to investigate the fate of the large amount of food administered and its effect on the total metabolism. During the years 1911 and 1912 it was possible to make 134 determinations of the respiratory exchanges of patients taking the high-calory diet, and the results have been embodied in the following report. Some of the experiments were reported briefly on a former occasion.[4]

Numerous investigations have been made by other observers, but practically all their patients were examined in the fasting state, that is, from six to thirteen hours after the last meal. Moreover, these patients were on diets of low caloric value and were not receiving enough food during the fever to maintain themselves in nitrogen and weight equilibrium. In 1891, Kraus,[5] working with the Zuntz-Geppert apparatus, found that in fever the respiratory quotient depended on the kind of food previously eaten and on the state of nutrition of the body. Following this a number of articles were published in which many of the cited respiratory quotients were so low that they could be explained only on the assumption of a profound change in the laws of metabolism occurring in fever. Chief among those who

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1. Shaffer and Coleman: Protein Metabolism in Typhoid Fever, THE ARCHIVES INT. MED., 1909, iv, 538.

2. Du Bois: The Absorption of Food in Typhoid Fever, THE ARCHIVES INT. MED., 1912, x, 177.

3. Coleman: The High Calory Diet in Typhoid Fever, a Study of 111 Cases, Am. Jour. Med. Sc., 1912, cxliii, 77; Weight Curves in Typhoid Fever, ibid., 1912, cxliv, 659.

4. Coleman: Diet and Metabolism in Fever, Tr. Fifteenth International Cong. on Hyg. and Demog., Washington, 1912, ii, 602.

5. Kraus F.: Ueber den respiratorischen Gasaustausch im Fieber, Ztschr. f. klin. Med., 1891, xviii, 160.

found these low quotients were Robin and Binet,[6] Rolly and Hörnig,[7] Rolly and Meltzer,[8] and E. Grafe.[9] Subsequently, Rolly[10] and Grafe,[11] questioning the correctness of their results, reinvestigated the subject and concluded that the types of apparatus first used were not suitable for the study of the respiratory metabolism in fever. In their later work Rolly and Grafe obtained no quotients below the normal limits, thus confirming the observations of Kraus made many years before. In the meantime Svenson[12] had carefully investigated the metabolic processes of convalescence and had found that the oxygen consumption fell below normal in the first week, rising again above normal during the second week. He found also that a heavy meal increased the metabolism from 30 to 65 per cent., and that during convalescence from typhoid a given amount of work was performed with a greater expenditure of energy than in health. Löning[13] took up the subject of the influence of food on metabolism in fever, and his work indicated that sugar was very rapidly oxidized, the respiratory quotient dropping to its original level within three or four hours after its administration. Glucose had no marked effect in raising the oxygen consumption.

Figure 1 shows graphically all the work done on typhoid patients by Kraus[5] and Svenson[12] and all the later work of Grafe[11] and Rolly.[10] The work of these investigators was selected because it dealt with patients on low diets examined from six to fourteen hours after their last meal; in other words, the basal or *nüchtern* metabolism was determined. This work was selected also because it contained very few quotients below 0.7 and therefore seemed to be technically correct. We have arbitrarily arranged the observations under the headings of "Continued Temperature Period," corresponding to the second week, "Early Steep Curve Period," corresponding to the third

6. Robin and Binet: Etudes cliniques sur le chimisme respiratoire, Arch. gén. de méd., 1896, i, 641, ii, 385 and 515.

7. Rolly and Hörnig: Stoffwechseluntersuchungen an Typhuskranken mit besondere Berücksichtigung des Verhaltens des respiratorischen Quotienten, Deutsch. Arch. f. klin. Med., 1908-1909, xcv, 74.

8. Rolly and Meltzer: Stoffwechseluntersuchungen bei Fieber, etc., Deutsch. Arch. f. klin. Med., 1909, xcvii, 252.

9. Grafe, E.: Gaswechseluntersuchungen bei fortgeschrittenen Erkrankungen der Lungen und der Zirkulationsorgane, Deutsch. Arch. f. klin. Med., 1909, xcv, 543.

10. Rolly, G.: Experimentelle Untersuchungen über den Stoffwechsel im Fieber und in der Rekonvalescenz, Deutsch. Arch. f. klin. Med., 1911, ciii, 93.

11. Grafe, E.: Untersuchungen über den Stoff- und Kraftwechsel im Fieber, Deutsch. Arch. f. klin. Med., 1911, ci, 209.

12. Svenson, N.: Stoffwechselversuche an Rekonvalescenten, Ztschr. f. klin. Med., 1901, xliii, 86.

13. Löning, Karl: Ueber den respiratorischen Gaswechsel im Fieber unter dem Einfluss der Nahrungsaufname, Klin. Jahrb., 1908, xix, 183.

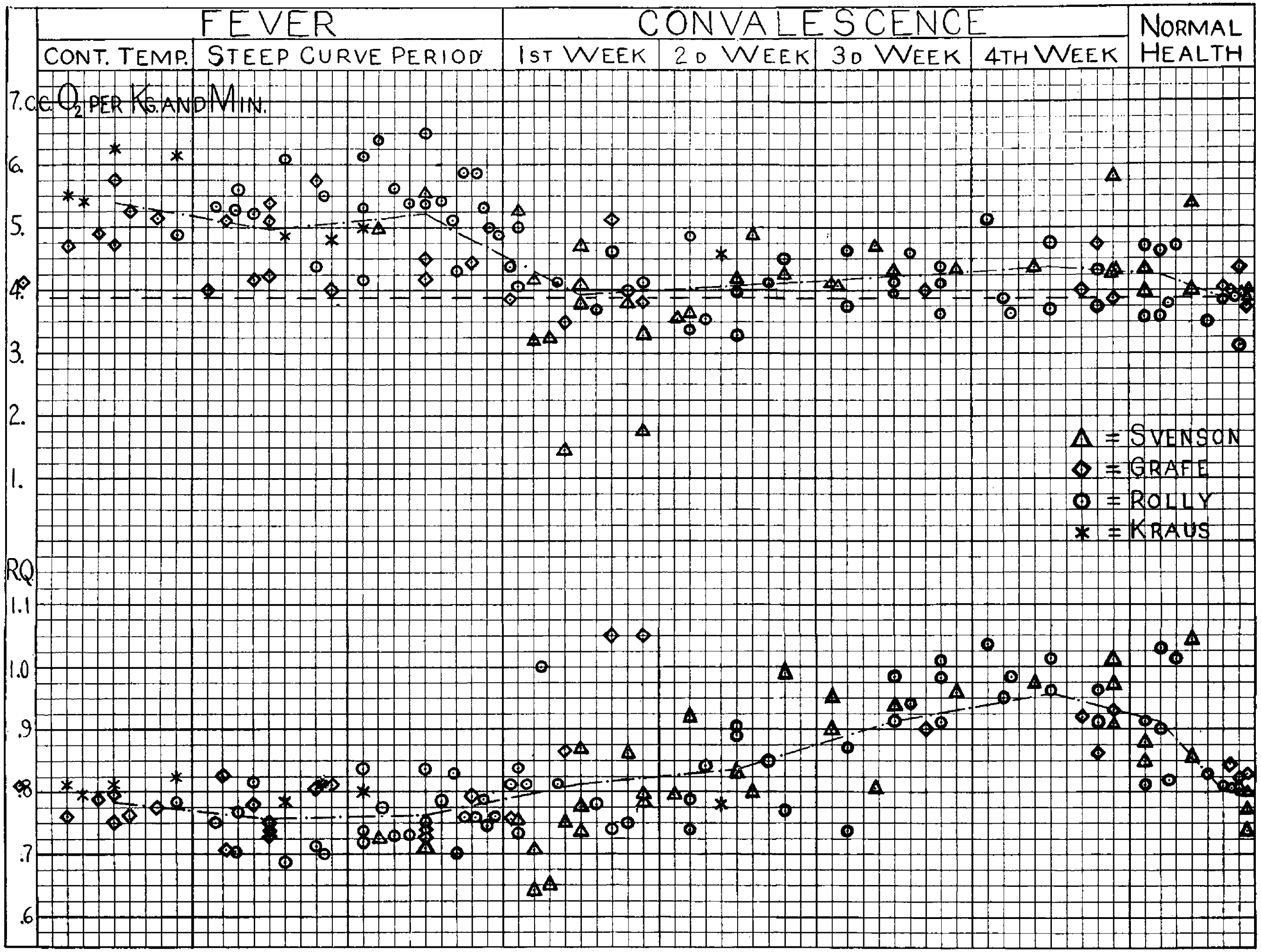

Fig. 1.—The oxygen consumption and respiratory quotients of typhoid patients on low diets examined by Kraus, Svenson, Grafe and Rolly from twelve to fourteen hours after the taking of food.

week, and "Late Steep Curve Period," corresponding to the fourth week of the disease and finally the various weeks of convalescence. In the last column are the results obtained on those patients whose metabolism was investigated several weeks or several months after their recovery.

For purposes of comparison the work on the high-calory cases is summarized in Figure 2, which corresponds to Figure 1 in every particular except that the last column represents the metabolism during relapses.

The high-calory diet used in the cases here reported has been fully described in previous publications.[1, 2, 3]

In brief, it may be said that as soon as typhoid patients are admitted to the hospital they are given food in amounts which are increased as rapidly as their digestions will permit. By the end of a week patients are usually taking a liter of milk, from 300 to 400 c.c. of 20 per cent. cream, from 100 to 200 gm. of lactose, two or three eggs, a couple of slices of toast and from 10 to 30 gm. of butter. This furnishes between two and three thousand calories. One or two thousand more calories are gradually added in the form of larger amounts of the foregoing or in the form of rice, oatmeal, mashed potato, cream of wheat, apple-sauce, custard or ice-cream. It was found that patients could be brought into nitrogen and weight equilibrium even in the active stages of the disease when the temperature was still high.[1] The absorption of the large amounts of food given in this diet was investigated,[2] and it was found that protein and carbohydrates were absorbed as well as in health. The nitrogen of the feces averaged 1.12 gm. a day, which was 7.1 per cent. of the average nitrogen of the food. Carbohydrates were completely absorbed unless more than 300 gm. a day was given, in which case 2 or 3 gm. appeared in the stools. Fats were absorbed in huge amounts, and the loss amounted to only 7.2 per cent. during the first three weeks of the fever and 4.5 per cent. in the later stages of the disease. On an average the patients lost in the feces only 5 per cent. of the calories ingested.

EXPERIMENTAL PROCEDURE

The type of apparatus selected for the investigation was the small "unit" or "universal apparatus" of Benedict.[14] In 1911 the machine resembled that described in Benedict's first publication, except that

14. Benedict, F. G.: An Apparatus for Studying the Respiratory Exchange, Am. Jour. Physiol., 1909, xxiv, 345; Ein Universalrespirationsapparat, Deutsch. Arch. f. klin. Med., 1912, cvii, 156.

