PROTEIN METABOLISM IN TYPHOID FEVER *

PHILIP A. SHAFFER, Ph.D., and WARREN COLEMAN, M.D.

WITH THE ASSISTANCE OF

Michael Somogyi, E. A. Reinoso and Edna Cutler

NEW YORK

It has long been known that during the febrile reaction to acute infections the katabolism of protein is intensified, resulting in an increased excretion of nitrogenous substances in the urine. This phenomenon is of such constant occurrence that it may properly be considered a characteristic of fever.

Because of this increased katabolism and of the disproportion between the anabolism and katabolism of protein the subject becomes poorer in nitrogenous substances. After the termination of the disease the protein katabolism falls in intensity to or even below the normal limit, the anabolic process becomes more prominent, and during this reverse disproportion between the processes of assimilation and destruction the organism repairs its losses of protein and other substances.

These conditions, fever and convalescence, afford two of the most interesting fields for the investigation of the complicated principles of physiological and pathological nutrition, as has been demonstrated by the numerous papers on these subjects.

During the past two years we have been engaged in a study of the protein metabolism in typhoid fever. The main object of the investigation was a study of certain aspects of the febrile katabolism of body protein. We hoped to determine to what extent, if at all, the loss of body protein during the disease could be prevented or retarded by different forms of food, and to establish the physiological characters of the diets best suited for this purpose. The experiments to be reported concern chiefly the effect of diets rich in carbohydrate. We have also accumulated much material concerning the quantitative composition of the urine from which we hoped some further knowledge might be obtained of the degree of abnormality in the intermediary metabolism of nitrogenous substances in this disease.

* From the Laboratory of Pathological Chemistry, Department of Experimental Pathology, Cornell University Medical College, and the Second Medical Division of Bellevue Hospital, New York City.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

For a critical review of the extensive literature relating to the metabolism in fever and allied subjects the reader is referred to various papers, especially that by Kraus, in von Noorden's "Handbuch der Pathologie des Stoffwechsels." We shall cite in the following pages only a few of the papers having an immediate bearing on our experiments.

THE LOSS OF BODY PROTEIN

The loss of body protein, calculated from the minus balance of nitrogen, is very great in typhoid fever. F. Müller's patient who lost 86.4 gm. of body nitrogen, the equivalent of 2.5 kg. of muscle tissue, in eight days is not very unusual. In an experiment reported by Leyden and Klemperer[2] the subject lost 109.4 gm. of body nitrogen, the equivalent of 3.2 kg. muscle tissue, in twelve days. In neither instance do the figures given represent by any means the total loss of body protein during the whole course of the disease in these patients. The loss for short periods is often relatively much greater, a loss of 15 to 20 gm. nitrogen per day not being very unusual in the early stages of severe attacks in muscular individuals.

This loss of body protein, which apparently occurs during all acute infectious fevers, is due both to an increased destruction and to a decrease in the regenerative processes, both changes serving to intensify the disproportion between the anabolism and katabolism of protein.

The increased katabolism is at present generally believed to be due to at least two fairly distinct causes: to the pyrexia itself and to the action of bacterial toxins on the body cells or fluids, quite apart from the pyrexia. The decrease in the anabolism, the regenerative processes, is largely the result of a lowered or insufficient food-supply; the latter point may be better appreciated after considering the factors involved in the febrile katabolism.

EFFECT OF SIMPLE PYREXIA

An artificial raising of the body temperature above the normal for some hours results in an increased katabolism of protein. Fritz Voit[3] observed that, if the temperature of a fasting dog was raised to 40 or 41 C., the nitrogen excretion was increased about 37 per cent. This increase was obtained only after maintaining the higher temperature for twelve hours, and Voit concluded that the increase of protein metabolism

1. Müller: Centralbl. f. klin. Med., 1884, v, 596.
2. Leyden and Klemperer: von Leyden's Handbuch der Ernährungstherapie, 1904, ii, 345.
3. Voit, F.: Sitzungsb. d. Gesellsch. f. Morphol. u. Physiol. in München, 1895, xi, 120.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

took place after the greater part of the store of glycogen had been exhausted. Schleich,[4] Linser and Schmid,[5] and others have performed similar experiments. Schleich found the urea excretion of a man to be noticeably increased on raising the body temperature for several hours by means of hot baths to 39.5 C. Linser and Schmid found an increase of protein metabolism on raising the body temperature of a normal man, as well as of a subject of ichthyosis hystrix, above 39 or 40 C. The last-mentioned investigators believe that a simple pyrexia causes an increase in the protein metabolism only when the temperature is above 39 C. (102 F). It appears, therefore, that the febrile temperature in typhoid fever may be one of the factors which increase the protein metabolism.

THE EFFECT OF TOXINS

The human subject of an infectious fever excretes, during the height of the disease, much more nitrogen in his urine than does either a starving man or a man whose body temperature has been raised by artificial means. The same rule holds true for animals experimentally infected with pathogenic organisms or injected with bacterial toxins.

Neither simple pyrexia nor the degree of starvation alone is sufficient to explain the whole of the increase in protein katabolism, and it becomes necessary to seek some further factor which may act in this direction. Most writers call this factor the "toxic" or "toxogenous" destruction, meaning merely the effect of the bacterial toxins on the katabolic processes.

While there seems to be no doubt that the toxins have a distinct part in the cause for the febrile katabolism, the mechanism of this "toxic" action is not known. One hypothesis is represented by the statement of Krehl[6] that it is "very probable that the agent causing the fever actually destroys the cell proteids in various parts of the body." According to this idea the increase in febrile katabolism involves only protein.

Benedict and Surányi,[7] on the other hand, deny the existence of this sort of a toxic destruction, believing that the increased protein katabolism is merely a part of an increase in the total metabolism which Aronsohn[8] believes may be caused by the action of toxins on either enzymes or the nervous mechanism controlling the consumption of food and body materials.

---

4. Schleich: Arch. f. exper. Path. u. Pharmakol., 1875, iv, 82.
5. Linser and Schmid: Arch. f. klin. Med., 1904, lxxix, 514.
6. Krehl: The principles of clinical pathology, Philadelphia, 1905, p. 394; transl. by Hewlett from 3rd German ed.
7. Benedict and Surányi: Ztschr. f. klin. Med., 1903, xlix, 502.
8. Aronsohn: Ztschr. f. klin. Med., 1907, lxi, 153.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Krehl's view of the toxic destruction appears to be supported by the results of May,[9] who studied the total metabolism in fasting rabbits infected with hog cholera and found a marked increase in protein katabolism, but no increase in the consumption of fat; though May concluded from his experiments that the increased protein destruction was chiefly the result of an insufficient carbohydrate supply.

Stähelin,[10] on the other hand, working with a dog infected with surra, found an increase in the consumption of fat as well as protein, thus indicating that non-nitrogenous substances also take part in the increase of febrile katabolism.

PARTIAL STARVATION

If a subject does not receive food of a sufficient caloric value to meet the daily energy exchange, his body material is drawn on to supply the deficit. This factor is responsible, in most cases of typhoid fever, for a part of the loss of body protein. The caloric value of the diets now used in the disease is lower than would maintain equilibrium in even a normal subject, with the result that there is not only a decrease in the anabolic processes, but the body tissues or fluids are further drawn on for an additional supply of energy.

The degree of this partial starvation and the amount of the contingent (starvation) loss of body protein is determined both by the food intake and by the total requirement for energy. No satisfactory general estimate of the amount of the latter factor can be made at present; it will vary greatly with different subjects and at different stages of the disease.

It is certain that the energy requirement of such subjects is not lower than the normal (about 33 cal. per kilo[11]), but we cannot predict how much greater it is than the normal in any individual case unless we know the extent of the febrile increase in total katabolism. According to Krehl,[12] the febrile increase in heat production varies between 10 per cent. and 60 per cent.; the latter estimate would give a requirement of about 53 cal. per kg.

---

9. May: Ztschr. f. Biol., 1894, xxx, 1.
10. Stähelin: Arch f. Hyg., 1904, L, 77.
11. At ordinary rest the heat production of a normal fasting individual is about 30 cal. per kg. body weight. The heat production at complete rest is lower than this, Johannson recording about 22 and Atwater, in an experiment during sleep, 22.8 cal. per kg. Typhoid patients are, however, rarely at complete rest; the restless movements in bed and the shivering after frequent "tubs" or sponges appear sufficient to justify accepting at least 30 cal. per kg. as the basis for this calculation. To this starvation requirement we must add 10 per cent. to allow for the dynamic stimulation of metabolism caused by food (Rubner.)
12. Krehl: The Principles of Clinical Pathology, Philadelphia, p. 382.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

We have attempted above to outline the factors, so far as they are at present known, which are responsible for the febrile loss of body protein. We have seen that the increased katabolism of body protein is due on the one hand to the febrile temperature of the subject and on the other to the action of bacterial toxins; and that this katabolism may be, and usually is, further increased by an inadequate food-supply and the consequent burning of body material as a source of energy. What are the possibilities of retarding the protein katabolism by dietetic means? It is obvious that the increased katabolism of body materials and the loss of body protein due to simple starvation may be prevented by sufficient food.

And if the view held by Benedict and Surányi, Aronsohn, and in a qualified form by May[13] be true, that the effect of the pyrexia and of the action of toxins is merely an increase in the total katabolism, resulting in a greater demand for energy-producing material, the situation with these factors also becomes one of undernourishment. The body protein, together with fat, is drawn on as in simple starvation to meet the demand for fuel, though in larger amounts on account of the increased heat production. The chief obstacle to this view has been the apparent impossibility of preventing a loss of body nitrogen in a fever subject, even though he be given food of such caloric value as supposedly to cover his energy exchange; and the lack of success in such efforts is, in fact, largely responsible for the conception of a "toxic" destruction of body protein, in the meaning of Krehl. But, according to our experiments, the reason for this lack of success is not that it is impossible to prevent this febrile loss of body protein, as would be the case were Krehl's conception true, but that food of sufficient fuel value and of suitable character has not been used.

Voit, and Linser and Schmid, were able to retard the increased protein katabolism of simple pyrexia by giving additional carbohydrate in the food.

To retard or to prevent the excessive katabolism of body protein due to the action of toxins has been found very difficult; the experiments of Weber[14] are the only ones in which success is clearly shown. This investigator injected extract of glanders bacilli into a sheep and obtained a loss of nitrogen, although the animal received a diet which had previously maintained nitrogen equilibrium. In a second experiment, with food equivalent to 73 cal. per kg., the animal gained nitrogen during six days of fever. The gain, however, was less than during the normal

13. May: Ott: Chemische Pathologie der Tuberculose, Berlin, 1903, p. 259.
14. Weber: Arch. f. exper. Path. u. Pharmakol., 1901, xlvii, 19.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

periods. He was able, therefore, wholly to prevent a loss of body protein which, with less food, would have been caused both by the pyrexia and by the direct action of the toxins on the protein metabolism.

In a subject of typhoid or other infectious fever it is difficult, and usually impossible, to study the effect singly of partial starvation, pyrexia, or the action of toxins on the protein katabolism, and one must ordinarily be content with determining the combined effect. This is essentially what has been done by Weber, by May with rabbits, and by Puritz,[15] and Leyden and Klemperer, with human subjects of typhoid fever.

All these experiments give some indication, it seems to us, that the total protein katabolism in fever, and the loss of body protein, may be influenced by the caloric value of the food. May and Weber drew this conclusion from their experiments, but the principle involved does not appear to have been accepted as generally applicable, and the results of these experiments have had no effect upon the dietetic treatment of febrile conditions in the human subject. Puritz believed the loss of body protein to be less with high protein diets; Leyden and Klemperer, though of the same opinion, conclude that the "toxic" loss of protein cannot be affected by any dietary régime.

There are other reasons for believing that food of high caloric value and especially rich in carbohydrate should be effective in protecting the body protein from excessive destruction in fever. The work of Lusk,[16] Sivén,[17] Landergren,[18] Folin,[19] Murlin,[20] and others has shown the superior value of carbohydrate in sparing body protein in afebrile conditions.

Fat alone fed to an animal retards the loss of body protein little or not at all, but spares an equivalent quantity of body fat.[21]

Protein when alone must be given in extremely large amount before nitrogen equilibrium is obtained, because of the large specific dynamic effect (Rubner) of protein in increasing the total metabolism. Carbohydrate alone, on the other hand, may reduce the amount of nitrogen excreted by 50 per cent. to 70 per cent. of the starvation excretion.

Our experiments were undertaken with the hope, based on the considerations stated in the preceding pages, that the total febrile destruc-

15. Puritz: Virchow's Arch. f. path. Anat., 1893, cxxxi, 327.
16. Lusk. Ztschr. f. Biol., 1891, xxvii, 459.
17. Sivén: Skand. Arch. f. Physiol., 1901, xi, 308.
18. Landergren: Skand. Arch. f. Physiol., 1903, xiv, 112.
19. Folin, Otto: Am. Jour. Physiol., 1905, xiii, 66.
20. Murlin: Am. Jour. Physiol., 1907, xx, 234.
21. A portion of the carbohydrate of a maintenance diet may be replaced by fat without materially affecting the protein katabolism. The above statements refer to previously starved animals.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

tion of body protein might be decreased even to normal limits by the addition to the food of large quantities of carbohydrate. It seemed to us probable that carbohydrates might exert the same or similar protecting influence on the body protein during the febrile reaction in man as they do during partial starvation.

These expectations have been realized to the extent that we have found it possible, by giving diets of unusually high caloric value, and consisting principally of carbohydrate, very greatly to diminish and in some instances wholly to prevent the loss of body protein as indicated by the nitrogen balance. Our investigation includes work on twenty-four subjects of typhoid fever, the results from all of which show, with a fair degree of uniformity, though to varying extents, that other factors, such as temperature, intensity of the febrile process, protein intake, etc., being the same or comparable, the loss of body protein becomes less the higher the caloric value of the food. The results from only seven subjects need be given. The results and conclusions from the work with other subjects are in substantial agreement with these.

PLAN OF EXPERIMENTS

The procedure was varied with the different subjects. A constant diet from day to day was frequently impossible, but the amount of food taken in each twenty-four hours was accurately recorded. The protein, fat and carbohydrate, as well as the caloric value of the food, has been calculated from the following data, based in part on our own analyses made from time to time and in part upon König's and Atwater and Bryant's tables.

	Protein %	Carbohydrate %	Fat %
Milk (by volume)	3.3	5.0	5.0
Cream (by volume	2.0	3.0	30.0
Butter (by weight)	..	..	85.0
Toast	11.0	60.0	..
Eggs (selected to weigh about 60 gm. gross)	12.0	..	9.0
One egg	(7.2 gm.)	..	5.4 gm.)
Lactose	....	100.0	..
"Somatose"	12.4% nitrogen		
Liebig's meat extract	9.2% nitrogen		
Whisky	40.0% alcohol		

The energy value of the diets is calculated on the basis of Rubner's figures:

1 gm. protein .... 4.1 cal.
1 gm. carbohydrate .... 4.1 cal.
1 gm. fat .... 9.3 cal.
Nitrogen × 6.25 = protein.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

The urines were collected in twenty-four hour quantities. The collection of complete twenty-four-hour urines from bed patients who are acutely ill is not an easy task, and in a large and busy ward in a general hospital is frequently very difficult. For the success of an investigation of the nature here reported it is necessary that one have every possible assurance, rather than only an assumption, that the urines are complete. During the last half of the work two special nurses, who had no other duties than attendance on the patients being studied, were detailed through the courtesy of Dr. S. T. Armstrong, superintendent of the hospital, and of Miss Goodrich, superintendent of nurses. To the care of these nurses is due the infrequency of the loss of urines as well as the successful and accurate administration of the food.

The following is a form of printed blanks which were written up and signed by the nurses and sent to the laboratory with each bottle of urine or feces:

METABOLISM IN FEVERS

Name ....Ward..........Bed..........

Urine for 24 hours, ending at.......... a. m. / p. m. (date)..........................

Feces for............days, from...... a. m. / p. m. ....to........ a. m. / p. m. ....

Temperature: lowest.......at...... a. m. / p. m. ....; highest......at...... a. m. / p. m.

Weight of patient..........lbs. at........ p.m. / a. m. (date)....................

NURSES: | Quantity of Urine.

.... |

Each nurse, when she goes off duty, will please sign her name above stating the time she was in charge of the patient. If no accidents concerning the administration of food (as refusal to take all or part, or loss of through vomiting—if patient vomits, state hour) or the collection of the *complete excreta* have occurred, she should write O. K. after her name. Otherwise, she should describe on the back of this sheet the amount of food refused or left or vomited, and the approximate quantity of urine or feces lost and how it was lost. Please send this sheet to the laboratory with its corresponding specimen.

When this sheet is used for a specimen of feces, data concerning urine, temperature and weight may be omitted.

By this means responsibility for the collection of excreta and administration of food was centered on individuals, with the result that accidents of this nature were rare, and, more important still, were accurately recorded when they did occur.[22]

22. A similar blank had been previously used by Folin and one of us (Shaffer) at the McLean Hospital. Printed blanks also were used daily for recording in the ward the amount and kind of food taken by each patient. To the advantages derived from the use of these blanks we attribute in large measure the technical success of our experiments.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

The urines were analyzed at once for total nitrogen, kreatinin, kreatin, and in many instances for other substances. In some cases "composites" representing a number of days, were made by mixing aliquot parts of consecutive urines. These composites were then analyzed for the substances stated in the tables.

The feces, marked off by charcoal, were collected and analyzed for total nitrogen during a part of some experiments, but not in all. It is to be regretted that the limited capacity of the laboratory prevented further work on the feces. For the calculation of the nitrogen balance we have used nitrogen figures for each day's urine, and, except where the feces were analyzed, have arbitrarily taken 15 per cent. of the food nitrogen as representing the amount of nitrogen in the feces.

This latter assumption is admittedly a source of error, but this error is probably fairly constant with individual patients and, we believe, does not affect the validity of our conclusions, based as they are on comparative figures.[23]

The analytical methods used were:

Kjeldahl method for total nitrogen; Folin's method for urea, kreatinin, kreatin, total sulphur[24] and its partition among inorganic, ethereal and neutral sulphur, titrated acidity[25] and indican;[26] Boussingault-Shaffer method for ammonia;[27] Folin-Shaffer method for uric acid; Salkowski method for xanthin bases; Volhard method for chlorids; Fehling's or Pavy's methods for sugar; Shaffer's method for beta-oxybutyric acid,[28] and a modified Messinger-Huppert method[28] for acetone plus diacetic acid. The fraction called "rest" nitrogen is the difference between the total nitrogen of the urine and the sum of urea-, ammonia-, kreatinin-, kreatin- and uric-acid nitrogen.

DETAIL OF EXPERIMENTS

Patient 1.—R—n, male, aged 23, tailor, fairly well nourished, admitted the seventh day of the disease. Positive serum reaction. Illness severe. Duration of the fever thirty-five days. Two recrudescences.

---

23. The feces of Hoesslin's typhoid subjects (Virchow's Arch. f. path. Anat., 1882, lxxxix, 317) contained on the average about 1 gm. nitrogen per day. Leyden and Klemperer's subjects excreted usually between 1 and 2 gm. nitrogen in the feces, the amount increasing with the nitrogen of the food. In one case the last-named worker assumed the feces-nitrogen to be 10 per cent. of the food nitrogen. In our own analyses, the feces-nitrogen amounts to between 10 and 20 per cent. of the food-nitrogen.
24. Folin, O.: J. Biol. Chem., 1906, i, 131.
25. Folin, O.: Am. Jour. Physiol., 1903, ix, 265.
26. Folin, O.: Am. Jour. Physiol., 1905, xiii, 53.
27. Shaffer, P.: Am. Jour. Physiol., 1903, viii, 330.
28. Shaffer, P.: Jour. Biol. Chem., 1908, iv, 211.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 1.—PATIENT 1, R—N: TEMPERATURE AND FOOD

Day of Disease.	Temp. F. High.	Temp. F. Low.	Food. Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein.	Fat.	C.H.
				PERIOD I					
12	104.8	103.0	1200	95	460	2	60.0	99	523
13	104.0	102.0	1080	120	610	2	52.5	101	668
14	104.4	101.0	1200	60	515	2	55.0	89	577
15	104.0	101.4	1470	...	450	2	63.0	84	523
16	103.0	101.6	1000	60	365	2	48.6	79	417
17	102.6	100.6	990	120	420	2	49.5	86	473
18	102.6	99.0	1200	150	455	2	57.0	116	520
19	103.6	100.0	1290	150	510	2	60.0	120	579
Average							55.7	97	535
				PERIOD II					
20	104.4	101.0	1380	150	500	3	70.0	130	574
21	102.0	98.0	1200	180	500	3	64.8	130	565
22	102.8	98.4	1260	150	480	3	65.2	124	547
23	102.6	98.4	1200	270	500	4	74.2	132	565
24	102.6	99.0	1200	300	505	3	67.0	166	574
25	102.0	99.0	960	300	510	2	52.0	149	567
Average (omitting last day)							68.2	136	565
				PERIOD III					
26	102.4	99.2	240	420	515	1	23.3	143	540
27	103.6	100.6	....	540	520	..	10.8	162	536
28	104.8	99.6	....	600	515	..	12.0	180	533
29	102.8	101.6	....	630	475	..	12.6	189	494
Average							15.4	162	536
				PERIOD IV					
30	102.2	99.0	2400	...	...	..	79.2	120	120
31	100.6	99.0	2400	...	...	..	79.2	120	120
32	104.6	101.0	2400	...	...	..	79.2	120	120
33	101.0	99.6	2400	...	...	..	79.2	120	120
34	102.0	99.0	2400	...	...	..	79.2	120	120
35	100.2	98.4	2160	...	...	..	71.5	108	108
Convales-cence.		Average (omitting last day)					79.2	120	120
				PERIOD V					
1	99.0	98.0	1200	270	357	2	59.4	152	425
2	98.4	97.0	1440	210	500	3	73.3	151	578
3	99.0	97.6	1440	210	500	4	80.5	156	578
4	99.4	97.2	1440	240	505	5	88.3	171	584
5	100.0	99.0	1410	240	510	4	80.0	164	588
6	99.6	98.4	1500	240	510	5	90.3	174	592
7	99.6	99.0	1560	150	485	5	90.5	150	567
8	99.0	98.0	1620	330	395	5	96.0	207	485
Average (omitting first day)							85.0	167	564