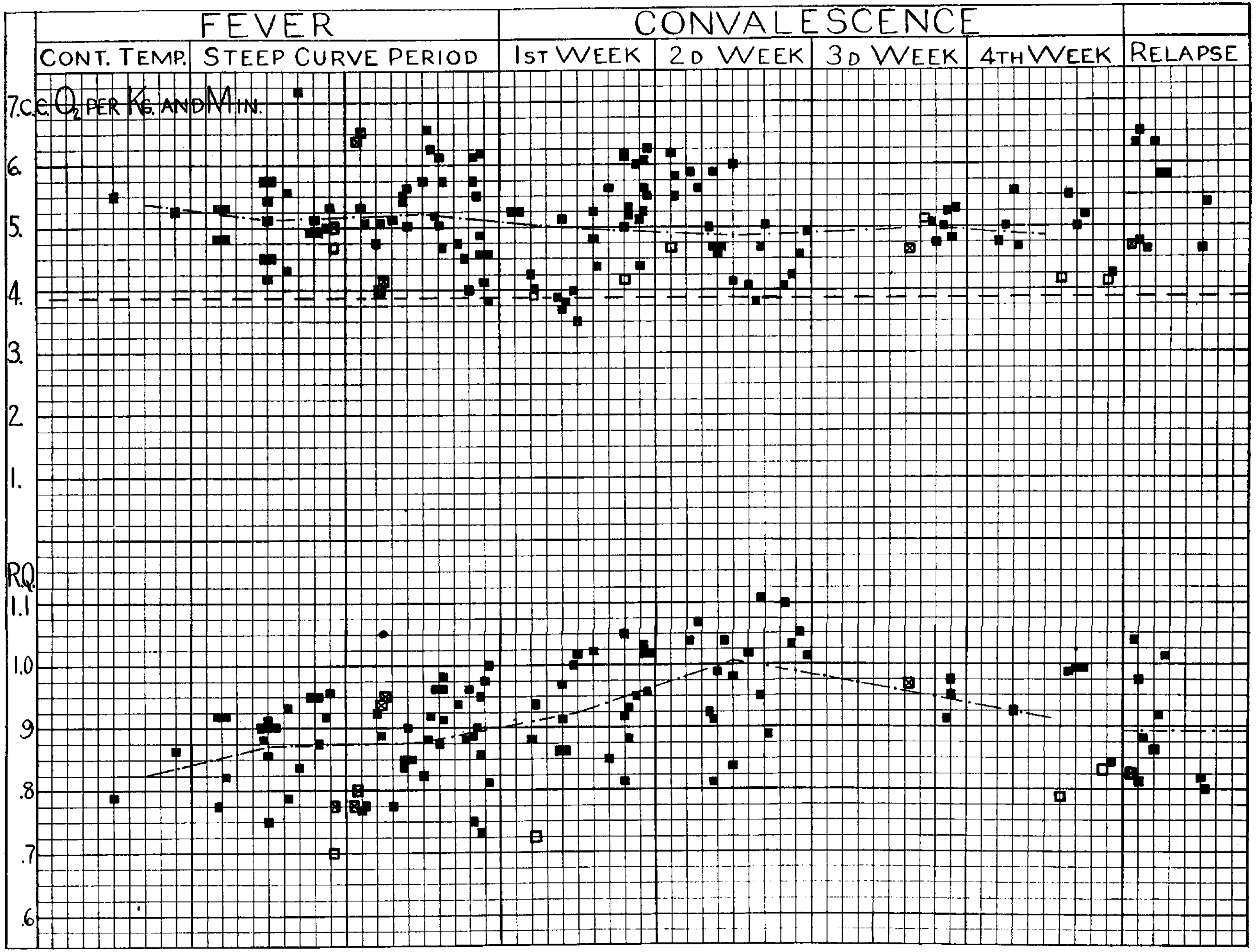

Fig. 2.—The oxygen consumption and respiratory quotients of typhoid patients on high-calory diet. Solid squares indicate observations made shortly after meals; open squares, fasting observations; crossed squares, observations, made from five to seven hours after the last meal or shortly after a very light meal.

Williams bottles[15] were used instead of the Woulfe bottles and Kipp generators, thus reducing the volume of air within the apparatus.

During 1912 a spirometer was substituted for the rubber bag, and the apparatus more closely resembled that described in Benedict's second publication. The old style of air-moistener and the single absorber system were retained but, unfortunately, the work-adder was not attached until the typhoid season was over. The nose-pieces require a special description, as they differed from Benedict's model. A soft rubber tube, reinforced by a spiral of brass wire, was substituted for the glass core used by Benedict, and the finger-cot was tied around this as shown in Figure 3. In order that the direction of the nose-pieces might be changed to fit different noses, a pair of wire spreaders, also shown in Figure 3, was attached. With some of the patients it was difficult to secure an air-tight joint when the finger-cot between the core and the inside of the nose was inflated. The flexibility of the new nose-pieces and the spreaders improved conditions considerably, but it seemed necessary to take the precaution of lathering the joint between nose-piece and nose with soap. This lather was watched during the whole experiment by one or two observers, and leaks were sometimes discovered which would otherwise have passed unnoticed. The use of lather with this apparatus is strongly recommended, since the loss of any quantity of air increases by a corresponding amount the apparent consumption of oxygen.

The experimental procedure is important enough to require a detailed description. The respiration apparatus was wheeled to the patient's bed and the oxygen bomb and the CO_2 absorbing system weighed to within 0.01 gm., all weighings being checked by an assistant. The bottles were then connected with the machine and the whole tested for leaks under a slightly increased pressure while the air was circulating at full speed. This was continued for some time in order to bring the various parts of the machine to a constant temperature. Meanwhile the subject's mouth was sealed with adhesive plaster, and the nose-pieces inserted, blown up and lathered. All this time a valve was turned so that the patient was breathing room air. Next the pressure within the machine was brought almost to zero and the level of the oil manometer carefully recorded. Then while the patient was breathing quietly and regularly, the valve was turned at the end of a normal expiration and he began to breathe the air which was circulating in the machine. During the experiment the pulse and respiration were counted at least three times and the character of respiration recorded. Note was made of each movement of the patient, although none of them did more than move a hand or leg

15. Williams, H. B.: Animal Calorimetry, First Paper, A Small Respiration Calorimeter, Jour. Biol. Chem., 1912, xii, 317.

a few inches. As the experiment progressed, oxygen was admitted by means of a reducing valve on the oxygen cylinder, and the rubber bag kept at approximately the same level. At the end of a period, which was almost always fifteen minutes, the valve near the nose-piece was quickly reversed, exactly at the end of a normal expiration. The air was then kept in circulation for two or three minutes in order to remove the last traces of carbon dioxid which might be in the passageways of the machine. Next oxygen was gradually admitted until the oil manometer gave the same reading as at the start of the experiment. Both readings were made about one minute after the circulation of the air was stopped. In 1912, when the spirometer was used,

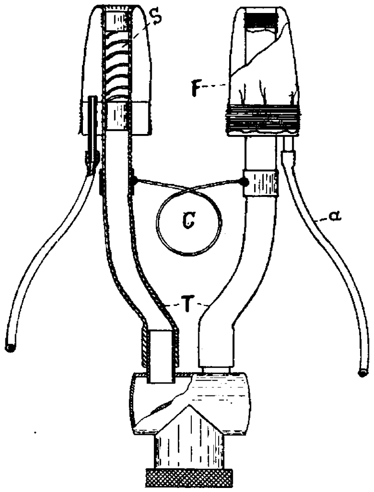

Fig. 3.—Diagram of modified nose-pieces: *S*, flexible spiral spring; *F*, finger-cot; *C*, spreaders for adjustment of nose-pieces; *T*, soft rubber tubes; *A*, small rubber tube for inflating finger-cots.

graphic records of the respiration were made in the manner described by Benedict,[16] and the oxygen was admitted until the original level of the spirometer was reached. The carbon dioxid absorbers and oxygen bomb were immediately weighed and the calculations made as follows:

$$\frac{CO_2 \text{ gm.} \times 0.509}{O_2 \text{ gm.} \times 1.004 \times 0.669} = \frac{CO_2L}{O_2L} = \text{Respiratory Quotient.}$$

The correction of adding 0.4 per cent. to the oxygen was made, since the Linde Air Product Company's oxygen was found on analysis to contain the same percentage of impurity that Benedict[16] found.[17]

16. Benedict, F. G: Universalrespirationsapparat, Deutsch. Arch. f. klin. Med., 1912, cvii, 156.

17. Shortly before this article was ready for publication, our attention was called to the fact that G. W. Morey of the United States Bureau of Standards had discovered that 98 per cent. of the impurity in the Linde Air Product Company's oxygen was argon and not nitrogen as had been previously supposed.

In all cases in which the urinary nitrogen was determined, the method described by Loewy[18] was used. This showed that in every case except one (Frank W.), protein furnished very close to 15 per cent. of the total calories. It was therefore possible to use the tables of Magnus-Levy[19] in those cases in which it was impossible to obtain the urinary nitrogen. These two sets of tables gave the caloric value of the oxygen for each experiment and made it easy to calculate the calories produced by the patient during each fifteen-minute period. That this method of indirect calorimetry corresponds very closely to the direct calorimetry has been shown by the animal experiments of Lusk and by unpublished experiments on human subjects.

The accuracy and general utility of the Benedict respiration apparatus have been proved by Benedict and his coworkers[20] in many comparisons with the Atwater-Rosa-Benedict respiration calorimeters. It must be remembered that all experimental difficulties are greatly increased in working with typhoid patients. It is almost impossible to keep a patient on a rigidly specified diet, and in the case of patients with high fever it is not justifiable to make more than two or three experiments a day. As a rule, the patients are somewhat nervous the first time they use the apparatus, and it has seemed advisable to leave unpublished the first observations on all except two phlegmatic individuals who showed absolutely no apprehension. Patients soon become accustomed to the procedure, however, and rather enjoy the break in the day's monotony, since they suffer no discomfort.

It was difficult to begin the experiments on schedule time since leaks would often be discovered at the nose just before the start. After the start a rising and falling bubble in the lather around the nose-pieces sometimes made it necessary to interrupt the period for a few minutes and readjust the apparatus. If the bubble broke or

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(The Occurrence of Argon in Commercial Oxygen made from Liquid Air, Jour. Am. Chem. Soc., 1912, xxxiv, 491). On account of the difference in the atomic weights of these gases, the correction should have been —0.6 per cent. instead of +0.4 per cent. This means that all the oxygen figures are about 1 per cent. too high and that the respiratory quotients are a trifle too low. The error is so small that it has seemed unnecessary to recalculate all the results given in this article and in the publications from Benedict's laboratory, which have been used as controls.

18. Loewy: Oppenheimer's Handbuch. der Biochemie, 1911, iv,[1] 277.

19. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906, i, 207.

20. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Inst. of Washington, 1910, Bull. 136; A Study of Metabolism in Severe Diabetes, ibid., 1912, Bull. 176; Benedict, Emmes and Riche: The Influence of the Preceding Diet on the Respiratory Quotient After Active Digestion has Ceased, Am. Jour. Physiol., 1911, xxvii, 383.

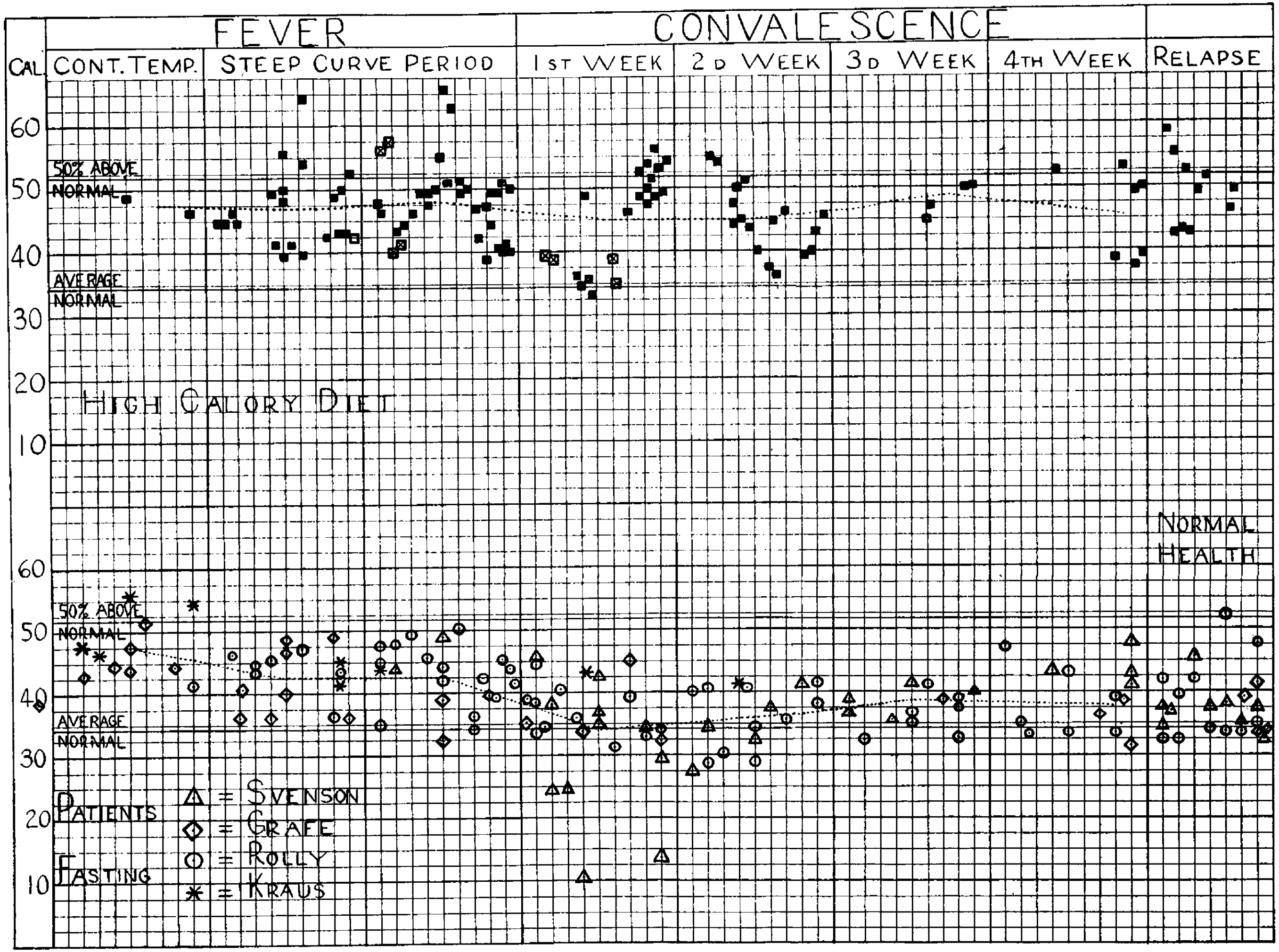

Fig. 4.—Results expressed in terms of calories per square meters of body-surface per hour. Comparison of high-calory cases examined shortly after meals and the fasting cases of Kraus, Svenson, Grafe and Rolly.

if there were any other leak, the experiment was discarded. The chief technical difficulty, however, lay in the tendency of some of the patients to increase the frequency or depth of their respirations shortly after the period was started. A few of the febrile patients persisted in this type of breathing, and it was necessary to give them up as experimental subjects. Two patients, Louis M. and Frank W., who had been breathing normally during the fever, developed this tendency early in convalescence, but their data were retained and grouped in a special table. The cause of the trouble is not clear; it might be due to nervousness on the part of the patient or to some unknown mechanical effect of the apparatus.