TABLE 2.—PATIENT 1, R—N: DAILY NITROGEN BALANCE

Day of Disease.	Calories. Total.	Calories. Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake.	Nitrogen Balance. Excretion.*	Nitrogen Balance. Balance.
			PERIOD I			
12	3310	61	40	9.6	14.3	—4.7
13	3890	70	51	8.4	10.8	—2.4
14	3430.	63	44	8.8	13.8	—5.0
15	3180	59	40	10.1	14.8	—4.7
16	2645	49	32	7.8	15.0	—7.2
17	2940	54	36	7.9	15.7	—7.8
18	3440	64	39	9.1	16.0	—6.9
19	3735	69	44	9.6	11.4	—1.8
			PERIOD II			
20	3850	71	43	11.2	11.9	—0.7
21	3790	70	43	10.4	10.9	—0.5
22	3660	68	41	10.4	9.7	+0.7
23	3850	71	43	11.9	8.9	+3.0
24	4170	77	43	10.7	8.7	+2.0
25	3920	73	43	8.3	8.8	—0.5

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 2.—(Continued)

			Period III			
26	3640	67	41	3.7	7.0	—3.3
27	3750	70	41	1.7	5.1	—3.4
28	3900	72	40	1.9	5.8	—3.9
29	3840	71	38	2.0	....	.....
			Period IV			
30	1928	36	9	12.7	11.3	.....
31	1928	36	9	12.7	16.6	—3.9
32	1928	36	9	12.7	16.3	—3.6
33	1928	36	9	12.7	15.0	—2.3
34	1928	36	9	12.7	15.5	—2.8
35	1740	..	..	....	....	.....
			Period V			
Convalescence.						
1	3390	63	32	9.5	11.0	—1.5
2	4070	75	43	11.7	10.3	+1.4
3	4150	77	43	12.9	9.3	+3.6
4	4340	80	44	14.1	....	.....
5	4260	79	44	12.8	10.3	+2.5
6	4420	82	45	14.4	10.3	+4.1
7	4090	76	43	14.5	10.5	+4.0
8	4300	80	37	15.3	12.2	+3.1

* "Excretion"=Total nitrogen of urine + 15 per cent. of food nitrogen.
Weight on twenty-seventh day of disease, 54 Kg.

TABLE 3.—PATIENT 1, R—N: DAILY ANALYSES OF URINE

	Urine					Per Cent. of Total Nitrogen.	
		Gm. Nitrogen.					
Day of Disease.	Volume c.c.	Total.	Kreatinin.	Kreatin.	Rest.*	Urea + NH_3	Rest.*
			Period I				
12	700	12.9	0.54	0.08	1.62	82.8	12.5
13	600	9.5	0.44	0.10	1.52	78.4	16.0
14	800	12.5	0.58	0.09	1.19	85.1	9.5
15	900	13.3	0.60	....	1.70	82.6	12.8
16	960	13.8	0.54	0.21	1.23	84.7	8.9
17	980	14.5	0.54	0.28	1.56	83.6	10.8
18	1580	14.6	0.54	0.42	1.37	84.3	9.4
19	940	10.0	0.53	0.29	0.73	84.7	7.3
			Period II				
20	1180	10.2	0.54	0.25	0.94	83.0	9.2
21	1170	9.3	0.50	0.03	0.84	85.3	9.0
22	1120	8.1	0.44	0.03	0.81	84.3	10.0
23	840	7.1	0.40	0.03	1.01	79.7	14.3
24	810	7.1	0.35	0.00	1.38	75.7	19.4
25	930	7.6	0.47	0.00	1.17	78.5	15.4
			Period III				
26	975	6.4	0.40	0.00	1.10	76.5	17.3
27	1140	4.8	0.42	0.00	0.55	79.5	11.5
28	900	5.5	0.55	0.05	0.95	71.8	17.4
29	Urine lost.						
			Period IV				
30	1450	9.4	0.50	0.00	....	....	....
31	1560	14.7	0.62	....	....	....	....
32	1280	14.4	0.52	0.09	....	....	....
33	1560	13.1	0.47	....	....	....	....
34	970	13.6	0.49	....	....	....	....
35	Urine lost.						
			Period V				
Day of Convalescence.							
1	910	9.6	0.32	....	....	....	....
2	950	8.6	0.39	....	....	....	....
3	780	7.4	0.39	....	....	....	....
4	Urine lost.						
5	1100	8.4	0.49	....	....	....	....
6	1080	8.2	0.45	....	....	....	....
7	940	8.3	0.35	....	....	....	....
8	1160	9.9	0.41	....	....	....	....

* "Rest" includes uric-acid-nitrogen.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 4.—PATIENT 1, R—N: AVERAGES FROM PERIODS

Figures given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food: Cal. Per Kg. Total.	Food: Cal. Per Kg. Fat.	Food: Cal. Per Kg. C. H.	Food: Nitrogen. Gm.	Excretion N.	Balance N.	Urine: Kreatinin N.	Urine: Kreatin N.	Urine: "Rest" N. Gm.	Urine: "Rest" N. Per Cent. Total N.	Kreatinin Coef.
						Period I						
8	104.8-102.6	62	16	41	8.9	13.9	—5.0	0.54	0.21	1.49	11.8	10.0
						Period II*						
5	104.4-102.0	71	23	43	10.9	10.0	+0.9	0.45	0.02	1.02	12.2	8.3
						Period III						
3	104.8-102.4	70	28	41	2.4	5.9	—3.5	0.46	0.02	0.87	15.6	8.5
						Period IV†						
4	104.6-100.6	36	21	9	12.7	15.8	—3.1	0.52	0.09‡	....	....	9.6
						Period V†						
6	Normal	77	29	43	13.6	10.5	+3.1	0.41	....	....	....	7.6

* Last day of period omitted from average.

† First day of period omitted from average.

‡ Result of third day of period.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

The experiment began on the twelfth day of the disease and continued thirty-two days, during the last eight of which the temperature was normal.

With the exception of six days, when a strict milk diet was given, the patient received food of high caloric value; and during four days the protein intake was kept very low, maintaining at the same time the high caloric value of the food. The detailed results of this experiment are given in Tables 1, 2 and 3. Throughout the whole experiment there is a fairly close relation between the nitrogen balance and the caloric and protein value of the food.

This experiment may be conveniently divided into five periods, the average results of which are given in Table 4, to which the attention of the reader is particularly directed.

During the first period of eight days (twelfth to nineteenth days of disease) when receiving food equivalent to 62 calories per kg. and 8.9 gm. of nitrogen, the patient *lost an average of 5 gm. of body nitrogen each day.* This is just the type of result which led von Leyden and Klemperer and others to conclude that the harmful effect of the toxins in causing a destruction of body protein cannot be prevented. But, as we shall see, the loss during this period was undoubtedly much less than would have occurred with food of a lower caloric value. In the second period, when the temperature was still fairly high, and the fever process certainly still active, the food was further increased to 71 calories per kg. and 10.9 gm. of nitrogen, with the result that the subject *gained an average of 0.9 gm. nitrogen each day!* Although the nitrogen intake was increased by 2 gm., the excretion was decreased by 3.9 gm. It is clear that during this period the whole of the febrile increase in protein katabolism was either prevented by the large food supply, or was more than compensated for by a retention of food protein.

In interpreting an experiment of this sort we must, of course, remember that the condition of the subject or the intensity of the febrile process is constantly changing, and we must so far as possible make allowance for this factor. The difference between the nitrogen balance of Periods I and II is undoubtedly due in part to such a change in the intensity of the processes involved. On the other hand, we certainly have no reason for believing that the febrile katabolism, including the action of the toxins, had ceased during Period II, and, if this action was still at work, we can scarcely avoid the conclusion that the loss of body protein which would otherwise have taken place was prevented by the high caloric value of the food. In Period I the katabolism was more intense, the demands were greater than the supply, and the subject lost body protein; in

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Period II the katabolism was less intense, the food supply was greater than the demand, and the subject gained protein.

In Period IV, the last of fever, pathologic katabolism was still taking place. The food contained more protein (12.7 gm. nitrogen), but equaled only 36 cal. per kg. and the subject lost 3.1 gm. nitrogen per day. In the absence of any increased katabolism, this food should maintain equilibrium. In Period VI, the first six days of normal temperature, the food was again increased to 77 cal. per kg. and the subject gained 3.1 gm. nitrogen per day.

Period III is of interest as showing the importance of at least a moderate amount of protein in the food. The fat and carbohydrate intake was kept practically the same as in Period II, which gave a plus balance of 0.9 gm. nitrogen, but the protein was decreased to a very small amount (average 2.4 gm.) with the result that the patient lost 3.5 gm. nitrogen per day. This loss, however, seems remarkably small under the circumstances; the nitrogen excretion was reduced to 5.9 gm.

It should be noted that the marked sparing of body protein observed during this experiment was accomplished by food very rich in carbohydrate. In four periods the subject received each day carbohydrate equivalent to more than 40 cal. per kg.

The kreatin excretion of this subject is also significant. We shall have frequent occasions to refer to the excretion of kreatin and the following explanation of the bearing of this substance may be stated at this point. Endogenous kreatin is not excreted under normal conditions, but, as has been shown,[29] kreatin is excreted when muscle tissues are being broken down or absorbed. One of the most marked instances of a large excretion of kreatin is in women during the first week postpartum, when, as is known, the involution of the muscular wall of the uterus is proceeding most rapidly. The nitrogen derived from this absorbed protein is excreted at the same time in the urine, resulting in a marked minus balance.[30] This relation is also shown in dogs by the experiments of Murlin.[31]

If, as seems probable to us, the belief is correct that endogenous kreatin is excreted only when protein of muscle tissue is being katabolized, it should be possible to determine from the amount of kreatin excreted approximately the extent of the abnormal destruction or consumption of muscle tissues. While recognizing that this conception has

29. Shaffer: Am. Jour. Physiol., 1908, xxiii, 1.
30. Slemons: Johns Hopkins Hospital Rep., 1905, xii, 121.
31. Murlin: Unpublished work.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

not been definitely proved, it appears sufficiently clear to justify its use in the interpretation of our results.

The amount of kreatin excreted in Period I very nearly corresponds with the loss of nitrogen, indicating that the body nitrogen lost was in this period wholly derived from muscles; 0.21 gm. kreatin-nitrogen = 0.65 gm. kreatin. Human muscle contains about 0.4 per cent. kreatin; then 0.65 gm. kreatin = 163 gm. muscle, which (× 3.4 per cent. nitrogen) equals 5.55 gm. nitrogen. The sudden drop of kreatin on the second day of Period II (Table 3) from 0.25 to 0.03 nitrogen probably indicates a sudden and marked diminution in the pathologic metabolism of muscle protein; whether as a result of the increased food-supply or of a change in the patient's condition it is difficult to decide. Perhaps both are responsible. In the third period, although there was a loss of nitrogen, kreatin was excreted on only one day, indicating that the nitrogen lost was not directly derived from muscle tissues.

During Period IV kreatin unfortunately was determined on only two days, the result on the third day (0.09 gm. nitrogen) being equivalent to about 2.4 gm. muscle-protein-nitrogen. Accepting this day as representative of the period, the kreatin indicates that the greater part of the protein lost was derived from muscle, in which we may suppose the katabolism to have been increased as a result of the decrease in fuel value of the food.

Patient 2.—U—h, male, aged 24, laborer, well nourished and of good development, admitted on the tenth day of disease. Blood culture positive. Illness severe. Duration of fever thirty-five days.

The experiment began on the tenth day of the disease and ran for thirty days, during the last eight of which the temperature was normal. This experiment may also be divided into five periods, the average results of which are given in Table 8. The detailed results are given in Tables 5, 6 and 7.

With this subject we see again the marked sparing of the body protein by food rich in carbohydrate, though nitrogen equilibrium was not attained during the fever. In the first period the food contained 9.7 gm. nitrogen and was equivalent to 31 cal. per kg., which fairly represents the diet commonly used in typhoid fever. The patient lost 8.9 gm. of nitrogen each day, and excreted an average of 0.18 gm. kreatin-nitrogen, the latter corresponding to about 4.7 gm. of muscle-protein-nitrogen, and indicating that about half of the nitrogen loss was directly derived from muscle tissue.

In the second period with the temperature fairly high (third week of the disease) the food was increased to 63 cal. per kg., 43 of which were given as carbohydrate. The loss of nitrogen was decreased 5 gm. and the

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

kreatin almost disappeared, the latter, we think, indicating that the pathologic katabolism of muscle protein was practically stopped.

During the third period the diet was again reduced in fuel value to 31 calories per kg., while the protein intake was somewhat increased. The temperature was lower than in the previous periods, but the loss of nitrogen was very considerably increased. Both kreatin and uric acid were slightly higher than in the second period, indicating an increase in the protein katabolism taking place in the muscles. The amount of kreatin excreted was, however, equivalent to only 1 gm. of muscle-protein-nitrogen, or one-seventh of the amount of the minus balance. The greater part of the nitrogen lost was, therefore, probably derived from the blood or tissue fluids.

The food in the fourth period, the last six days of fever, was again of high caloric value, 66 calories per kg., and the subject was almost in nitrogen equilibrium. The kreatin excreted was about the same as during the preceding period, and just about corresponds to the amount of the minus balance (0.7 gm.) of nitrogen, assuming the latter to have been derived wholly from muscle-protein.

The fifth period consists of seven days of convalescence, during which the food was about the same as during Period IV, except for a slight increase in protein. The subject showed a plus balance of 2.5 gm. nitrogen per day. The small amount of kreatin excreted probably indicates that muscle protein was still being absorbed in very slight degree, though the loss of nitrogen from this muscle protein is more than compensated for by the retention of food nitrogen.

The experiment shows that the addition to the food of carbohydrate equivalent to 32 calories per kg. was followed by a decrease in the nitrogen loss of 5 gm., and the subsequent withdrawal of this carbohydrate resulted in an increase of 3 gm. in the nitrogen loss. On again increasing the carbohydrate intake to 43 carbohydrate calories per kg. the subject lost an average of only 0.7 gm. of nitrogen during the last six days of fever and gained 2.5 gm. (average) during the first seven days of normal temperature.

PATIENT 3.—Z—o, male, aged 20, laborer, well nourished, admitted the fourth day of the disease. Blood culture positive. Illness moderately severe. Sputum blood-stained but no tubercle bacilli could be found, nor any signs of tuberculosis in the lungs.

The experiment began on the ninth day of the disease and continued for thirty-two days, on the last seven of which the temperature was normal. In this experiment, which is divided into six periods, the total nitrogen, kreatinin and kreatin were determined in the urine of each day

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

as usual, while all of the other determinations were made in "composite" urines representing the whole of the several periods. The latter results are given in Table 12. A summary of results in periods is given in Table 11, and the daily detailed data in Tables 9 and 10.

This is one of the most interesting experiments of the series. During the first period, *at the height of the disease with food equivalent to 72 calories per kg.* and 13.9 gm. nitrogen, the subject *lost only 0.9 gm. nitrogen per day.* The amount of kreatin excreted (0.05 gm. nitrogen) is equivalent to 1.3 gm. muscle-protein-nitrogen. This roughly corresponds to the nitrogen balance and indicates that the nitrogen lost was derived wholly from muscle tissues.

On the other hand, the amount of kreatin excreted as well as the minus balance of nitrogen, was very small. From results of our experiments with other subjects there can be no doubt that with food of lower caloric value this patient would at that time have excreted much kreatin and would have shown a large minus balance of nitrogen during this period. That he did not excrete much kreatin indicates not only a protection afforded to the protein of blood and tissue fluids (circulating protein) from being drawn on as a source of fuel or for other purposes, but a protection of muscle proteins from the mechanism of the "toxic" destruction. Whatever the nature of this protection, it was certainly accomplished by the high caloric value of the food.

In the next period (II) the diet was increased to 85 calories per kg. by the addition of cream, and the subject was practically in nitrogen equilibrium. Only 0.02 gm. of kreatin-nitrogen was excreted, though the temperature was still high, and it seems fair to believe that a pathologic destruction of muscle and other body protein would have taken place but for the large food-supply.

In the third period the diet was kept the same, with the important exception of withdrawing 600 gm. (!) of carbohydrate. The subject received food equivalent to 45 calories per kg., but lost an average of 8.5 gm. nitrogen per day. That the effect of withdrawing carbohydrate is even greater than the above figure indicates is shown by the daily analyses (Table 10). The excretion of nitrogen increased progressively to the last day of the period and might have gone higher. This is probably to be explained by the protection of glycogen stored during the preceding period of high carbohydrate diet. Calculated on the basis of the last two days of the period, the daily loss would be 10.2 gm. of nitrogen.

The kreatin excretion during this period also was small, making it probable that the nitrogen lost was not derived from muscle tissues. Assuming the muscles to be an important seat of the "toxic" destruction,

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 5.—PATIENT 2, U—H: TEMPERATURE AND FOOD

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein Gm.	Fat Gm.	C. H. Gm.
				Period I						
10	...	104.0	103.0	540	220	180	5	58.0	120	214
11	...	104.0	102.4	600	150	130	3	44.4	91	204
12	...	104.0	102.2	600	225	120	4	50.0	119	157
13	60?	103.5	101.4	2070	...	...	..	68.3	104	104
14	...	103.4	101.6	2160	...	...	..	71.3	108	108
15	...	103.4	101.0	2160	...	...	..	71.3	108	108
Average								60.5	108	149
				Period II						
16	...	103.4	101.0	1200	120	310	6	85.2	128	374
17	...	103.2	100.0	960	120	480	2	48.4	95	532
18	58?	103.0	101.0	1170	45	540	2	54.0	83	600
19	...	103.4	100.0	1200	120	540	2	56.4	107	604
20	...	103.4	100.0	1200	120	540	2	56.4	107	604
Average (excluding 16th day)								53.8	98	585
				Period III						
21	...	103.2	100.8	2160	...	...	..	71.3	108	108
22	...	102.4	99.6	2160	...	...	..	71.3	108	108
23	56?	101.0	99.4	2160	...	...	..	71.3	108	108
24	...	101.0	99.2	2160	...	...	..	71.3	108	108
Average								71.3	108	108
				Period IV						
25	...	102.0	98.0	1140	120	480	2	54.4	104	540
26	...	102.0	99.4	975	120	485	2	49.0	95	537
27	56?	101.0	98.4	990	150	550	2	50.0	105	603
28	...	101.0	98.0	1200	180	550	2	57.6	125	615
29	...	101.0	98.4	1200	240	500	2	58.8	143	567
30	...	100.4	98.4	1200	150	540	2	5.70	116	604
Average (excluding 25th day)								54.5	117	585
				Period V						
Convalescence.										
1	...	99.0	98.0	1170	180	490	2	56.6	123	553
2	...	99.2	98.0	1290	150	515	2.5	63.0	123	584
3	55.0	98.8	98.2	1110	270	500	3	63.6	152	563
4	...	99.2	98.2	1230	300	455	3	68.0	167	525
5	...	99.2	98.2	1200	300	490	3	67.0	166	559
6	55.5	99.0	98.2	1230	240	515	2	59.7	145	584
7	...	98.8	98.4	1140	240	515	3	64.0	145	579
8	...	98.8	98.2	1200	180	500	2	57.8	125	565
Average								63.0	146	566

TABLE 6.—PATIENT 2, U—H: DAILY NITROGEN BALANCE

Day of Disease.	Food. Total Calories.	Cal. Per Kg. Total.	Cal. Per Kg. Fat.	Cal. Per Kg. C. H.	Nitrogen Gm.	Excretion * N Gm.	Balance N Gm.
			Period I				
10	2230	37	19	15	9.3	20.8	—11.5
11	1860	31	14	14	7.1	....	......
12	1960	33	19	11	8.0	16.3	— 8.3
13	1670	28	16	7	10.9	20.2	— 9.3
14	1730	29	17	7	11.4	17.9	— 6.5
15	1730	29	17	7	11.4	17.9	— 6.5
			Period II				
16	3070	53	20	26	13.6	19.3	— 5.7
17	2360	56	15	38	7.8	14.2	— 6.4
18	3450	59	13	42	8.6	13.3	— 4.7
19	3710	64	17	43	9.0	11.6	— 2.6
20	3710	64	17	43	9.0	11.2	— 2.2

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 6.—(CONTINUED)

			PERIOD III				
21	1740	31	18	8	11.4	18.0	— 6.6
22	1740	31	18	8	11.4	19.6	— 8.2
23	1740	31	18	8	11.4	18.0	— 6.6
24	1740	31	18	8	11.4	18.0	— 6.6
			PERIOD IV				
25	3410	61	17	40	8.7	14.3	— 5.6
26	3280	59	16	39	7.8	11.2	— 3.4
27	3650	65	17	44	8.0	8.7	— 0.7
28	3920	70	21	45	9.2	9.5	— 0.3
29	3900	70	24	42	9.4	9.5	+ 0.1
30	3780	68	19	44	9.1	8.4	+ 0.7
			PERIOD V				
Day of convalescence.							
1	3640	66	21	41	9.0	....	......
2	3790	69	21	43	10.1	8.5	+ 1.6
3	3980	72	25	42	10.2	8.8	+ 1.4
4	3980	72	25	39	10.9	8.1	+ 2.8
5	4100	74	25	41	10.7	6.7	+ 3.0
6	3970	72	24	43	9.5	6.9	+ 2.6
7	3980	72	24	43	10.2	6.5	+ 3.7
8	3720	67	21	42	9.3	7.4	+ 1.9

* "Excretion." — Total nitrogen of urine. + 15 per cent. of food nitrogen.