An increasing rate of ventilation (*Auspumpung*) has a very serious effect on the carbon dioxid determination, especially if the experimental period be a short one. Between the tissues whose carbon dioxid production we wish to estimate and the apparatus, there are from 3 to 5 liters of blood and 2.5 liters of residual air. While the carbon dioxid content of these does not change if the rate of ventilation be uniform, there is an immediate decrease of the carbon dioxid of the alveolar air when the alveolar ventilation is increased. This, in turn, removes some of the carbon dioxid from the blood, in which a large part is held in loose combination. Consequently, there is a "pumping out" of carbon dioxid from blood and residual air. There are no similar depots for oxygen in the body as has been shown by Katzenstein,[21] Zuntz and Geppert[22] and Loewy,[23] and the increased ventilation causes practically no change in the oxygen consumption. The percentage of oxygen in alveolar air may be slightly increased, as may the relatively small amount of oxygen held in solution in the blood-plasma. There may also be a slight increase in oxygen consumption because of the extra work of the muscles of respiration. It is evident that if stored carbon dioxid is exhaled in addition to the normally produced carbon dioxid and the oxygen remains constant, the respiratory quotient will be too high.

The effects of such increased ventilation (*Auspumpung*) are shown in a series of experiments on normal persons (Table 1). The first subject was examined during a period with natural breathing

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21. Katzenstein: Ueber die Einwirkung der Muskelthätigkeit auf den Stoffverbrauch des Menschen, Arch. f. d. ges. Physiol. (Pflüger's), 1891, xlix, 330.

22. Zuntz and Geppert: Ueber die Regulation der Athmung, Arch. f. d. ges. Physiol. (Pflüger's), xlii, 189.

23. Loewy: Die Wirkung ermüdende Muskelarbeit auf dem respiratorischen Stoffwechsel, Arch. f. d. ges. Physiol (Pflüger's), 1891, xlix, 405; Der respiratorische und der Gesamtumsatz, Oppenheimer's Handbuch der Biochemie, 1911, iv, p. 154, 161.

which gave his true oxygen and carbon dioxid. One hour later another fifteen-minute experiment was made in which the breathing was as deep and as rapid as possible. This increased the oxygen consumption 21 per cent., since the muscular work was severe. A second subject breathed deeply but not excessively during the first ten of the fifteen minutes and raised the respiratory quotient from 0.75 to 1.05, but increased the oxygen intake by only 5 per cent. The next subject was Louis M., one of the typhoid patients who had developed the tendency to *Auspumpung* during convalescence. Five months after leaving the hospital cured he returned to serve as a normal control. His fasting metabolism and respiratory quotient were determined in a respiration

TABLE 1.—Experiments in "Auspumpung" on Normal Persons from Fourteen to Seventeen Hours After Last Meal

	Periods 15 Min. Start of Exper. a. m.	Per Kg. and Min.		R. Q.	Increase in O_2 from *Auspumpung,* Pct.
		CO_2 c.c.	O_2 c.c.		
D. B., wt. 75.3 kg.:					
Oct. 31, normal breathing.....	10:35	2.69	3.48	0.77	
Breathing as deep and as fast as possible	11:35	4.62	4.21	1.10	21
J. R., wt. 66 kg. (approx.):					
Nov. 25, deep breathing first 10 minutes	10:37	4.43	4.24	1.05	5
Normal breathing	11:35	3.04	4.06	.75	
Louis M., wt. 51.7 kg.:					
March 26, normal breathing, 6 hours in calorimeter	10:10	3.36	4.34	.77	
March 29, unintentional *Auspumpung*	11:11	4.97	4.52	1.10	4
March 29, unintentional *Auspumpung*	11:55	5.03	4.57	1.10	5

calorimeter in which *Auspumpung* was impossible, and two days later, under exactly similar conditions, two observations were made with the small Benedict apparatus. Curiously enough, the abnormal type of breathing had persisted and it was possible to compare his unintentional *Auspumpung* with a faultless calorimeter experiment. The increase in oxygen consumption amounted to 4 and 5 per cent. in the two periods with the small apparatus.

The *Auspumpung* of the few typhoid patients who exhibited this phenomenon was of the type which, in the controls, raised the oxygen figures from 4 to 5 per cent. and never approached the maximal effort of the first normal subject. Since the carbon dioxid and respiratory quotient of all *Auspumpung* observations are too high, it has been necessary to group the experiments in which this phenomenon probably occurred in a special table. The quotients have been discarded, but the oxygen figures are so slightly changed that it seemed advisable to include them in the graphic chart (Fig. 2) and in the table of averages.

While the present work was in progress, Rolly and Rosiewitz[24] published an article on typhoid describing a modification of the Benedict apparatus changed to meet certain objections which they raised in regard to the original machine. These objections have been fully answered by Benedict,[16] but the best answer is to be found in the close agreement between the small apparatus and the large respiration calorimeters of the Nutrition Laboratory in Boston and the Russell Sage Institute of Pathology in New York. The latter apparatus has not yet been described.*

Kraus[5] and Svenson[12] used with apparent success the Zuntz-Geppert apparatus. Grafe,[11] in his recent work on typhoid, used a respiration cabinet of the Jacquet type in which he kept his patients from three to six hours. In this manner he avoided all possibility of *Auspumpung.*

CALCULATION OF FOOD

In the season of 1911 it was impossible to weigh and analyze each kind of food as was done in 1912. The patients, however, were under the personal charge of the head nurse who had assisted in metabolism experiments for three years. Milk and cream, the chief articles of the diet, were carefully measured and were analyzed from time to time. Lactose was also measured in a specially graduated cup. The other foods were given in standard portions which were checked up at frequent intervals. Calculations were based on analyses made in this clinic and on the tables of Atwater and Bryant.[25] In reckoning the calories of the food the factors of Rubner, 9.3 for fat and 4.1 for protein and carbohydrate, were used.

In 1912, it was possible to secure the services of three nurses for the typhoid cases alone. In this year cereals which had been analyzed were weighed raw and each portion separately cooked. Bread, eggs, ice-cream and a few other foods were analyzed and weighed out in the moist condition, and milk and cream were measured in graduates.

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* A preliminary report will appear shortly in the Jour. Am. Med. Assn.

24. Rolly and Rosiewitz: Deutsch. Arch. f. klin. Med., 1911, ciii, 58; Rolly: Bemerkungen zu dem Aufsatz von F. G. Benedict, Ein Universalrespirationsapparat, ibid., 1912, cvii, 593.

25. Atwater and Bryant: The Chemical Composition of American Food Materials, U. S. Dept. of Agric., Bull. 28, Revised Edition, 1906.

NORMAL CONTROLS

Twelve fasting experiments on three normal controls were made with the Benedict apparatus and the results grouped in Table 2. All the controls were men thoroughly familiar with the apparatus. D. B. was a physician aged 30, 5 feet 9¾ inches in height. F. C. G. was a chemist aged 29, 5 feet 8½ inches in height. Louis M., a barber, was the typhoid patient mentioned above, who returned five months after his attack in order to serve as a control. His type of respiration on the machine remained abnormal and it was necessary to use the respiratory quotient of a calorimeter experiment to obtain the caloric value of the oxygen.

The heat production of these controls has been calculated in two ways for purposes of comparison. In the first column use has been made of the urinary nitrogen, and the tables of Loewy[18] have furnished the caloric value of the oxygen according to the non-protein respiratory quotient. In the second column the simpler and somewhat less exact method of reckoning that the protein furnished 15 per cent. of the calories as given by Magnus-Levy[19] has been used. It will be seen that the two columns agree very closely.

The same controls served as subjects for experiments with the respiration calorimeter of the Russell Sage Institute of Pathology. The figures for the direct calorimetry and for the indirect calorimetry, using the tables of Loewy, are given in Table 3. Unfortunately the calorimeter leaked a little air in both experiments on F. C. G., and his oxygen consumption and indirect calorimetry were not determined. Table 4 gives the averages of all the calorimetric determinations by the four different methods, and shows a striking agreement between all four. Benedict[26] has repeatedly demonstrated the fact that figures obtained with his small apparatus correspond closely with those obtained with the calorimeter.

Table 5 gives the average oxygen consumption and heat production of forty-eight normal controls whose metabolism was investigated in short periods. Twenty-three of these are taken from Benedict, Bulletin 176, Table 131; four from Benedict, Bulletin 136, Table 166; nineteen from Loewy and Magnus-Levy, quoted by Benedict in Bulletin 136, Table 161. Our two normal controls, D. B. and F.C.G., have been included in the list. The tables as published by Benedict do not give the indirect calorimetry, and this has been calculated. The average respiratory quotient of Benedict's cases in Bulletin 176 is 0.834, of Loewy's and Magnus-Levy's cases, 0.781, of our cases, 0.779.

26. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Inst. of Washington, 1910, Bull. 136; A Study of Metabolism in Severe Diabetes, ibid., 1912, Bull. 176.

TABLE 2.—Basal Metabolism of Normal Controls Determined with Benedict Respiration Apparatus from Fourteen to Eighteen Hours After Last Meal

Subject, Date and Weight (kg.)	Start of Experiment	Average Pulse-Rate	Average Respiration Rate	R. Q.	Per Kg. and Min.			Cal. Per Kg. and 24 Hrs. Indirect Calorimetry	
					CO_2 c.c.	O_2 c.c.	N. of Urine, Mg.	Reckoned from Tables of Loewy, Using Urinary N	Reckoned from Tables of Magnus-Levy (15% Cal. from Protein)
D. B., Oct. 31, 1912, 75.3	9:30 a. m.	62	12	0.71	2.66	3.73	0.132	25.0	25.1
	10:35 a. m.	61	13	.77	2.69	3.48	0.132	23.5	23.7
D. B., Dec. 13, '12, 75.3	11:34 a. m.	60	12	.73	2.62	3.59	0.116	25.0	24.2
	12:14 p. m.	60	12	.74	2.93	3.97	0.116	27.6	26.8
	12:51 p. m.	62	12	.79	2.79	3.56	0.116	24.9	24.4
	1:29 p. m.	61	12	....	2.77	3.68	0.116	25.6	25.0
F. C. G., Dec. 16, '12, 56.5	11:55 a. m.	76	12	.81	3.26	4.05	0.138	27.7	27.9
	12:16 p. m.	74	13	.86	3.29	3.84	0.138	26.6	26.8
F. C. G., Dec. 17, '12, 56.5	11:32 a. m.	75	15	.78	3.24	4.15	0.107	28.2	28.3
	11:52 a. m.	71	14	.82	3.13	3.82	0.107	26.2	26.4
	12:13 p. m.	70	13	.78	2.99	3.86	0.107	26.2	26.4
Louis M., March 29, '13, 53.35. *Auspumpung*	11:11 a. m.	75	15	1.10*	4.97*	4.52	0.199	....	30.8*
	11:55 a. m.	85	17	1.10*	5.03*	4.57	0.199	....	31.1*

* Caloric value of oxygen for respiratory quotient of 0.77 as determined two days previously in respiration calorimeter used instead of the caloric values for these quotients, which are too high on account of *Auspumpung*.

TABLE 3.—Basal Metabolism of Normal Controls Determined with Respiration Calorimeter from Fourteen to Eighteen Hours After Last Meal

Subject, Date and Weight	Time of Experiment	R. Q.	Per Kg. and Min.			Calories per 24 Hours per Kilogram		Cal. per Hour per Square Meter Body-Surface
			CO_2 c.c.	O_2 c.c.	N. of Urine, Mg.	Indirect Calor-imetry	Direct Calor-imetry	
D. B., March 13, '13, 73.52	9-35-11:35	0.82	3.03	4.11	0.126	25.5	24.5	36.29
D. B., May 17, 75.51...	9:30-12:30	.83	2.84	3.41	0.116	23.4	22.7	34.60
F. C. G., March 17, 56.50	9:02-12:02	....	3.38	....	0.145	....	24.3	32.80
F. C. G., April 22, 54.87	9:45- 2:45	....	3.37	....	0.095	....	26.6	35.17
Louis M., March 26, 51.7	10:10- 4:10	.77	3.36	4.34	0.168	29.3	30.0	37.74
Average normal*......		....	....	....	....	....	....	34.20

* Average of 12 normal controls in the bed calorimeters of the Russell Sage Institute of Pathology, unpublished, and the Nutrition Laboratory in Boston, 3.44.