TABLE 7.—PATIENT 2, U—H: DAILY ANALYSES OF URINE

Day of Disease.	Urine							Per Cent. of Total Nitrogen.		
	Volume c.c.	Gm. Nitrogen as								
		Total.	NH_3	Kreatinin.	Kreatin.	Uric Acid.	Rest.	Urea.	NH_3	Rest.
					PERIOD I					
10	920	19.4	1.45	0.74	0.27	0.15	1.29	80.0	7.5	6.6
11	Urine lost.									
12	800	15.1	1.38	0.60	0.07	0.12	1.27	77.4	9.1	8.5
13	1400	18.6	1.77	0.66	0.13	0.14	1.04	79.9	9.5	5.6
14	860	16.2	1.37	0.58	0.17	0.13	0.99	80.1	8.5	6.1
15	880	16.2	1.39	0.64	0.26	0.13	0.93	79.4	8.6	5.7
					PERIOD II					
16	820	17.3	1.51	0.63	0.05	0.13	1.91	75.6	8.8	11.0
17	660	13.0	0.97	0.54	0.04	0.11	1.11	78.7	7.5	8.6
18	760	12.0	1.10	0.56	0.00	0.11	1.00	77.0	9.1	8.3
19	540	10.3	....	0.55	....	....	....	....	...	....
20	670	9.9	0.88	0.54	0.00	0.09	0.64	77.1	8.9	6.5
					PERIOD III					
21	1360	16.3	....	0.56	0.00?	. .	1.29	....	...	8.0
22	1390	17.9	0.94	0.53	0.08	0.12	0.90	85.8	5.2	5.0
23	1500	16.3	0.82	0.48	0.02	0.12	0.76	86.5	5.0	4.7
24	1400	16.3	0.79	0.54	0.03	0.12	0.87	85.6	4.9	5.4
					PERIOD IV					
25	1130	13.0	0.63	0.53	0.05	0.10	0.83	83.6	4.9	6.4
26	1020	10.0	0.57	0.50	0.03	0.09	0.83	79.8	5.7	8.3
27	900	7.5	0.50	0.40	0.03	0.07	0.60	78.8	6.7	9.3
28	1240	8.1	0.56	0.47	0.00	0.07	0.50	80.5	6.8	6.1
29	1120	8.1	0.57	0.47	0.05	0.04	0.68	77.6	7.0	8.4
30	1350	7.0	0.52	0.45	0.03	0.05	0.52	77.6	7.4	7.4
					PERIOD V					
Day of Convalescence: 1, urine lost.										
2	1060	7.0	0.45	0.40	....	0.05	0.72	77.1	6.4	10.2
3	1260	7.3	0.46	0.45	....	0.03	0.45	81.0	6.3	6.2
4	1080	6.5	0.38	0.39	0.05	0.03	0.51	79.1	5.8	7.9
5	1040	5.1	0.37	0.31	0.00	0.03	0.63	73.7	7.3	12.4
6	1440	5.5	0.44	0.40	....	0.03	0.77	69.9	8.0	14.1
7	850	5.0	0.38	0.39	0.00	0.04	0.43	75.5	7.5	8.6
8	940	6.0	0.45	0.41	0.01	0.04	0.64	74.3	7.5	10.7

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 8.—PATIENT 2, U—H: AVERAGES FROM PERIODS

Figures given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food: Cal. Total.	Food: Cal. Per Kg. Fat.	Food: Cal. Per Kg. C. H.	Food: Nitrogen Gm.	Excretion N.	Balance N.	Urine: Kreatinin N.	Urine: Kreatin N.	Urine: Uric Acid N.	Urine: "Rest" N. Gm.	Urine: "Rest" N. Total N.	Kreatinin Coef.
						Period I							
6	104.0-103.4	31	17	10	9.7	18.6	— 8.9	0.64	0.18	0.13	1.10	6.4	10.6
						Period II*							
5	103.4-103.0	61	16	41	8.6	12.6	— 4.0	0.55	0.01	0.10	0.64	8.1	9.5
						Period III							
4	103.2-101.0	31	18	8	11.4	18.4	— 7.0	0.52	0.04	0.12	0.95	5.7	9.3
						Period IV*							
6	102.0-100.4	66	19	43	8.7	9.4	— 0.7	0.47	0.03	0.07	0.72	8.8	8.4
						Period V*							
7	Normal	71	24	42	10.1	7.6	+ 2.5	0.39	0.01	0.03	0.59	9.7	7.0

* First day of period omitted from average.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 9.—PATIENT 3, Z—O: TEMPERATURE AND FOOD

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein Gm.	Fat. Gm.	C. H Gm.
				Period I						
9	....	104.0	102.4	1950	...	590	3	86.0	113	687
10	60.0	103.6	102.0	2000	...	600	3	87.6	116	700
11	....	103.2	101.6	2000	...	600	3	87.6	116	700
12	....	103.2	101.0	2000	...	600	3	87.6	116	700
Average								87.2	115	697
				Period II						
13	60.6	103.6	101.4	2000	300	600	3	93.6	206	709
14	....	103.2	101.2	2000	300	600	3	93.6	206	709
15	....	102.8	101.0	2000	300	600	3	93.6	206	709
16	61.6	103.2	104.4	2000	300	600	3	93.6	206	709
17	61.3	103.6	101.2	2000	300	600	3	93.6	206	709
18	....	103.6	101.0	2000	300	600	3	93.6	206	709
Average								93.6	206	709
				Period III						
19	....	103.6	101.0	2000	300	...	3	93.6	206	109
20	....	103.6	100.6	2000	300	...	3	93.6	206	109
21	60.4	103.8	100.4	2000	300	...	3	93.6	206	109
22	....	103.4	100.2	2000	300	...	3	93.6	206	109
Average								93.6	206	109
				Period IV						
23	....	103.6	99.8	2000	300	670	3	93.6	206	779
24	....	103.4	100.4	2000	300	700	3	93.6	206	809
25	60.0	103.8	99.8	2000	300	750	3	93.6	206	859
26	....	104.8	100.4	2000	300	680	3	93.6	206	789
27	60.0	102.6	100.6	2000	300	690	3	93.6	206	799
28	....	101.8	99.8	1800	270	600	3	86.5	187	695
29	....	101.4	99.2	1800	270	600	3	86.5	187	695
30	....	101.6	99.4	1800	270	600	3	86.5	187	695
Average (excluding first day)								90.6	198	763
				Period V						
31	59.5	100.8	99.2	1800	270	600	3	86.5	187	695
32	....	100.4	98.6	1800	270	660	3	86.5	187	755
33	....	100.4	98.2	1800	270	660	3	86.5	187	755
Convalescence.										
1	....	99.4	98.4	1800	270	660	3	86.5	187	755
2	....	99.8	98.4	1800	270	660	3	86.5	187	755
3	....	99.6	97.8	1800	270	420	3	86.5	187	515
Average								86.5	187	705
				Period VI						
4	....	99.6	98.0	1800	270	...	3	86.5	187	98
5	....	99.6	98.0	1800	270	...	3	86.5	187	98
6	....	99.4	97.8	1800	270	...	3	86.5	187	98
7	....	99.2	97.6	1600	240	...	3	79.2	168	87
Average								84.7	182	95

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 10.—PATIENT 3, Z—O: DAILY NITROGEN BALANCE AND URINE

During Periods III, XIII and XIV, the food contained "somatose."

Day of Disease.	Calories Total.	Calories Per Kg.	Calories C. H. Cal. Per Kg.	Nitrogen Balance Intake Gm.	Nitrogen Balance Excretion* Gm.	Nitrogen Balance Balance.	Urine Volume c.c.	Urine Nitrogen Total.	Urine Nitrogen Kreatinin.	Urine Nitrogen Kreatin.
PERIOD I										
9	4220	70	47	13.7	15.8	— 2.1	780	13.8	0.67	0.02
10	4330	72	48	14.0	13.1	+ 0.9	640	11.0	0.59	0.03
11	4330	72	48	14.0	15.8	— 1.8	840	13.7	0.59	0.11
12	4330	72	48	14.0	14.5	— 0.5	1140	12.4	0.65	0.05
PERIOD II										
13	5200	85	48	15.0	15.2	— 0.2	1210	13.0	0.65	0.00
14	5200	85	48	15.0	....	......	....	....	....	....
15	5200	85	48	15.0	14.7	+ 0.3	1220	12.5	0.52	0.02
16	5200	85	48	15.0	14.0	+ 1.0	1260	11.8	0.55	0.04
17	5200	85	48	15.0	14.9	+ 0.1	1210	12.7	0.53	0.03
18	5200	85	48	15.0	16.6	— 1.6	1660	14.4	0.58	0.02
PERIOD III										
19	2750	45	7	15.0	21.8	— 6.8	2050	19.6	0.63	0.06
20	2750	45	7	15.0	21.5	— 6.5	1720	19.3	0.56	0.00
21	2750	45	7	15.0	24.4	— 9.4	1520	22.2	0.60	0.03
22	2750	45	7	15.0	25.9	—10.9	1730	23.7	0.61	0.00
PERIOD IV										
23	5490	91	53	15.0	21.7	— 6.7	1320	19.5	0.63	0.03
24	5620	94	55	15.0	17.3	— 2.3	1040	15.1	0.63	0.02
25	5820	97	59	15.0	15.9	— 0.9	1080	13.7	0.60	0.00
26	5530	92	54	15.0	16.5	— 1.5	1600	14.3	0.60	0.00
27	5580	93	55	15.0	19.9	— 4.9	1260	17.7	0.64	0.00
28	4940	82	47	13.8	17.3	— 3.4	1060	15.1	0.53	0.00
29	4940	82	47	13.8	16.7	— 2.8	900	14.5	0.51	0.05
30	4940	82	47	13.8	17.9	— 4.0	1100	15.7	0.53	0.02
PERIOD V										
31	4940	83	48	13.8	12.4	+ 1.4	790	10.3	0.43	0.01
32	5180	87	52	13.8	14.2	— 0.4	880	12.1	0.50	....
33	5180	87	52	13.8	13.9	— 0.1	840	11.8	0.52	....
1	5180	87	52	13.8	11.8	+ 2.0	740	9.7	0.45	....
2	5180	87	52	13.8	11.6	+ 2.1	700	9.5	0.47	....
3	4200	71	35	13.8	11.6	+ 2.1	860	9.5	0.45	....
PERIOD VI										
4	2490	42	7	13.8	13.5	+ 0.3	1340	11.4	0.44	....
5	2490	42	7	13.8	13.0	+ 0.8	1210	10.9	0.45	....
6	2490	42	7	13.8	14.2	— 0.4	1600	12.1	0.46	....
7	2240	38	6	12.7	15.0	— 2.3	2000	12.9	0.54	....

* "Excretion"=Total nitrogen of urine + 15 per cent. of food-nitrogen.

TABLE 11—PATIENT 3, Z—O: AVERAGES FROM PERIODS

Figures are given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food Cal. Per Kg. Total.	Food Cal. Per Kg. Fat.	Food Cal. Per Kg. C. H.	Food Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.	Kreatin N.	Kreatinin Coef.
PERIOD I										
4	104. -103.2	72	18	48	13.9	14.8	—0.9	0.63	0.05	10.5
PERIOD II										
6	103.6-102.8	85	32	48	15.0	15.2	—0.2	0.56	0.02	9.2
PERIOD III										
4	103.8-103.4	45	32	7	15.0	23.5	—8.5	0.60	0.02	10.0
PERIOD IV *										
8	104.8-101.4	89	31	52	14.5	17.3	—2.8	0.58	0.01	9.6
PERIOD V										
6	100.8- 99.4	83	29	48	13.8	12.6	+1.2	0.47	....	7.9
PERIOD VI										
4	Normal	41	28	7	13.5	13.8	(—2.3) —0.3	0.47	....	7.8

* First day of period omitted from average.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 12.—PATIENT 3, Z—O: DETERMINATIONS MADE IN "COMPOSITE" URINES

Figures given for 24 hours.

Total. N. of Urine.	NH_3 N.	Uric Acid. N.	"Rest." N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N. Urea.	Per Cent. Total N. NH_3	Per Cent. Total N. "Rest."	Sulphur Gm. Total.	Sulphur Gm. Inorganic.	Sulphur Gm. Ethe-real.	Sulphur Gm. Neutral.	Per Cent. of Total S. Inor-ganic.	Per Cent. of Total S. Ethe-real.	Per Cent. of Total S. Neutral	Indi-can.	Sugar.	Al-bumin.	Titrated Acidity. c.c. $\frac{N}{10}$	Chlorin. Gm.	$\frac{\text{Total N.}}{100\times\text{Tot. S.}}$
									PERIOD I											
12.7	1.91	0.24	1.00	23	71.9	15.0	7.9	1.005	0.726	0.040	0.239	72.2	4.0	23.8	0	Trace	Slight +	520	2.6	7.9
									PERIOD II											
13.0	1.25	0.24	0.79	38	78.4	9.6	6.1	0.925	0.710	0.037	0.178	76.8	4.0	19.2	0	0	Trace	543	2.2	7.1
									PERIOD III											
21.0	0.86	0.22	1.09	47	86.9	4.1	5.2	1.408	1.129	0.069	0.210	80.2	4.9	14.9	10	0	Trace	772	2.8	6.7
									PERIOD IV											
15.6	1.09	0.22	1.14	..	79.6	7.0	7.3	1.155	0.919	0.055	0.181	79.5	4.8	15.7	15	Trace	0	610	2.7	7.4
									PERIOD V											
10.4	0.77	0.12	0.70	..	79.8	7.5	6.7	0.746	0.580	0.061	0.105	77.7	8.2	14.1	3	0	0	540	2.7	7.2
									PERIOD VI											
11.5	0.72	0.21	0.62	..	82.2	6.3	5.5	0.810	0.589	0.076	0.145	72.7	9.4	17.9	20	0	0	550	3.6	7.1

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

it is surprising that in this period, when much body nitrogen was being lost, the muscle protein was not being in part drawn on. It may be that the muscles are protected until the circulating protein has sustained a certain loss, or in this instance the muscles may have been protected during this period of four days by a reserve supply of glycogen accumulated during the previous periods. This explanation is not wholly satisfactory; but the fact remains that those of our subjects who were not given diets of high caloric value excreted, as a rule, much kreatin at the time when they were losing much body protein, while those who received food of high fuel value excreted much less kreatin and, even on withdrawing fat or carbohydrate, these latter patients showed, as a rule, no very considerable amounts of kreatin in the urine. And if our premise is correct, that the appearance of endogenous kreatin in the urine indicates the destruction of muscle protein, the conclusion is warranted that by the diets of large caloric value we in some way protect the muscle tissues from this pathologic katabolism.

In the fourth period much carbohydrate was again added, the food representing 89 calories per kg., 52 of which were in the form of carbohydrate. Excluding the first day of the period, the average balance was minus 2.8 gm. of nitrogen. Why the loss was greater here than in Period II is not clear, but it was much less than in Period III.

During half of Period V the subject had a normal temperature. With food equivalent to 83 calories per kg. there was an average daily gain of 1.2 gm. nitrogen. In Period VI most of the carbohydrate was again withdrawn and the nitrogen excretion rose, giving on the last day a minus balance of 2.3 gm. nitrogen. The temperature was normal and the food contained 13.5 gm. nitrogen and 41 calories per kg. The average balance (— 0.3 gm.) does not fairly represent the period because of the effect, during the first days, of the carbohydrate stored from the preceding period.

Patient 4.—W—d, male, aged 23, hotel clerk, well-nourished, taken ill one week before admission. Illness severe. Fever lasted twenty-six days, with mild relapse of seven days' duration. Blood-culture negative. The serum did not react to the typhoid bacillus but was not tried against the intermediates. The whole clinical picture, however, was that of typhoid fever.

The experiment with this patient is to some extent the opposite of the last described (Z—o), and again shows very strikingly the great protection from the loss of body protein afforded by food rich in carbohydrate.

The daily detailed results are given in Tables 13 and 14; Table 15 contains the averages of periods for the nitrogen balance, etc.; and

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 13.—PATIENT 4, W—D: TEMPERATURE AND FOOD

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk.	Lactose.	Toast.	Butter.	Protein.	Fat.	C. H.
				PERIOD I						
10	....	104.4	102.6	2160	...	...	..	71.3	108	108
11	....	104.4	103.2	2160	...	...	..	71.3	108	108
12	....	103.8	102.6	2400	...	...	..	79.2	120	120
13	63.?	103.6	102.0	2340	...	...	..	77.2	116	116
14	....	103.6	102.0	2400	...	...	..	79.2	120	120
15	....	103.6	102.4	2400	...	...	..	79.2	120	120
16	....	103.4	101.8	2400	...	...	..	79.2	120	120
17	....	103.2	101.8	2400	...	...	..	79.2	120	120
18	....	102.6	101,6	2400	...	...	..	79.2	120	120
Average								78.9	119	119
				PERIOD II						
19	....	102.8	101.0	2400	450	...	..	79.2	120	570
20	....	102.4	101.0	2400	405	...	..	79.2	120	525
21	....	101.0	99.6	2400	450	...	..	79.2	120	570
22	....	102.2	99.8	2400	585	...	..	79.2	120	705
23	....	100.6	99.6	2400	600	...	..	79.2	120	720
24	61.0	100.6	99.0	2310	560	...	..	76.2	116	676
Average								78.7	119	628
				PERIOD III						
Normal Temperature.										
1	....	99.8	98.8	2400	...	...	..	79.2	120	120
2	....	99.4	98.8	2400	...	...	..	79.2	120	120
3	60.2	99.2	98.4	2400	...	...	..	79.2	120	120
4	59.8	98.8	98.0	2400	...	...	..	79.2	120	120
5	....	100.0	98.2	2400	...	...	..	79.2	120	120
Relapse.										
1	....	100.8	99.2	2400	...	90	4	89.0	123	174
Average								79.2	120	120
				PERIOD IV						
2	....	102.4	99.4	2400	505	90	8	89.0	127	679
3	....	102.8	100.6	2400	600	90	48	89.0	161	774
4	61.6	102.8	100.8	2400	600	60	32	85.8	147	756
5	....	101.2	100.0	2400	600	90	24	89.0	140	756
6	61.4	100.2	99.0	2400	600	90	24	89.0	140	756
Convalescence.										
	....	99.8	98.6	2400	600	90	24	89.0	140	756
2	62.3	99.6	98.0	2400	600	90	24	89.0	140	756
3	....	99.6	98.0	2400	600	90	16	89.0	134	756
Average								88.5	143	754
				PERIOD V						
4	62.7	99.2	98.0	2400	...	90	24	89.0	140	174
5	....	99.4	98.0	2400	...	90	24	89.0	140	174
6	....	99.2	98.0	2160	...	90	16	81.2	121	162
7	....	99.6	97.6	2400	...	120	24	93.4	140	192
8	63.0	99.4	97.8	2400	...	120	48	93.4	161	192
9	....	99.4	97.6	2400	...	120	48	93.4	161	192
Average								90.1	145	182