As a mean of these the quotient of 0.8 has been selected to give the caloric value of the oxygen. According to the table of Magnus-Levy, with a quotient of 0.8, 1 liter of oxygen represents 4.77 calories. This factor has been used for all the controls.

TABLE 4.—Normal Controls: Comparison of Atwater-Rosa-Benedict Respiration Calorimeter and Benedict Respiration Apparatus; Averages of all Experiments from Fourteen to Sixteen Hours After Last Meal

Subject	C.C. O_2 Per Kg. and Min.		Calories Per Kg. and Twenty-Four Hours			
			Direct Calorimetry Bed Calorimeter	Indirect Calorimetry		
				Calorimeter	Benedict Apparatus	
	Calorim.	Benedict.			Reckoned from Urinary Nitrogen	Reckoned from Tables of Magnus-Levy
D. B.	3.76	3.67	23.6	24.3	25.3	24.9
F. C. G....	....	3.95	25.4	....	27.0	27.2
Louis M...	4.34	4.54	30.0	27.3	....	31.0

TABLE 5.—Normal Oxygen Consumption and Heat Production: Averages of Forty-Eight Normal Controls from Various Sources Grouped According to Body-Weight

Weight, Kg.	Number of Subjects	O_2 C.C. Per Kg. and Min.			Av. Calories	
		Min.	Max.	Average	Per Kg. per 24 Hours	Per Sq. M. Body Surface per Hour
40-50	6	3.68	4.57	4.06	27.9	33.6
50-60	17	3.32	4.41	3.86	26.5	34.1
60-70	15	3.47	5.50	3.71	25.5	34.5
70-80	4	3.15	3.73	3.48	23.9	34.1
80-90	6	2.76	3.60	3.16	21.7	32.3

The subjects have been grouped according to body-weight, and it will be seen that the calories produced per kilogram, as is well known, decrease as the weight increases. On the other hand, there is a striking uniformity in the column showing calories per square meter of body-surface, as Rubner demonstrated many years ago. The surface area was calculated from Meeh's formula, using the body-weights of 45, 55, 65, etc., and using the average heat production of individuals of the same weight group. The subjects between 80 and 90 kg. show an unexpectedly low average metabolism, and it would be interesting to see if a larger number of controls of this weight would give the same results. Seven normal controls have been studied in the respiration calorimeter of the Russell Sage Institute of Pathology, and they have been averaged with five normal controls from figures published by Benedict.[27] The average heat production per square meter of body-surface per hour is 34.2 calories with a variation 10 per cent. above or 10 per cent. below this point. The results will shortly be published in detail.

It is more accurate to express the results of respiration experiments in calories per square meter of body-surface, since it then becomes possible to compare individuals of different weights. In the tables of respiration experiments, both calculations are given, but the final comparisons are made according to body-surface. For the clinicians' purposes calculations based on a twenty-four-hour period are best, but from the point of view of the experimenter the one-hour period is preferable since it is much closer to the actual experimental time of all types of apparatus, except a few of the large respiration cabinets. The habit of comparing results in cubic centimeters of carbon dioxid and oxygen per kilogram and minute has nothing to recommend it except the fact that previous observers have used the method and have made it necessary to follow their example for purposes of comparison.

HISTORIES OF PATIENTS

Joseph T., weight 58.4 kg., aged 35, of medium build. Typhoid fever of severe type. Admitted Oct. 13, 1911, the twenty-fifth day of disease. Discharged November 21. Fever lasted forty-one days, no relapse. Vomited once; otherwise no gastric or intestinal disturbance. Not restless. See table for clinical data.

John H., colored, weight 54.3 kg., aged 27, of medium frame. Typhoid fever, moderately severe type. Admitted Oct. 23, 1912, on sixteenth day of disease. Discharged December 28. Fever lasted thirty-three days. Took food fairly well. Not delirious or restless. See table for clinical data.

Frank W., weight 54.5 kg., aged 27, short and stout. Typhoid fever of severe type. Admitted Nov. 23, 1911, tenth day of disease. Discharged February 8. Original fever lasted thirty-two days. A relapse of moderate severity began on the forty-seventh day and lasted to the sixty-first day. Glycosuria appeared on the fifteenth day, lasting till the twenty-first day. No history of diabetes in patient's family or in himself. Severe sore throat, January 7. Vomited at start; could not take milk with lactose. Soon began to take food better, but barely reached 3,000 calories a day until temperature was falling to normal. No diarrhea or tympanites. Not restless. See table for clinical data.

27. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Inst. of Washington, 1910, Bull. 136.

Davide G., weight 56.1 kg., aged 27, short and muscular. Typhoid fever of severe type. Admitted Oct. 27, 1911, twenty-first day of disease. Discharged December 5. Fever lasted forty days, no relapse. Ugly tempered. Took food poorly in early stage. Appetite began to improve November 1. No diarrhea. Not restless.

Twenty-seventh day of disease, T. 101.2-104; 63 food calories per kilogram. Twenty-eighth and twenty-ninth days, T. 99.8-103.2; 72-73 calories per kilogram. Thirtieth day, T. 99.0-102; 71 calories per kilogram. Thirty-first day, T. 99.2-101.4; 64 calories per kilogram. Thirty-second day, T. 99.2-100.4; 76 calories per kilogram. Thirty-third day, T. 99.5-101.2; 80-89 calories per kilogram. Thirty-seventh day, T. 98.6-100.2; 78 calories per kilogram.

John C., weight 62.3 kg., build, medium, slight. Typhoid of severe type. Admitted to medical service Aug. 22, 1911, probably twenty-eighth day of disease (transferred from Psychopathic Pavilion). Discharged to Psychopathic Pavilion October 5. Original fever lasted about fifty days. No relapse. Looked sick. Diarrhea on admission, none later. No tympanites. Took food well at the start — not so well later. Gained 1 pound a day from thirty-first to thirty-eighth days. Slept greater part of time. Mental condition recorded as dull and stupid.

Thirty-fifth day of disease, T. 100.0-102; 54 food calories per kilogram. From the thirty-sixth to the thirty-eighth day, T. 99.2-104.7; from 63 to 71 calories per kilogram. Thirty-ninth day, T. 100.2-103.2; 53 calories per kilogram.

Abe B., weight 74.8 kg., aged 20, short and stout. Typhoid fever of mild type. Admitted to genito-urinary service for gonorrheal epididymitis, Oct. 29, 1911, probably the twenty-first day of the typhoid. Transferred to medical service on the thirty-second day. Discharged December 19. Long, low fever uninfluenced by epididymitis, temperature rising to 100.6 the day before discharge on the seventy-second day. Nausea only twice. No diarrhea. Not restless.

Thirty-seventh day, T. 99.0-101.0; 55 food calories per kilogram. Thirty-eighth day, T. 99.4-100.3; 46 calories per kilogram. Thirty-ninth day, T. 98.4-101.2; 64 calories per kilogram. From the twentieth to the forty-second days, T. 99.1-101.6; 57-64 calories per kilogram. Forty-third day, T. 98.2-100.7; 48 calories per kilogram.

Anton V., weight 62.3 kg., aged 32, tall and spare. Typhoid of severe type. Admitted Aug. 13, 1911, the twenty-eighth day of disease. Discharged October 11. Original fever lasted thirty-four days. Patient was afebrile for six days and then had relapse of eleven days' duration. Complicated by phlebitis September 4. Took food well. No gastric or intestinal disturbance. Not restless.

Thirty-third day of disease, T. 99.2-100.6; 40 food calories per kilogram. Convalescence, from the first to the third day, from 51 to 58 calories per kilogram. Relapse, first to sixth days, T. 97-104.2; from 56 to 61 calories per kilogram. Seventh day, T. 98.8-101.8; 47 calories per kilogram. Eighth day relapse to ninth day convalescence, from 71 to 110 calories per kilogram. Tenth day, 108 calories per kilogram. Eleventh to twentieth days, from 86 to 117 calories per kilogram. Twenty-first day food not measured; approximately 100 calories per kilogram.

Frank R., weight 61.6 kg., aged 18, of medium build. Typhoid fever of severe type. Admitted Oct. 2, 1911, twenty-first day of disease. Discharged November 22. Original fever lasted twenty-eight days. No relapse. No gastric or intestinal disturbance. Not restless.

Charles S., weight 57.7 kg., aged 21, of medium height. Typhoid fever of moderate severity. Admitted Aug. 5, 1911, the third day of disease. Discharged convalescent, October 13. Original fever lasted twenty-one days. Relapse on eighteenth day, fever continuing to fifty-first day. Last experiment on twen-

TABLE 6.—Clinical Data, Frank W.

Day of Disease	Temperature		Food					Urine, N.	Feces, N.	N, Balance	Urine, Glucose*	Urine, Kreatinin	Body - Wt., kg.
	Min.	Max.	Total Cal.	Cal. per Kg.	Fat, Gm.	Carb., Gm.	N., Gm.						
11	103.0	104.4	2,140	39	105	160	14.0	11.0	1.4†	+1.6	0.0	....	
12	102.0	104.0	2,850	52	139	290	14.1	14.1	1.4†	—1.4	....	1.01	54.5
13	102.0	105.4	2,100	39	110	192	11.2	16.3	1.1†	—6.2	±	1.4	
14	103.2	104.4	1,910	35	67	276	5.9	18.5	1.4	—14.0	±	1.67	
15	102.4	104.0	3,380	62	170	334	16.9	15.2	1.4	+0.3	7.7	1.28	54.5
(Early Steep-Curve Period)													
16	102.2	103.0	2,510	46	125	267	9.7	14.3	1.4	—6.0	8.0	1.27	53.6
17	101.2	103.0	3,700	68	199	343	17.4	18.9	1.4	—2.9	15.5	1.35	
18	101.0	103.0	3,860	71	192	397	17.2	19.9	1.4	—4.1	31.6	1.59	
19	100.4	103.0	3,700	69	190	373	15.4	17.9	1.4	—3.9	79.6	1.29	
20	99.4	102.4	2,130	40	202	173	17.0	13.8	1.0	+2.2	11.0	.99	
21	99.2	103.6	2,670	50	183	128	17.1	19.9	1.0	—3.8	8.5	1.17	
22	100.0	103.0	1,860	35	139	65	11.4	12.9	1.0	—2.5	0.0	1.05	
(Late Steep-Curve Period)													52.7
23	98.0	101.0	2,860	54	200	131	17.9	18.8	.8	—1.7	0.0	1.11	
24	98.4	100.8	3,980	76	282	202	20.5	16.5	.8	+3.2	0.0	....	52.5
25	98.8	101.8	4,100	78	288	218	20.6	14.3	.8	+5.5	1.6	1.12	
26	98.6	101.4	3,750	71	265	195	19.0	11.9	.8	+6.3	1.6	....	
27	98.4	100.4	3,740	71	257	203	20.1	12.3	.8	+7.0	1.8	1.06	53.9
28	98.3	101.3	4,100	76	288	215	21.1	17.4	.8	+2.9	1.6	1.29	
29	98.4	100.4	3,910	73	266	221	20.6	13.9	2.1†	+4.1	1.2	1.01	53.9
30	98.2	100.2	3,670	68	249	206	19.9	....	.....	....	....	.6	
31	98.6	100.0	4,000	74	275	237	18.7	12.0	1.9†	+4.8	1.1	.9	54.3
(Convalescence)												1.21	
1	98.0	99.2	3,990	73	275	224	20.1	14.3	2.0†	+3.8	1.6	.....	
2	98.2	99.8	3,860	71	247	276	17.2	12.2	1.7†	+3.3	0.0	.89	
3	98.0	98.8	3,930	72	248	294	16.0	9.1	1.6†	+5.3	1.0	.88	
4	98.0	99.2	4,590	83	306	301	20.3	12.3	2.0†	+6.0	1.5	1.34	55.1
5	98.0	99.2	2,300	42	151	151	10.5	9.8	1.0†	—0.3	0.0	....	
6	97.7	99.1	3,700	68	258	208	17.7	10.5	1.8†	+5.5	1.4	1.05	54.8
7	98.2	98.8	2,710	49	180	160	14.5	8.7	1.4†	+4.3	0.0	.94	
8	98.0	99.4	3,840	71	241	274	18.3	10.0	1.8†	+6.5	0.0	1.11	54.1

* In this column, ± means trace.
† Feces nitrogen assumed to be 10 per cent. food nitrogen, in cases in which feces were not analyzed.

tieth day. Severe recurrent epistaxis from the twenty-sixth to the thirty-eighth day caused a suspension of the observations. Took food well. No diarrhea or tympanites. Not restless.