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 14—PATIENT 4, W—D: DAILY NITROGEN BALANCE AND URINE

Day of Disease.	Calories Total.	Calories Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance Intake.	Nitrogen Balance Excretion.	Nitrogen Balance Balance.	Urine Volume c.c.	Urine Nitrogen as Total.	Urine Nitrogen as Kreatinin.	Urine Nitrogen as Kreatin.
					PERIOD I *					
10	1740	28	07.0	11.4	....	......	1010	12.4	0.78	....
11	1740	28	07.0	11.4	18.0	— 6.6	1320	16.7	0.67	....
12	1930	31	07.8	12.7	25.2	—12.5	2300	23.9	0.82	....
13	1870	30	07.5	12.3	25.0	—12.7	1570	23.7	0.68	....
14	1930	31	07.8	12.7	24.7	—12.0	2330	23.4	0.70	....
15	1930	31	07.8	12.7	23.9	—11.2	2300	22.6	0.69	....
16	1930	31	07.8	12.7	22.9	—10.2	2550	21.6	0.65	....
17	1930	31	07.8	12.7	23.3	—10.6	2100	22.0	0.62	....
18	1930	31	07.8	12.7	22.6	— 9.9	1660	21.3	0.66	....
					PERIOD II					
19	3770	60	38.0	12.7	....	......	2060	19.7	0.60	0.05
20	3600	57	35.0	12.7	....	......	2210	16.4	0.59	0.02
21	3770	60	38.0	12.7	....	......	1660	14.9	0.63	....
22	4320	70	47.0	12.7	13.6	— 0.9	1320	11.7	0.45	....
23	4390	72	48.0	12.7	13.3	— 0.6	2000	11.4	0.48	....
24	4160	68	45.0	12.2	14.2	— 2.0	1790	12.4	0.49	....
					PERIOD III					
Normal Temperature.										
1	1930	32	08.0	12.7	....	......	2300	13.9	0.46	....
2	1930	32	08.0	12.7	17.0	— 4.3	2050	15.1	0.45	....
3	1930	32	08.0	12.7	16.7	— 4.0	2080	14.8	0.44	....
4	1930	32	08.0	12.7	16.3	— 3.6	2010	14.4	0.43	....
5	1930	32	08.0	12.7	15.3	— 2.6	2000	13.4	0.45	....
Relapse.										
1	2220	37	12.0	14.2	15.9	— 0.9	1720	13.0	0.54	0.00
					PERIOD IV					
2	4330	72	46.0	14.2	....	......	1820	11.2	0.61	0.00
3	5040	83	52.0	14.2	11.0	+ 3.2	2000	8.9	0.61	0.00
4	4830	79	50.0	13.7	10.3	+ 3.4	1930	8.1	0.57	0.00
5	4760	78	50.0	14.2	10.8	+ 3.4	1720	8.7	0.56	0.00
6	4760	78	50.0	14.2	10.5	+ 3.7	1730	8.4	0.47	0.03
Convalescence.										
1	4760	77	50.0	14.2	11.1	+ 3.1	1320	9.0	0.47	0.02
2	4760	77	50.0	14.2	10.3	+ 3.9	1730	8.2	0.44	....
3	4710	76	50.0	14.2	9.8	+ 4.4	1420	7.7	0.45	0.00
					PERIOD V					
4	2380	38	11.0	14.2	....	......	1620	9.2	0.43	0.02
5	2380	38	11.0	14.2	11.9	+ 2.3	1770	9.8	0.41	0.00
6	2130	34	11.0	13.0	12.0	+ 1.0	1600	9.9	0.45	0.01
7	2470	39	13.0	14.9	12.8	+ 2.1	2300	10.6	0.45	0.02
8	2670	43	13.0	14.9	12.5	+ 2.4	2000	10.3	0.46	0.00
9	2670	43	13.0	14.9	13.5	+ 1.4	2180	11.3	0.43	0.05

* Feces in Period I contained 1.26 gm. nitrogen per day.
"Excretion in Period I=total nitrogen of urine + 1.26 gm.
"Excretion in other periods=total nitrogen of urine + 15 per cent. of food nitrogen.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Table 16 the results of sulphur and nitrogen partitions in composite urines representing the several periods.

During the first nine days of the experiment, which began on the tenth day of the disease and continued for thirty-five days, the patient received a strict milk diet, so frequently used in typhoid fever. The food was equivalent to 31 calories per kg. and contained 12.6 gm. of nitrogen. Excluding the first two days of this period, which clearly show the effect of food of high fuel value given during several days before the beginning of the experiment, the average loss per day was 11.3 gm. of nitrogen. Kreatin unfortunately was not determined during this period. During the following six days the food remained the same, except for the addition of much carbohydrate in the form of lactose, the average

TABLE 15.—PATIENT 4, W—D: AVERAGES FROM PERIODS

No. of Days.	Range of Maximum Temp. F. During Period.	Food: Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.
				Period I				
9	104.4-102.6	31	18	8	12.6	23.9*	—11.3	0.69
				Period II				
6	102.8-100.6	65	18	42	12.6	13.7†	— 1.1	0.54
				Period III				
6	99.8-100.8	32	18	8	12.7	16.3‡	— 3.6	0.44
				Period IV				
8	102.4- 99.6	77	21	50	14.2	10.5§	+ 3.7	0.51
				Period V				
6	Normal	40	22	12	14.4	12.6	+ 1.8	0.44

* First two days of period excluded from average.
† First three days of period excluded from average.
‡ First and last days of period excluded from average.
§ First day of period excluded from average.

fuel value of the diet then being 65 calories per kg. There resulted a rapid decline of the nitrogen excretion so that, on the last three of the six days of the period, the subject lost only 1.1 gm. nitrogen each day. This result is perhaps due in part to the simultaneous fall in temperature; but that the added carbohydrate was very largely responsible is shown by the next period (III), when the patient had a normal temperature except on one day. The lactose was withdrawn and there was at once an increase in the nitrogen excretion, giving an average minus balance of 3.6 gm.[32]

32. The first and last days of this period are excluded from the average; the first because of the effect of glycogen stored in the preceding period, the last because of the increase in protein intake.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 16.—PATIENT 4, W—D: DETERMINATIONS MADE IN "COMPOSITE" URINES—AVERAGES FOR 24 HOURS

Total. N.	NH_3 N.	Uric Acid. N.	"Rest." N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N. Urea.	Per Cent. Total N. NH_3	Per Cent. Total N. "Rest."	Sulphur Gm. Total.	Sulphur Gm. Inorganic.	Sulphur Gm. Ethereal.	Sulphur Gm. Neutral.	Per Cent. of Total S. Inorganic.	Per Cent. of Total S. Ethereal.	Per Cent. of Total S. Neutral.	Chlorin. Gm.	Titrated Acidity. c.c. $\frac{N}{10}$	Indican.	Sugar.	Albumin.	$\frac{100 \times \text{Tot. S.}}{\text{Total N.}}$
									PERIOD I											
21.0	0.93	0.29	1.10	91	85.6	4.4	5.2	1.570	1.090	0.090	0.390	69.5	5.7	24.8	1.9	420	10	0	Trace	7.5
									PERIOD II											
14.4	0.65	0.23	1.13	37	82.7	4.4	7.5	1.000	0.731	0.034	0.235	73.1	3.4	23.5	1.5	250	20	0	0	7.0
									PERIOD III											
14.2	0.36	0.19	0.56	53	89.0	2.5	4.0	0.901	0.704	0.032	0.165	78.2	3.5	18.3	1.8	210	8	0	0	6.35
									PERIOD IV											
8.7	0.40	0.17	0.77	30	78.5	4.7	8.8	0.638	0.461	0.048	0.129	72.3	7.5	20.2	2.3	240	10	0	0	7.35
									PERIOD V											
10.3	0.32	0.18	0.60	87	85.3	3.1	5.8	0.672	0.521	0.005?	0.146	77.4	0.8?	21.8	3.3	184	20	0	0	6.5

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Except for the one day on which the temperature rose to 100.8 F. and which is excluded from the average, this was clinically a period (III) of convalescence; and yet with food equivalent to 32 calories per kg. and to 12.7 gm. of nitrogen the subject lost 3.6 gm. of body nitrogen per day. The conclusion seems warranted that the food was not of sufficient fuel value to prevent or compensate for the excessive protein destruction which was still taking place. It is obvious that the excessive protein katabolism of this period was not due to pyrexia since the temperature was normal.

The following period (IV) includes five days of a relapse and three days of normal temperature. Food of high fuel value, 77 calories per kg., was given throughout and the subject gained nitrogen on each day of the period, the average balance being plus 3.7 gm. Practically no kreatin was excreted. The interpretation seems wholly justified that the large food-supply, consisting chiefly of carbohydrates, completely prevented in this instance the excess of protein katabolism which undoubtedly would otherwise have taken place.

During Period III the temperature was normal, but the subject lost 3.6 gm. nitrogen each day on a diet containing 32 total calories and 8 carbohydrate calories per kg.; during Period IV, in spite of relapse during five of the eight days, he gained 3.7 gm. nitrogen each day on a diet containing 77 total calories and 50 carbohydrate calories per kg. As compared with Period III there was a sparing during Period IV of at least 7.3 gm. (3.7 — [— 3.6] = 7.3) of nitrogen per day, which gain is presumably wholly referable to the difference in diet.

Food.	Period III gm.	Period IV gm.
Total cal. per kg	32.0	77.0
Total cal. per kg	32.0	77.0
Carbohydrate cal. per kg	8.0	50.0
Fat—cal. per kg	18.0	21.0

The only marked difference in the diets is in the carbohydrate calories. It appears fair to interpret these figures as showing that the addition of 42 carbohydrate calories per kg. has in this patient spared 7.3 gm. nitrogen or 45.5 gm. of body protein.

In the last period, with normal temperature, the subject showed an average plus balance of 1.8 gm. of nitrogen on a diet equivalent to 40 calories per kg. The increased katabolism had probably ceased and the food was, under the conditions, more than sufficient to maintain equilibrium. The situation here is in sharp contrast with that in Period III when, with normal temperature and food equivalent to 32 calories per

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

kg., a minus balance of 3.6 gm. was observed; in the latter period the pathologic increase in katabolism was doubtless still taking place.

The comparison of the results in these two periods of normal temperature again illustrates the importance of the intensity of the katabolic process in determining the degree of sparing of body protein accomplished by any given food. This factor explains the difficulty in comparing, quantitatively, a result from one subject with that of another, or even the results from two different periods on the same subject.

Patient 5.—B—t, male, aged 23, driver, well-nourished, admitted to hospital on seventh day of disease. Positive blood-culture. Illness moderately severe.

This experiment was intended primarily to determine the relative value of fat versus carbohydrate in protecting the body protein in fever, but it was not carried out as planned and the conclusion on this point is not clear. The experiment does again show the marked effect of carbohydrate, and is of interest also for other reasons.

The experiment began on the ninth day of the disease and continued for thirty-four days, including fifteen days of the original fever and a relapse of eight days. The averages representing the five periods into which the experiment is divided are given in Table 19. Other data are given in Tables 17, 18 and 20.