Tenth day of disease, T. 99.5-100.8; 75 food calories per kilogram. Eleventh day, T. 99.5-101; 67 calories per kilogram. Twelfth day, T. 99.5-101.4; 49 calories per kilogram. Thirteenth and fourteenth days, T. 98.4-100.0; from 61 to 76 calories per kilogram. Fifteenth day, T. 99.8-102.7; 77 calories per kilogram. Sixteenth to eighteenth days, T. 96.8-99.8; from 75 to 78 calories per kilogram. One day relapse, T. 100.8-102.8; 54 calories per kilogram. Second day, T. 102-103; 67 calories per kilogram.

William M., weight 67.3 kg., aged 32, of moderate height, rather stout. Typhoid moderately severe. Admitted October 16, 1911, the twentieth day of disease. Discharged November 9. Complication serofibrinous pleurisy. Original fever lasted thirty-eight days. No relapse. Good appetite. No gastric disturbance or diarrhea. Not restless.

Twenty-third day of disease, T. 102-103; 89 food calories per kilogram. Twenty-fourth day, T. 100.5-103; 92 calories per kilogram. Twenty-fifth day, T. 100.2-103; 83 calories per kilogram. Twenty-sixth to thirtieth days, T. 99.2-102; from 68 to 87 calories per kilogram. Thirty-first day, T. 99-101; 76 calories per kilogram. Thirty-second day, T. 98.8-101; 66 calories per kilogram.

Archie C., weight 48.2 kg., aged 35, tall and thin. Typhoid of mild type. Admitted to alcoholic service, September 24, 1911, the sixth day of disease. Transferred to medical service, September 26. Discharged, November 8. Fever lasted thirty-one days. No relapse. Patient irrational at times, at first probably from alcoholism. Suffered from severe nausea and vomiting early in disease, probably from alcoholic gastritis. Slight diarrhea to nineteenth day.

Seventeenth day, T. 101-103; 87 food calories per kilogram. Eighteenth to twenty-fourth days, T. 99.8-103.5; from 55 to 83 calories per kilogram. Twenty-fifth day, T. 99.4-102.2; 102 calories per kilogram.

Hugh K., weight 66.8 kg., aged 32, large and muscular. Typhoid fever of very severe type. Admitted Sept. 29, 1911, probably fifth day. Discharged, November 9. Original fever lasted thirty days. No relapse. Took food extremely well. No gastric or intestinal disturbance. Was given whisky till October 10. Not restless.

Twenty-first day of disease, T. 101.2-103; 81 food calories per kilogram. Twenty-second and twenty-third days, T. 99.8-102; from 73 to 92 calories per kilogram. Twenty-fourth day, T. 99-101; 92 calories per kilogram.

Salvatore L., weight 43.9 kg., aged 17, a thin, growing boy. Typhoid fever of mild type. Admitted, Sept. 5, 1911, seventh day of disease. Discharged, October 11. Original fever lasted eleven days. Patient was afebrile for five days and then had a relapse of seven days' duration. Patient suffered from slight nausea at times but for the most part took food well. No restlessness.

Convalescence first to sixth days, from 37 to 76 calories per kilogram in food. Relapse, first and second days, T. 97.6-102; 76 calories per kilogram. Third day, T. 97.8-102; 141 calories per kilogram. Fourth day, T. 98.3-102; *170 calories per kilogram.* Fifth day, T. 98.2-101.6; 125 calories per kilogram. Second convalescence, first to fourth days, from 86 to 94 calories. Fifth to ninth days, from 140 to 166 calories per kilogram.

Alexander C., weight 58.9 kg., aged 36, of medium frame. Typhoid fever, severe type. Admitted July 14, 1911, eighth day of disease. Discharged, October 3. Original fever lasted ten days followed by relapse of thirty days' duration. Complications on admission, severe bronchitis with pleurisy. Took food poorly. Patient suffered from tympanites until well along in disease. Was incontinent of urine and feces much of the time. Irrational at times.

Sixth to tenth days of convalescence, from 86 to 89 food calories per kilogram. Eleventh day, 104 calories per kilogram. Twelfth day, 89 calories per kilogram. Thirteenth to seventeenth days, from 83 to 113 calories per kilogram. Eighteenth day, 78 calories per kilogram. Nineteenth day, 112 calories per kilogram. Twentieth day, 113 calories per kilogram.

Louis M., weight 48.6 kg., aged 22, short and slight. Typhoid fever. Admitted Sept. 7, 1912, the ninth day of the disease. Discharged convalescent, October 30. Type of disease severe, fever lasting twenty-eight days. No relapse. Took food well. No diarrhea or gastric disturbance. Returned in March, 1913, to serve as a normal control.

Seventh to eleventh days of convalescence, from 64 to 69 food calories per kilogram.

Hugo T., weight 63.2 kg., aged 17, tall and muscular. Typhoid fever of severe type. Admitted Aug. 28, 1912, recorded as sixth day of disease but uncertain. Discharged Oct. 25, 1912. Fever lasted to thirty-second day. Delirious early. Did not take food well until steep-curve period. In convalescence took up to 7,000 calories a day. No diarrhea or tympanites. Not restless.

Twenty-first day of disease, T. 101.2-103; 81 food calories per kilogram. Twenty-second and twenty-third days, T. 99.8-102; from 73 to 92 calories per kilogram. Twenty-fourth day, T. 99-101; 92 calories per kilogram.

TABLE 7.—Clinical Data, John H.

Day of Convalescence	Total Calories	Cal., Per kg.	Food			Urine, N.	Feces, N.†	N, Balance	Body Wght., kg.
			Fat, gm.	Carb. gm.	Nitrogen, gm.				
2	3,144	58	265	107	9.7	8.9	1.0	—0.2	
3	2,500	46	179	150	7.9	8.5	0.8	—1.4	54.3
4	4,220	78	216	430	17.2	9.2	1.7	+6.3	54.4
5	4,100	74	219	413	14.6	9.2	1.5	+3.9	55.1
6	3,550	64	181	353	16.2	9.2	1.6	+5.4	55.6
7	2,950	53	26	587	11.9	8.7	1.2	+2.0	55.8
8	3,010	53	26	600	11.1	7.0	1.1	+3.0	56.4
9	3,020	53	26	612	10.3	5.9	1.0	+3.4	56.4
10	2,950	52	26	594	10.3	6.9	1.0	+2.4	56.6
11	3,202	56	129	425	10.2	6.1	1.0	+3.1	56.8
12	2,980	52	26	604	10.3	7.7	1.0	+1.6	57.6
13	3,140	55	119	434	9.8	7.0	1.0	+1.8	57.5

† Assumed 10 per cent. of food N.

The tables of clinical data, Tables 6 to 8, need little explanation. In three cases, John H., Frank W. and Joseph T., the clinical and experimental data have been given in full. In the rest of the cases the lengthy tables have been abbreviated as much as possible. The days of the disease are numbered from the time when the patient first began to feel definitely sick and not from the time he first took to bed, since many typhoid patients take to bed only when the disease is well advanced. The febrile period has been divided, somewhat arbitrarily perhaps, in order to make it possible to compare the different cases. No observations were made in the period of ascending temperature ("First Week"), and only two in the continued temperature period ("Second Week"). During the so-called early steep-

TABLE 8.—Clinical Data, Joseph T.

Day of Disease	Min. Temp.	Max. Temp.	Food, Total Cal.	Food, Cal. per Kg.	Food, Fat, Gm.	Food, Carb., Gm.	Food, N., Gm.	Urine, N.	Feces, N.*	N, Balance	Body Wght., Kg.
(Early Stee	p-Curve Per	iod)									
30	101.2	103.0	1,940	33	115	165	7.7				
31	101.0	102.4	2,200	38	141	156	9.7				
32	101.0	103.0	3,820	65	209	355	16.6	12.3	1.7	+ 2.6	58.4
33	100.4	102.2	3,530	60	219	256	17.5	16.3	1.8	— 0.6	
34	99.8	103.0	4,080	70	135	614	12.2				
35	100.0	102.2	4,350	74	188	525	17.2	....	....	....	58.9
(Late Steep	-Curve Peri	od)									
36	99.4	102.0	3,940	67	172	474	15.5				
37	99.2	101.8	4,450	75	193	534	18.2	....	....	....	58.9
38	99.4	101.8	4,120	70	182	491	16.2				
39	99.0	100.2	5,330	90	192	741	19.8	....	....	....	59.2
40	98.4	100.0	3,690	62	158	447	15.1				
(Convale	scence)										
1	98.0	99.2	6,240	05	319	655	23.0				
2	98.2	99.0	4,970	82	252	523	18.8	....	....	....	60.7
3	98.2	99.0	5,700	94	272	615	25.2	11.4	2.5	+11.3	
4	98.0	99.0	5,380	87	265	598	18.0	9.4	1.8	+ 6.8	61.8
5	97.8	99.1	5,360	87	267	593	17.3				
6	98.0	99.2	5,500	89	292	518	25.7	....	....	....	61.8

* 10 per cent. of food nitrogen.

curve period ("Third Week"), when the temperature made sharp remissions but never touched normal, twenty-one experiments were recorded. In the late steep-curve period ("Fourth Week"), with a temperature dropping to normal almost every morning, there were thirty-three observations; five observations were made during a relapse. During convalescence, the days are numbered from the first day of normal temperature, and the results grouped in actual weeks

TABLE 9.—RESPIRATION—

Day of Disease	Start of Experiment	Recent Food				During Experiment		
		Time	Fat, gm.	Carb., gm.	Prot., gm.	Temp.	Average Pulse	Average Resp.
(Contin.	Temp.)							
11	p. m.	9:00 a.m.	8	12	15			
	2:38†	1:30 p.m.	7	11	14	103.6	111	27
14	....	9:00 a.m.	12	33	2			
	2:27	1:00 p.m.	..	70	..	103.2	112	26
(Early Steep-	Curve Period)							
16	....	9:00 a.m.	25	42	3			
	2:57	11:00 a.m.	..	70	..	103.0	100	22
18	....	12:00 m.	37	42	25			
	3:17	2:30 p.m.	4	12	2	102.8	104	24
21	....	12:00 m.	33	29	24			
	3:41	2:30 p.m.	17	10	7	103.0	104	18
22	3:06	9:00 a.m.	17	10	7	102.8	115	17
(Late Steep-	Curve Period)							
24	....	12:00 m.	37	28	25			
	3:06	2:30 p.m.	17	10	7	100.2	105	16
28	....	12:00 m.	43	30	26			
	3:25	2:30 p.m.	23	12	7	99.8	118	19
30	....	12:00 m.	43	30	26			
	2:33	2:20 p.m.	17	10	7	99.0	107	18
§	3:30	....	..	...	..	99.0	107	16

* Unusually low total nitrogen in urine on this day. † First experiment with this patient.

of seven days. In 1911 the twenty-four-hour specimens of urine were collected by the head nurse personally, preserved with thymol and chloroform and analyzed the day the specimen ended. In 1912 each voiding was kept separate and preserved in an ice-box with the addition of toluene. The voidings for the whole day were either united or analyzed separately if it were necessary to fractionate the urine. Nitrogen determinations were made by the Kjeldahl method, glucose by the methods of Stanley R. Benedict[28] and creatinin by Folin's[29] method. In 1912 these analyses were made by Mr. Gephart. The cases in which the stools were analyzed, Charles S. and Frank R., have been described in a previous publication.[2] In all other cases the fecal nitrogen was estimated at 10 per cent. of the food nitrogen. The patients were weighed as frequently as possible by means of the scales previously described.[30]

—EXPERIMENTS, FRANK W.

Per Kg. and Min.		R. Q.	Calculated Heat Production					Food for 24 Hours, Cal. Per Kg.
			Per Cent. Calories from			Cal. Per Sq. M., Per Hr.	Cal. Per Kg. Per 24 Hours	
CO_2, c.c.	O_2, c.c.		Prot.	Fat	Carb.			
4.35	5.48	0.79	13.7?*	....	...	48.3	37.6	39
4.48	5.22	.86	25	29	46	46.0	35.8	35
4.10	5.33	.77	19	65	16	46.1	35.9	46
4.93	5.71	.86	25	28	47	50.0	39.2	71
4.25	4.89	.87	29	23	48	42.5	33.5	50
3.86	5.01	.77	19	64	17	42.8	33.7	35
3.94	5.10	.77	24	61	15	43.3	34.2	76
4.67	5.71	.82	22	46	32	49.5	38.8	76
4.63	4.87	.95	15‡	..	..	44.2	34.7	68
3.92	4.58	.86	15‡	..	..	40.7	3.19	

‡ Estimated. § *Auspumpung* in all subsequent experiments.

The calculation of the urinary nitrogen for the fifteen-minute period is necessarily somewhat inaccurate; no method is entirely satis-

28. Benedict, Stanley R.: The Detection and Estimation of Glucose in Urine, Jour. Am. Med. Assn., 1911, lvii, 1193.

29. Folin, O.: Beiträge zur Chemie des Kreatinins und Kreatins im Harne, Ztschr. f. Physiol. Chem., 1904, xli, 223.

30. Coleman: Diet in Typhoid Fever, Jour. Am. Med. Assn., 1909, liii, 1145.

TABLE 10.—Respiration Experiments,—

Day of Disease	Start of Experiment	Recent Food				During Experiment		
		Time	Fat, gm.	Carb., gm.	Prot., gm.	Temp.	Average Pulse	Average Resp.
Joseph T.:								
(Early Steep-	Curve Period)							
31	....	12 m.	17	24	11			
	3:02 p. m.	2:45 p.m.	18	16	8	102.2	83	15
(Late Steep-	Curve Period)							
36	2:51 p. m.	12:00 m.	42	59	29	101.4	83	16
	4:09 p. m.	......	..	..	..	102.0	78	14
38	2:17 p. m.	12:00 m.	48	66	35	101.0	83	18
	3:41 p. m.	2:36 p.m.	..	125	..	101.8	85	21
39	....	12:00 m.	38	112	21			
	3:46 p. m.	2:16 p.m.	..	125	8	100.2	80	17
	4:22 p. m.	......	..	..	..	100.2	78	19
(Convales	cence)							
2	....	9:00 a.m.	38	47	17			
	3:21 p. m.	11:00 a.m.	..	125	..	99.0	73	16
	4:17 p. m.					99.0	74	15
4	....	9:00 a.m.	46	70	21			
	3:19 p. m.	11:00 a.m.	..	125	..	98.3	70	17
	4:17 p. m.‡	......	..	..	..	98.3	70	17
5	....	11:00 a.m.	..	125	..			
	4:04 p. m.	1:00 p.m.	46	115	15	99.2	93	16
6	....	12:00 m.	43	91	39	..	..	..
	3.47 p. m.	2:00 p.m.	18	69	8	98.2	81	15
		......	..	..	..	98.2	82	16
John H.:								
(Convales	cence)							
3	10:41 a. m.*	4:30 p.m*	62	28	16	98.5	66	15
11	....	5, 6, 7, 8, 9,						
	10:13 a. m.	10:00 a.m.	0	28	3	98.4	71	15
	10:49 a. m.	......	..	..	..	98.4	76	15
11	....	11, 12, 1, 2,						
	4:00 p. m.	3:00 p.m.	11	28	3	98.4	82	10
13	10:10 a. m.	10:00 a.m.	0	28	3	98.6	77	12
	10:54 a. m.†	......	..	..	..	98.6	74	12
	3:12 p. m.	3:00 p.m.	11	28	3	98.6	82	12
	4:03 p. m.	......	..	..	..	98.6	78	12

* Eighteen hours after last food.

† Seventeen-minute period.

Per Kg. and Min.		R. Q.	Calculated Heat Production					Food for 24 Hours, Cal. Per Kg.
			Per Cent. Calories from			Per Sq. M. Per Hour	Cal. Per Kg. Per 24 Hours	
CO_2, c.c.	O_2, c.c.		Prot.	Fat	Carb.			
4.07	5.42	0.75	..	..	..	48.3	36.7	38
4.07	5.32	.77	..	..	..	47.8	36.2	67
4.02	5.13	.78	..	..	..	46.3	35.1	
4.53	5.36	.85	..	..	..	49.2	37.2	70
4.56	5.08	.90	..	..	..	47.1	35.8	
4.03	4.57	.88	..	..	..	42.1	32.0	90
3.86	4.04	.96	..	..	..	38.1	28.9	
3.74	4.25	.88	..	..	..	39.6	29.8	82
3.77	4.03	.94	..	..	..	38.1	28.6	
3.95	3.97	1.00	14	0	86	38.9	29.1	87
3.55+	3.55—	1.02	15	0	85	35.0	26.1	
4.74	5.59	.85	..	..	..	52.0	38.9	87
4.98	6.16	.81	..	..	..	56.7	42.4	89
4.95	5.30	.93	..	..	..	49.0	37.6	
2.83	3.92	.72	16	83	1	33.7	26.3	46
4.11	4.05	1.02	10	0	90	38.1	29.3	52
4.24	3.82	1.11	10	0	90	36.4	28.0	
4.52	5.06	.89	8	31	61	46.3	35.6	
4.51	4.09	1.10	11	0	89	39.2	29.9	55
4.33	4.23	1.03	11	0	89	40.1	30.6	
4.78	4.56	1.05	10	0	90	43.4	33.1	
4.95	4.90	1.01	9	0	91	46.3	35.4	

‡ Twenty-minute period.

Day of Disease	Start of Experiment	Recent Food				During Experiment		
		Time	Fat, gm.	Carb., gm.	Prot., gm.	Temp.	Average Pulse	Average Resp.
Charles S.:								
(Early Steep-	Curve Period)							
10	....	12:30 p.m.	33	75	25			
	3:16 p. m.	2:30 p.m.	..	125	..	99.4	66	30
	3:57 p. m.	....	..	...	..	99.4	66	19
12	....	7:00 a.m.	18	70	10			
	11:41 a. m.	9:00 a.m.	13	52	8	100.2	58	18
	1:01 p. m.	1:35 p.m.	12	53	2	100.2	61	..
	2:37 p. m.	....	..	...	..	100.2	61	18
(Late Steep-	Curve Period)							
15	....	12:00 m.	58	132	47			
	3:25 p. m.	2:30 p.m.	13	52	8	101.2	64	16
	4:06 p. m.	....	..	...	..	101.2	65	17
(Relapse)								
20	....	6:45 p.m.	13	32	8			
(Second Day	of Relapse)							
	9:30 a. m.	7:00 a.m.	2	43	2	100.0	74	21
	10:35 a. m.	9:55 a.m.	12	53	2	100.0	72	19
	12:10 p. m.	....	..	...	..	100.2	78	17
William M.:								
(Early Steep-	Curve Period)							
23	....	12:00 m.*	58	119	42			
	4:11 p. m.	2:30 p.m.	18	30	8	102.2	89	17
24	....	12:00 m.*	74	99	45			
	3:42 p. m.	2:30 p.m.	35	78	14	102.8	97	17
25		12:00 m.*	72	130	45			
	2:36 p. m.	2:29 p.m.	25	95	12	101.5	92	17
	3:27 p. m.	....	..	...	..	102.0	90	14
(Late Steep-	Curve Period)							
31	....	9:00 a.m.	67	76	31			
	2:41 p. m.	12:00 m.*	64	93	49	100.0	97	14
	3:31 p. m.	....	..	...	..	100.0	95	16
	4:31 p. m.	....	..	...	..	100.2	90	15
32	9:00 a. m.	9:00 a.m.	35	68	14			
	2:52 p. m.	12:00 m.	73	121	52	100.3	91	16
Archie C.:								
(Early Steep-	Curve Period)							
17	....	11:45 a.m.	28	24	23			
	3:47 p. m.	3:07 p.m.	..	125	..	102.7	100	22
25	....	12:00 m.	44	82	27			
	4:22 p. m.†	2:30 p.m.	6	50	3	100.6	94	15
Hugh K.:								
(Early Steep-	Curve Period)							
21	....	12:00 m.	43	71	19	102.8	106	14
24		12:00 m.	65	96	44			
	3:23 p. m.	2:30 p.m.	..	75	..	100.4	109	18

* Whisky, 15 c.c., with noon meal.

Per Kg. and Min.		R. Q.	Calculated Heat Production		Food for 24 Hours, Cal. Per Kg.	Body-Weight, kg.
CO_2, c.c.	O_2, c.c.		Cal. per Sq. M. per Hour	Cal. Per Kg. Per 24 Hours		
4.41	4.82	0.92	44.8	34.1	75	
4.44	4.83	0.92	44.8	34.1		
3.94	4.47	0.88	41.2	31.4	49	
3.87	4.23	0.91	39.1	29.9		
4.02	4.46	0.90	41.2	31.4		
4.41	4.78	0.93	44.4	33.8	77	57.7
4.49	5.04	0.89	46.5	35.4		
3.89	4.70	0.83	42.5	32.4	67	58.6
3.86	4.76	0.81	43.2	32.8		
4.11	4.67	0.88	42.8	32.6		
4.56	5.09	0.90	49.2	35.8	89	
5.15	5.55	0.93	54.2	39.4	92	67.3
4.66	4.91	0.95	48.3	35.0	83	68.2
4.85	5.09	0.95	50.0	36.3		
4.93	5.16	0.96	51.0	36.8	76	68.6
4.86	5.04	0.96	50.2	36.2		
4.60	4.71	0.98	46.9	33.8		
4.49	4.77	0.94	47.1	34.0	66	69.3
4.38	5.33	0.82	44.8	36.4	87	
4.56	4.96	0.92	43.6	35.1	102	49.1
5.18	5.73	0.90	55.4	40.1	81	66.9
4.99	5.36	0.93	52.1	38.0	92	67.0

† Nine-minute period.

factory. A few well-trained patients were able to void every two hours, and the calculations are based on such fractional specimens. In most cases the twenty-four-hour specimen was used because it

TABLE 12.—

Day of Disease	Time After Last Meal, Hrs., Min.	Temperature During Experiment	Per Kg. and Min.	
			CO_2, c.c.	O_2, c.c.
Salvatore L.:				
(Last Day of	Fever)			
10	2-57	99.6	4.57	6.10
	3-46	99.6	4.48	6.16
(Relapse)				
4	1-23	102.2	6.62	6.32
	1-57	102.2	6.37	6.53
5	3- 7	100.2	5.47	6.34
	0-31	100.2	5.37	5.83
	1-17	100.2	5.85	5.81
(Second Con	valescence)			
6	1-58	98.2	6.43	6.12
7	2-39	98.4	5.70	5.98
	0.43	98.4	6.17	6.06
	1-37	98.0	6.01	6.27
9	0-41	98.0	6.12	5.87
	1-20	98.0	6.05	5.65
John C.:				
(Early Steep-	Curve Period)			
35	0-15	101.0	3.38	4.30
39	7-35	103.2	3.36	4.71
Abe B.:				
(Late Steep-	Curve Period)			
37	3- 0	100.2	3.75	3.95
	3-49	100.5	3.88	4.14
39	1-05	99.2	5.77	6.56
	1-54	99.4	5.70	6.22
43	1-26	99.6	3.98	4.09
	2- 0	99.8	3.82	3.82
Anton V.:				
(Late Steep-	Curve Period)			
33	2-51	100.0	3.69	4.55
(Convales	cence)			
3	2-33	98.4	3.35	3.89
	1-30	98.4	3.37	3.70
	3-28	98.4	3.28	3.82
(Relapse)				
7	7-56	101.6	3.80	4.65
	0-49	101.8	4.32	5.41
(Second Con	valescence)			
10	2–28	98.0	4.62	4.69
	3-43	98.0	4.71	4.55
	4-56	98.0	3.95	4.06
21	3-42	98.0	4.64	4.81

seemed fair to assume that with patients on a liberal diet of moderate nitrogen content, fed at frequent intervals, the protein metabolism would not vary greatly from hour to hour.

In most of the tables of the respiration experiments (Tables 9 to 11), the composition of all food administered within the five or six hours preceding the observations with the Benedict machine has been

—Respiration Experiments

R. Q.	Heat Production		Food for 24 Hours, Cal. Per Kg.	Weight
	Cal. Per Kg. Per 24 Hrs.	Cal. Per Sq. M. Per Hour		
.75	41.4	49.5	73	43.9
.73	41.5	49.6		
1.04	48.7	58.3	170	44.3
.97	46.7	55.8		
.86	43.9	52.5	125	
.92	40.9	49.2		
1.01	43.1	51.7		
1.05	44.0	53.5	149	
.95	42.7	52.1	166	46.1
1.02	43.7	53.2		
.96	44.8	54.6		
1.04	45.0	55.0	142	47.3
1.07	44.5	54.4		
.79	29.4	39.6	54	62.3
.70	31.7	42.5	53	62.7
.94	28.0	39.9	55	74.8
.95	29.2	41.7		
.88	45.9	65.8	64	
.92	43.9	62.9		
.97	29.2	41.7	48	74.5
1.00	28.1	40.1		
.81	29.8	39.9	40	62.3
.86	27.1	36.2	51	61.1
.91	26.1	34.7		
.86	26.6	35.4		
.82	32.1	46.7	47	59.8
.80	37.1	49.2		
.99	33.6	45.2	108	61.8
1.04	32.6	43.8		
.98	29.8	39.9		
.97	34.5	47.1	....	65.5

given, since different meals affect metabolism in different ways. In all cases in which the meal consisted of carbohydrate alone, nothing but lactose in lemonade was given. In the abbreviated tables (Tables

12 to 14), these data have been omitted for the sake of brevity. When the non-protein respiratory quotient was over 1, it has been assumed that carbohydrate was being converted into fat and the extra heat due to this has been calculated by the method described by Lusk,[31] in

TABLE 13.—

Day of Convalescence	Time After Last Meal, Hrs., Min.	Temperature During Experiment	Per Kg. and Min.	
			CO_2, c.c.	O_2, c.c.
Louis M.:				
7	0-46	99.2	5.75	5.58
	1-38	99.2	5.60	5.47
10	2-30	99.8	4.84	5.94
11	0-58	99.2	5.00	5.97
Hugo T.:				
24	1-18	98.2	5.11	5.54
26	14-26	97.8	3.29	4.16
	0-30	98.4	5.37	5.47
	1-16	98.4	5.03	5.06
	2- 7	98.4	5.13	5.18
32	17-30	98.0	3.42	4.11
	1- 9	98.4	3.53	4.22
Frank R.:				
3	0-43	98.0	4.96	5.10
5	3-34	98.2	4.92	4.81
Alex C.:				
6	0-42	98.4	4.64	5.03
	1-46	98.0	4.60	5.22
10	0-35	98.8	4.61	5.02
	1-38	99.2	4.30	4.70
12	1-38	99.0	4.47	4.70
18	5-42	99.0	4.48	4.62
20	0-44	99.8	4.78	5.23
	1-26	99.8	4.99	5.26
Davide G.:				
(Early Steep-	Curve Period)			
27	0-41	102.0	5.98	7.17
(Late Steep-	Curve Period)			
30	4-33	101.8	5.08	6.38
	5-23	101.8	5.04	6.53
32	2-17	100.2	4.62	5.51
	3-32	100.2	4.74	5.57
33	1-13	100.2	5.30	6.11
	2- 9	100.2	5.20	5.73
37	0-56	100.0	5.10	5.72
	1-39	100.0	4.94	5.48

which 1 liter of excess of carbon dioxid over and above the volume eliminated, when the respiratory quotient is unit, is given the value of 0.803 calories.

31. Williams, Riche and Lusk: Animal Calorimetry, Second Paper, Metabolism of the Dog Following the Ingestion of Meat in Large Quantity, Jour. Biol. Chem., 1912, xii, 358.

DISCUSSION OF RESULTS

As has been stated, the present investigation was undertaken primarily to discover the fate and general influence on metabolism of the large amount of food which is given to typhoid-fever patients in this clinic. So many factors enter into the figures appearing in the tables that it is difficult to classify the results. Moreover, most of the statements in the following discussion have been based on the averages obtained in the different periods of the disease, and it must be remembered that the limits of variation may be considerable as is shown in Figures 1 and 2.

—Respiration Experiments

R. Q.	Heat Production		Food for 24 Hours, Cal. Per Kg.	Weight, Kg.
	Cal. Per Kg. Per 24 Hrs.	Cal. Per Sq. M. Per Hour		
1.03	40.5	50.0	64	48.6
1.02	39.7	49.0		
.81	40.8	50.2	68	
.84	41.3	51.0	68	48.4
.92	39.2	52.8	87	63.2
.79	28.5	38.4	54	63.6
.98	39.4	53.1		
.99	36.5	49.2		
.99	37.3	50.2		
.83	28.2	37.9	29	62.5
.84	29.2	39.2		
.97	36.6	48.8	99	61.6
1.02	34.6	46.3	66	
.92	35.6	47.1	88	58.9
.88	36.6	48.3		
.92	35.4	47.1	86	59.5
.91	33.2	44.2		
.95	33.5	44.7	89	59.9
.97	33.1	44.7	78	
.91	36.9	50.0	113	63.6
.95	37.5	50.6		
.84	49.3	64.2	63	56.1
.80	43.3	56.3	71	55.7
.77	44.1	57.1		
.84	37.9	49.2	76	56.0
.85	38.4	49.8		
.87	42.4	55.0	88	55.2
.91	40.1	51.9		
.89	40.2	51.9		
.90	38.6	50.0		

The question of varying weights is fairly easily disposed of. The average weights of the high-calory cases investigated during the febrile period was 59.4 kg., and during convalescence 56.3 kg. The average weight of the cases of Kraus, Svenson, Grafe and Rolly which have been used for comparison was 53.7 kg. in the febrile period and 50.4 in convalescence. According to the table of normal controls this difference of about 6 kg. would make the lighter patients show an increase of only 2 or 3 per cent. in metabolism when the calories were

TABLE 14.—Respiration Experiments with "Auspumpung" (Carbon Dioxid and Respiratory Quotient Probably Too High on Account of Increasing Ventilation)

Day of Convalescence	Start of Exper.	Per Kg. and Min.		R. Q.	Cal. per Kg. for 24 Hrs.	
		CO_2, c.c.	O_2, c.c.		Produced Calculated from O_2	Food
Frank W.:						
1	2:46 p. m.	4.85	5.23	.93	36.7	73
	3:21 p. m.	5.17	5.21	.99	38.2	
4	2:38 p. m.	5.84	5.22	1.12	42.9	83
	4:22 p. m.	4.90	4.36	1.13	36.1	
6	9:49 a. m.*	4.02	4.15	.97	29.6	68
	10:22 a. m.	4.77	4.36	1.09	35.1	
	2:47 p. m.	5.67	5.11	1.10	41.7	
	3:29 p. m.	5.58	5.21	1.07	41.0	
8	9:47 a. m.*	5.44	4.69	1.16	39.9	71
Louis M.:	2:47 p. m.	6.61	5.82	1.14	48.5	
8	2:35 p. m.	6.50	6.22	1.05	45.3	65
	3:34 p. m.	6.47	5.48	1.18	40.7	
19	9:34 a. m.*	5.23	5.18	1.01	37.2	37
	11:16 a. m.	5.78	5.06	1.14	37.1	
	1:28 p. m.	5.52	4.77	1.16	35.3	
	3:15 p. m.†	5.40	4.98	1.08	36.4	
23	10:02 a. m.	5.16	4.77	1.08	34.8	40
	2:35 p. m.	6.00	4.94	1.22	36.8	
	3:41 p. m.	5.37	4.68	1.15	34.4	

* Seventeen hours after food. † Twenty minutes after period.

calculated according to body-weight. The metabolism of both the high-calory and fasting groups of typhoid cases can therefore be compared with the normals whose weights were between 50 and 60 kg. and whose heat production averaged 26.5 calories per kilogram.

Table 15 gives a direct comparison of the averages of the fasting and the high-calory cases in the different stages of the disease and convalescence. As with the normal controls, the metabolism of the fasting patients was calculated from the average oxygen consumption and the average quotient. The tables of Magnus-Levy were used, and although the protein furnished more than 15 per cent. of the total calories, it might have furnished 20 per cent. without making a difference of 1 per cent. in the caloric value of the oxygen. The calories per kilogram of the groups of high-calory cases are calculated in the same manner in one column, and next to it are given the averages of calculations made according to the more accurate method of Loewy, using the urinary nitrogen. The results of Kraus, Svenson, Grafe and Rolly have been recalculated according to calories per square meter of body-surface per hour for comparison with the high-calory cases. In the last two columns of the table a percentage comparison has been made showing that in the steep-curve period of typhoid fever the liberally fed patients have a metabolism from 36 to 40 per cent. higher than normal, while the fasting patients show an increase of 23 or 24 per cent. During convalescence the relation of the high-calory cases to normal is about the same, but the increase over the fasting patients is much greater. It is unfortunate that we have been unable to study a series of typhoid patients on low diets, but we have not felt it justifiable to withhold food. For this reason it has been necessary to use the work of others as a basis of comparison. The somewhat lower metabolism of the fasting cases of other observers may have been due to the low state of nutrition.

HEAT PRODUCTION

Febrile Period.—Since only two observations were made on the high-calory cases in the period of continued temperature, a percentage comparison of their heat production with that of the fasting cases would not be justified.

In the early steep-curve period the high-calory cases show an increase of 5 per cent. in metabolism over fasting patients, calculated according to body weight; in the late steep-curve period the increase amounts to only 2 per cent. Calculated according to surface area, the percentage increases are 11 and 13 per cent., respectively.

The absence of a greater increase in metabolism when patients were taking from 60 to 100 and more food calories per kilogram per day directly raises the question whether or not food exhibits a specific dynamic action in fever. This slight increase in metabolism is all the more noteworthy since the fasting patients were studied in the early morning when, it may be assumed, the temperature and metabolism were lowest for the day, while the high-calory patients were studied in the afternoon, usually shortly after food.

That the total metabolism of normal subjects is raised after the taking of food, and particularly after protein food, has been proved repeatedly by the work of Voit,[32] Rubner,[33] Magnus-Levy,[34] Lusk,[31, 35] Howland[36] and many others. Recent studies by Lusk[37] have shown that, in the case of protein, this is due to the stimulus of the amino-acids, and in the case of fat and carbohydrates to a plethora of fat and carbohydrate metabolites in the circulation.

These results of Lusk's confirm Rubner's observation that the specific dynamic action of a mixed diet does not represent the sum of the specific dynamic actions of the individual foodstuffs in the diet, but is considerably less than this.

TABLE 15.—Table of Averages: High-Calory Cases Compared with Normal—Grafe and—

	Number of Observations		O_2 c.c. Per Kg. and Min.		R. Q.	
	Fasting	High Calory	Fasting	High Calory	Fasting	High Calory
Normal controls, weight 50-60 kg.	17	..	3.86	....	...	....
Typhoid patients, continued temperature period	11	2	5.33	5.35	.78	0.83
Early steep-curve period	19	21	4.98	5.11	.76	0.87
Late steep-curve period	21	32	5.23	5.20	.76	0.88
Convalescence, first week	25	21	3.90	4.98	.82	0.93
Convalescence, second week	16	17	4.08	4.85	.84	1.01
Convalescence, third week	15	4	4.19	5.00	.92	0.95
Convalescence, fourth and fifth weeks	24	7	4.30	4.85	.96	0.91
Several months after recovery	10	..	3.85	....	.81	....

* Reckoned from calories per square meters body-surface.
† 12 Normal controls, weights from 50 to 83 kg. in bed calorimeters.

32. Voit, Carl: Physiologie des Stoffwechsels und der Ernährung, 1881, pp. 308, 311.

33. Rubner: Die Gesetze des Energieverbrauchs, 1902.

34. Magnus-Levy: Ueber die Grosse des respiratorischen Gasewechsels unter dem Einfluss der Nahrungsaufnahme, Arch. f. d. ges. Physiol. (Pflüger's), 1894, lv, 1.

35. Lusk: Third Paper, Metabolism After the Ingestion of Dextrose and Fat, Including the Behavior of Water, Urea and Sodium Chlorid Solutions, Jour. Biol. Chem., 1912, xiii, 27; Sixth Paper, The Influence of Mixtures of Foodstuffs on Metabolism, ibid., 1912, xiii, 185.

36. Howland: Der Chemismus und Energieumsatz bei schlafenden Kindern, Ztschr. f. Physiol. Chem., 1911, lxxiv, 1.

37. Lusk: Fifth Paper, The Influence of the Ingestion of Amino-Acids on Metabolism, Jour. Biol. Chem., 1912, xiii, 155; The Cause of the Specific Dynamic Action of Protein, The Archives Int. Med., 1913, xii, 485, and the references given in Footnote 35.

While our study of the specific dynamic action of food in typhoid fever is not yet completed, it is clear, from the figures in the tables, that, compared with fasting cases, the high-calory patients, even when taking enormous amounts of food, exhibit only a slight, if not negligible, increase in heat production, and we would suggest, tentatively, as the explanation that the stimulation of metabolism by the toxic agent of the disease is so intense that further stimulation by food is insignificant. This would be analogous to the absence of summation of the specific dynamic actions of foodstuffs in a mixed diet or to

—CONTROLS AND WITH FASTING (NÜCHTERN) LOW-CALORY CASES OF KRAUS, SVENSON,
—ROLLY

Cal. per Kg. per 24 Hours	Cal. per Kg. per 24 Hours High Calory		Cal. per Square Meters Body Surface		Percentage Increase Above* Normal Controls	
Fasting	Calculated from N. of Urine	Calculated from Av. O_2 and Av. R. Q.	Fasting	High Calory	Fasting Patients	High Calory Patients
26.5	....	....	34.2 †			
36.4	35.9	37.0	47.3	47.2	38	37
33.9	35.6	35.7	42.4	46.9	23	36
35.6	36.3	36.0	42.6	48.0	24	40
26.9	35.8	34.9	34.0	45.3	— 1	32
28.3	37.0	36.0	35.9	45.0	4	31
29.7	36.2	35.7	38.4	48.1	12	40
30.6	35.9	35.4	38.0	45.8	11	33
26.5	....	....	39.9			

the absence of specific dynamic action when the heat production is increased through subjection of a normal individual to the influence of cold.

Clinically the observation is important in that it proves unfounded the fear that large amounts of food in the febrile period of typhoid may cause too great an increase in heat production and, in turn, a rise of the fever temperature, thus confirming by scientific experiment the early clinical belief of von Hoesslin,[38] that large quantities of ingested food were without influence on the temperature or heat production in fever.

38. Von Hoesslin: Experimentelle Beiträge zur Frage der Ernähung fiebernder Kranker, Virchow's Arch. f. path. Anat., 1882, lxxxix, 95, 303; Ueber den Einfluss der Nahrungszufuhr auf Stoff und Kraftwechsel, ibid., p. 333.

Convalescence.—Throughout convalescence — at least into the fourth week—the metabolism of the liberally fed patients is just as high as during the fever. Yet the returning control of the heat-regulating mechanism permits rapid dissipation of the excess of heat, and the temperature remains normal. The reason for the continuance of the high metabolism into convalescence is not clear. It may be that, as the stimulation of metabolism, which the disease causes, disappears, the specific dynamic action of the food again becomes manifest; the convalescing organism may be doing its work uneconomically, as Svenson believes, or the basal metabolism of the typhoid convalescent may be high, as Howland and others have shown to be the case with normal growing infants. The solution of the problem must be left for future investigation.

TABLE 16.—Food Required to Bring Typhoid Patients Into Nitrogen Equilibrium

Name	Day of Disease	Range of Max. Temp.	Average Food Cal. Per Kg. Per 24 Hours	Average Food N. Per 24 Hours	Average N. Balance Per 24 Hrs.
R. N.*	20-24	104.4-102.0	71	10.9	+1.5
U. H.*	27-30	100.4-101.0	68	8.9	+0.4
Z. O.*	9-12	104.0-103.2	72	13.9	—0.2
Z. O.*	13-18	103.6-102.8	85	15.0	+0.6
Charles N.†..	28-31	102.0-101.8	69	18.7	+6.0
Michael K.†..	15-17	102.0-100.5	79	17.9	+1.5
Philip R.† ...	14-15	102.0-102.0	67	17.6	+2.7
John N.† ...	26-30	102.0-104.0	58	17.8	+1.9
Frank W.‡...	24-28	101.0- 99.6	74	20.3	+4.9
F. Ma.§	6- 8	103.1-103.6	45.5	10.5	—0.5
J. Gerl¶	9-10	103.6-103.8	59.5	7.5	+0.4
J. Gerl¶	16-21	100.9-103.4	76.6	8.1	+0.03

* Shaffer and Coleman (Footnote 1.) † DuBois (Footnote 2). ‡ This article (Table 6). § Rolland (Footnote 41). ¶ Rolland (Footnote 41) Boy aged 10, weight 26 kg.

The fasting convalescents of the earlier investigations[39] have a total heat production which is only slightly greater than normal until the third week, when there occurs an increase of from 12 to 18 per cent.

Relapse.—Three patients were studied during relapses. They showed an average heat production of 39 calories per kilogram. The average is high on account of the high metabolism of the boy Salvatore. The average for the other two cases is 36.6 calories per kilogram, or essentially the same as the general average in the original fever.

39. Rolly, F.: Experimentelle Untersuchungen über den Stoffwechsel im Fieber und in der Reconvalescenz, Deutsch. Arch. f. klin. Med., 1911, ciii, 93; Grafe, E.: Untersuchungen über den Stoff- und Kraftwechsel im Fieber, ibid., 1911, ci, 209.

In this connection it should be pointed out that a large excess of energy over the actual heat production must be supplied to the typhoid patient in order to maintain weight and nitrogen equilibrium. The influence of the high-calory diet on the weight of the patient has been considered in previous publications.[40] It is sufficient to state here that loss of weight may be prevented by giving the patient sufficient food.

The few reported cases in which nitrogen equilibrium was obtained have been grouped in Table 16. With the exception of one patient of Rolland's[41] (who almost reached balance on 45.5 calories), these cases were not brought into equilibrium until the patients were given from 60 to 85 calories per kilogram, and even with the larger amount of food, equilibrium was not established until the temperature had begun to fall. It is evident, therefore, that more than 85 calories per kilogram may be required by some patients to establish nitrogen equilibrium during the height of the fever.

Rolland has estimated 49 calories per kilogram as the mean heat production of the typhoid-fever patient. Basing her calculation on Grafe's[11] average of 35 calories per kilogram for fasting typhoids, she allowed from 10 to 15 per cent. for the specific dynamic action of food, from 10 to 15 per cent. for the excreta, and from 10 to 15 per cent. for muscular work in moving about the bed. Experimental work in this clinic has shown that her allowance for the first two factors is too liberal. It has already been pointed out that the specific dynamic action of the food in the high-calory cases is almost, if not entirely, masked by the increase in metabolism caused by the toxic agent, and it has been shown that the average loss of calories in the feces amounts to 5 per cent. of the intake. Though it is difficult to estimate accurately the increase in metabolism from bodily activity, yet in the high-calory cases it cannot be great—possibly not so great as in patients who are undernourished. The high-calory cases are not "tubbed," and are spared the shivering which ordinarily follows this practice. With rare exceptions they are not toxic and, therefore, not restless, and do not exhibit jactitation and subsultus tendinum. For the most part the patients lie quietly in bed, often reading for several hours a day. Without taking into consideration the reduction of metabolism during sleep, we believe that the increase in metabolism caused by bodily movement is amply covered by an allowance of 10 per cent.

40. Coleman: The High-Calory Diet in Typhoid Fever, a Study of 111 Cases, Am. Jour. Med. Sc., 1912, cxliii, 77; Weight Curves in Typhoid Fever, ibid., 1912, cxliv, 659; Diet in Typhoid Fever, Jour. Am. Med. Assn., 1909, liii, 1145.

41. Rolland, Anne: Zur Frage des toxogenen Eiweisszerfalls im Fieber des Menschen, Deutsch. Arch. f. klin., Med., 1912, cvii, 440.

Making this allowance, the average total heat production of the typhoid patient is 40 calories per kilogram per day.

If the supply of nitrogen be sufficient, a normal man may be maintained in nitrogen and weight equilibrium on a diet which just covers his heat production. It is clear, however, from Table 16 that typhoid patients, though producing an average of 40 calories per kilogram, cannot be brought into equilibrium unless they receive from 57 to 81 calories[42] and in some instances more. In other words, a patient of 65 kg., producing 2,400 calories a day, requires from 3,600 to 5,000 calories to maintain him in equilibrium.

The fate of this excess is a matter of great interest. There can be no doubt that the nitrogen of the urine furnishes an accurate index of protein metabolism in fever. The work of Magnus-Alsleben[43] and Mohr[44] proved that there is no abnormal loss of calories in carbon-containing compounds in the urine except in cases with glycosuria. Glycosuria has been observed but seldom in the Bellevue cases. It is difficult, but not impossible, to conceive that patients are able to store body-fat while there is a negative nitrogen balance and a steady loss of body-weight. A moderate storage of fat could, of course, be masked by a change in the water content of the body, but we are not prepared to offer this theory.

With the onset of convalescence, the amount of food required to maintain nitrogen equilibrium more nearly approaches the estimated heat production of the patient. For example, one of the patients reported by Shaffer and Coleman showed a positive nitrogen balance from the fifth to the ninth days of convalescence while receiving 37 calories per kilogram, yet a few days previously, during a relapse, 77 calories per kilogram were required. F. Müller[45] has reported a case which retained nitrogen from the third to the tenth days of convalescence from typhoid fever on a diet furnishing only 1,165 calories and 9.9 gm. of food nitrogen, which, on account of its low fuel value, would be incapable of maintaining nitrogen equilibrium in health.

These facts demonstrate that the need of the typhoid patient for the excess of energy over the heat production is in some way connected with the reaction of the host to the infecting agent; but so far we have failed to discover the purpose or fate of this excess, and we possess no data which even suggest a plausible hypothesis.

42. Five per cent. of the intake has been deducted to cover the loss of calories in the feces.

43. Magnus-Alsleben, E.: Ueber die Ausscheidung des Kohlenstoffs im Harn., Ztschr. f. klin. Med., 1909, lxviii, 358.

44. Mohr: Ueber den Stoffzerfall in Fieber, Ztschr. f. klin. Med., 1904, lii, 371.

45. Müller, F.: Stoffwechseluntersuchungen bei Krebskranken, Ztschr. f. klin. Med., 1889, xvi, 542.

RESPIRATORY QUOTIENTS

Febrile Period.—The averages of the respiratory quotients[46] in Table 15 give a great deal of information as to the different foods actually oxidized by the patients. The fasting individuals in the steep-curve period, with an average quotient of 0.76, were no longer oxidizing carbohydrate in quantity. It is estimated that from 20 to 25 per cent. of the calories were furnished by protein, from 5 to 10 per cent. by carbohydrate and the remainder by body-fat. The high-calory patients in the same period had respiratory quotients of 0.87 and 0.85, indicating that carbohydrate supplied from 40 to 50 per cent. of the energy. These results demonstrate that carbohydrate is oxidized by the fever patient whenever it is available, and are a farther justification of the clinical procedure of giving large amounts of this foodstuff.

Figure 2 brings out the fact that there is a definite tendency for the respiratory quotient to rise during the last days of the febrile period. We have interpreted this to mean that the reparative processes of convalescence are established before the fever subsides.

Convalescence.—The average respiratory quotient of the high-calory patient rises above 0.92 in the first week of convalescence. The fasting patients did not show a similar rise until the third week, which was probably the time when they began to take large amounts of food. The high average of the quotients is due to the large number above 1, obtained when the regenerating organism is transforming ingested carbohydrate into body-fat. It is extraordinary how long this process may continue after the last meal. Previous observers have repeatedly obtained quotients over 1 from twelve to fourteen hours after the last food, during the period of convalescence. The body apparently makes this transformation with very slight loss of energy, and it is in this manner that the fat depots of the body are in part replenished. It is impossible to say whether or not the body oxidizes any fat during the period when fat is being formed from carbohydrate. If there be any catabolism of this material, it is more than counterbalanced by anabolic processes.

Nineteen quotients over 1 were recorded in the first and second weeks of convalescence in experiments in which there was no question of *Auspumpung*. The highest quotients, 1.1 and 1.11, were found in John H. during convalescence when he was given 28 gm. carbohydrate every hour.

46. Nineteen respiratory quotients obtained on patients Frank W. and Louis M. have been omitted from the averages because of the possibility that the height of the quotients was due to *Auspumpung*.

The data concerning the quantitative effect of food on metabolism in individual patients is somewhat fragmentary, and we shall not attempt to formulate conclusions based on the results.

SUMMARY AND CONCLUSIONS

The Benedict "universal respiration apparatus" employed in this investigation was tested on normal controls and found to give accurate results. We believe that the apparatus is well adapted to clinical use if Benedict's technic is carefully followed, that is to say, if precautions are taken to prevent leaks, and if results obtained on patients whose breathing is irregular or labored are discarded. Leaks lower the quotient, irregular and labored breathing artificially raise it.

The metabolism of liberally fed typhoid patients exceeds that of normal individuals by from 36 to 40 per cent. Previous observers have found that the average basal metabolism during the febrile period of patients who are on diets containing less energy than they produce is 35.3 calories per kilogram per day. Comparing this figure with the averages obtained, after ingestion of food, on typhoid patients who received from 35 to 170 calories per kilogram daily, it is observed that the average metabolism per kilogram of body-weight shows an increase of from only 2 to 5 per cent. If the body-surface be made the basis of comparison, it is found that the increase is between 11 and 13 per cent. Since the variation in the metabolism of different normal persons may amount to 10 per cent. above or 10 per cent. below the normal average, it is obvious that the influence of a large ingestion of food cannot be of great importance in increasing heat production in the febrile stage of the disease. In other words, the large amount of food administered exhibits little or no specific dynamic action, thus removing the chief theoretical objection to the use of a liberal diet in typhoid fever.

In the high-calory cases approximately 10 per cent. must be added to cover the increase in metabolism caused by bodily exertion incident to moving about the bed. Accordingly the typhoid patients examined had an average theoretical requirement of 38.5 calories per kilogram per day. It has been found, however, that the theoretical requirement must be exceeded by from 50 to 110 per cent. in order to bring the patient into nitrogen and weight equilibrium. The fate of the excess has not yet been discovered.

In the steep-curve period and during relapses some patients derived from 84 to 89 per cent. of their calories from carbohydrate and, in addition, transformed some carbohydrate into body-fat. The majority of the high-calory patients showed a sharp rise in the level of the respiratory quotients during the last days of the fever, which we have interpreted to mean that the regenerative processes of convalescence begin before the temprature reaches normal.

We desire to express our gratitude to Prof. Graham Lusk for his unfailing interest in our work and for many valuable suggestions during its prosecution. We wish also to thank Dr. Francis G. Benedict, director of the Carnegie Nutrition Laboratory, for helpful advice respecting the handling of the Benedict "universal respiration apparatus" which we employed, and Mr. J. A. Riche for its construction. Our thanks are due to Mr. Frank C. Gephart and Mr. Rudolf H. Harries, of the Russell Sage Institute of Pathology, and to Mr. John M. Janson for aid in food and urine analyses and in the operation of the machine. We are indebted to Dr. Charles L. Dana for the privilege of studying cases in his service at the hospital. For the many food analyses we are indebted to Mr. Frank C. Gephart of the Russell Sage Institute of Pathology.

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