During the first period of eight days at the height of the disease, the fuel value of the food averaged 56 calories per kg., of which 36 were in fat and 16 in carbohydrates. The subject lost 5.5 gm. nitrogen per day. In the next period (II) the fat was in part withdrawn and more carbohydrate added, so that the average daily food equaled 69 calories per kg., of which 39 were in carbohydrate and 24 in fat. The loss of nitrogen was decreased by 2 gm. The situation is, however, complicated by the lower temperature and the higher total caloric and protein value of the food in the second period; and no conclusion seems to be justified regarding the relative value of fat versus carbohydrate in retarding the loss of nitrogen. There was, however, a marked sparing effect in both of these periods, as shown by Period III, when the temperature was lower than before. The food contained practically the same amount of nitrogen (16.1 gm.) as in Period II, but was equivalent to only 39 calories per kg.; excluding the first day, the average loss was 7.8 gm. nitrogen. On two days of this period the temperature remained below 100 F., while on two other days the highest temperature was only 100.2 and 100.4 F., respectively. On the last day of the period a relapse set in and the temperature reached 101.6. Except on this last day, the patient might be considered clinically almost in the condition of convalescence, but with food, which under normal circumstances would have main-

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 17.—PATIENT 5, B—T: DAILY TEMPERATURE AND FOOD

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose Gm.	Toast Gm.	Butter Gm.	Somatose Gm.	Protein Gm.	Fat Gm.	C. H. Gm.
						Period I							
9	....	103.2	101.0	2070	90	1	110	...	24	..	77.4	138	216
10	....	103.8	102.2	1290	480	2	140	60	82	..	73.0	289	255
11	....	103.6	102.4	1320	480	2	140	60	96	..	74.0	292	240
12	75.?	103.2	100.6	1260	420	1	170	90	69	..	67.0	253	300
13	....	?	.....	1290	570	1	170	90	69	..	71.0	299	305
14	....	101.8	100.0	1290	600	1	170	90	69	..	71.0	308	306
15	....	101.8	99.0	1440	540	3	170	90	69	..	90.0	309	312
16	....	101.6	99.2	1320	810	3	160	90	100	..	91.0	410	294
Average											76.8	287	279
						Period II							
17	....	100.6	98.4	2000	...	3	540	90	100	..	97.5	201	694
18	74.?	100.4	98.8	2000	...	3	500	90	84	..	97.5	187	654
19	....	100.2	98.8	2100	...	3	560	120	75	..	104.0	185	737
20	....	100.0	99.8	2100	...	3	560	120	79	..	104.0	188	737
21	....	100.0	98.4	2040	...	3	560	120	79	..	102.0	185	734
22	73.0	100.4	98.6	2000	...	3	495	120	111	..	101.0	210	667
Average											101.0	193	704
						Period III							
23	....	100.2	98.6	2000	...	3	...	120	64	..	101.0	170	172
24	....	99.4	98.4	2000	...	3	...	120	80	..	101.0	184	172
25	72.9	99.8	98.0	2000	...	3	...	120	80	..	101.0	184	172
Relapse.													
1	72.7	100.4	98.4	2000	...	3	...	120	80	..	101.0	184	172
2	....	101.6	99.2	2000	...	3	...	120	80	..	101.0	184	172
Average											101.0	184	172
						Period IV							
3	....	?	.....	2000	...	3	...	120	80	60	147.0	184	172
4	73.0	102.2	100.8	2000	...	3	...	120	80	60	147.0	184	172
5	....	101.8	99.8	2000	...	3	...	120	80	50	131.0	184	172
Average											142.0	184	172
						Period V							
6	73.2	?	99.6	2000	...	3	600	120	80	..	101.0	184	772
7	....	100.8	99.4	2000	60	3	600	120	80	..	102.0	202	775
8	....	100.4	99.0	2000	...	3	600	120	80	..	101.0	184	772
Convalescence.													
1	73.1	99.8	98.0	1800	...	4	540	120	80	..	101.0	179	700
2	....	99.6	98.4	2000	...	4	600	120	80	..	108.0	189	772
3	73.9	99.6	98.0	2000	...	4	600	120	80	..	108.0	189	772
4	....	98.8	98.0	2000	...	4	600	120	80	..	108.0	189	772
5	....	99.8	98.0	2000	...	4	600	120	80	..	108.0	189	772
6	....	99.6	98.2	2000	...	4	600	120	80	..	108.0	189	772
7	74.8	99.8	98.0	2000	...	4	600	120	80	..	108.0	189	772
8	....	99.4	98.0	2000	...	4	600	120	80	..	108.0	189	772
9	....	99.6	98.0	2000	...	4	600	120	80	..	108.0	189	772
Average											107.0	188	765

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 18.—PATIENT 5, B—T: DAILY NITROGEN BALANCE AND URINE

Day of Disease.	Calories: Total.	Calories: Per Kg.	Calories: C. H. Cal. Per Kg.	Nitrogen Balance: Intake.	Nitrogen Balance: Excretion.*	Nitrogen Balance: Balance.	Urine: Volume c.c.	Urine: Nitrogen as Total.	Urine: Nitrogen as Kreatinin.	Urine: Nitrogen as Kreatin.
					PERIOD I					
9	2480	33	12.0	12.4	18.4	—6.0	655	16.5	0.80	....
10	4040	54	14.0	11.7	15.6	—3.9	630	13.9	0.68	....
11	4030	54	13.0	11.8	17.4	—5.6	920	15.6	0.77	....
12	3860	51	16.0	10.7	19.2	—8.5	1420	17.6	0.88	....
13	4320	58	17.0	11.3	17.0	—5.7	1080	15.3	0.81	....
14	4400	59	17.0	11.3	18.0	—6.7	880	16.3	0.82	....
15	4530	61	17.0	14.4	18.0	—3.6	950	15.8	0.74	....
16	5400	72	16.0	14.5	19.3	—4.8	1150	17.1	0.67	....
					PERIOD II					
17	5120	69	38.0	15.6	19.1	—3.5	1220	16.8	0.67	0.08
18	4820	65	36.0	15.6	18.3	—2.7	1310	16.0	0.63	0.08
19	5170	70	41.0	16.6	20.6	—4.0	1620	18.1	0.65	....
20	5200	70	41.0	16.6	20.4	—3.8	1520	17.9	0.61	....
21	5150	70	41.0	16.3	20.3	—4.0	1680	17.9	0.61	....
22	5100	70	38.0	16.1	19.7	—3.6	1580	17.3	0.62	....
					PERIOD III					
23	2740	38	9.6	16.1	....	.....	1570	17.5	0.59	....
24	2870	39	9.6	16.1	23.6	—7.5	1850	21.2	0.63	....
25	2870	39	9.6	16.1	23.8	—7.7	1700	21.4	0.63	....
Relapse.										
1	2870	39	9.6	16.1	24.6	—8.5	1900	22.2	0.65	....
2	2870	39	9.6	16.1	23.7	—7.6	1540	21.3	0.65	....
					PERIOD IV					
3	3020	41	9.6	23.5	27.2	—3.7	1850	23.7	0.89	....
4	3020	41	9.6	23.5	27.5	—4.0	2920	24.0	0.84	....
5	2950	40	9.6	21.0	28.9	—7.9	1820	25.4	0.80	....
					PERIOD V					
6	5290	72	43.0	16.1	....	.....	1500	19.5	0.72	....
7	5470	75	43.0	16.3	....	.....	1780	20.5	0.72	0.04
8	5290	72	43.0	16.1	17.4	—1.3	1550	15.0	0.61	0.07
Convalescence.										
1	4950	68	39.0	16.1	16.6	—0.5	1500	14.2	0.62	0.01
2	5370	73	43.0	17.3	17.7	—0.4	1320	15.1	0.59	0.05
3	5370	73	43.0	17.3	17.8	—0.5	1140	15.2	0.60	0.00
4	5370	73	43.0	17.3	17.6	—0.3	1460	15.0	0.62	0.00
5	5370	72	43.0	17.3	17.5	—0.2	1530	14.9	0.63	0.00
6	5370	72	43.0	17.3	17.4	—0.1	1430	14.8	0.67	....
7	5370	72	43.0	17.3	17.2	+0.1	1230	14.6	0.62	0.02
8	5370	72	43.0	17.3	17.4	—0.1	1540	14.8	0.57	0.07
9	5370	72	43.0	17.3	17.1	+0.2	1520	14.5	0.62	0.00

* "Excretion"=total nitrogen of urine + 15 per cent. of food-nitrogen.

TABLE 19.—PATIENT 5, B—T: AVERAGES FROM PERIODS

No. of Days.	Range of Maximum Temp. F. During Period.	Food: Cal. Per Kg. Total.	Food: Cal. Per Kg. Fat.	Food: Cal. Per Kg. C. H.	Food: Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.	Kreatin N.
					PERIOD I				
8	103.8-101.6	56	36	16	12.3	17.8	—5.5	0.77	....
					PERIOD II				
6	100.6-100.0	69	24	39	16.2	19.7	—3.5	0.63	0.08
					PERIOD III				
5	101.6- 99.4	39	23	9	16.1	23.9*	—7.8	0.64	....
					PERIOD IV				
3	102.2-101.8	40	23	9	22.7	28.9†	—6.2	0.84	....
					PERIOD V				
12	100.8- 99.4	72	24	43	17.1	17.3‡	—0.2	0.63	0 02

* First day of period excluded from average.
† Excretion of last day taken as representing period.
‡ First two days of period excluded from average.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 20.—PATIENT 5, B—T: DETERMINATIONS MADE IN "COMPOSITE URINES

Figures given are for 24 hours.

Total. N.	NH_3 N.	Uric Acid. N.	"Rest." N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N. Urea.	Per Cent. Total N. NH_3	Per Cent. Total N. "Rest."	Sulphur Gm. Total.	Sulphur Gm. Inorganic.	Sulphur Gm. Ethereal.	Sulphur Gm. Neutral.	Per Cent. of Total S. Inorganic.	Per Cent. of Total S. Ethereal.	Per Cent. of Total S. Neutral.	Chlorin. Gm.	Titrated Acidity. c.c. $\frac{N}{10}$	Indican.	Sugar.	Albumin.	$\frac{100 \times \text{Tot. S.}}{\text{Total N.}}$
									Period I											
16.0	1.49	0.21	0.52	27	80.7	9.3	3.2	1.140	0.845	0.015	0.280	74.1	1.3	24.6	2.3	530	30	0	Trace	7.1
									Period II											
17.0	0.90	0.21	0.70	44	85.1	5.3	4.1	1.192	0.941	0.047	0.204	79.0	3.9	17.1	4.1	660	80	0	0	7.0
									Period III											
20.5	1.35	0.23	1.60	73	81.3	6.6	7.8	1.353	.....	.....	0.190	...	...	14.0	...	...	..	0	0	6.6
									Period IV											
24.3	0.77	0.27	2.30	81	82.8	3.2	9.5	1.660	1.405	0.040	0.215	84.7	2.4	12.9	4.3	615	6	0	0	6.8
									Period V											
15.5	0.89	0.22	0.60	73	84.6	5.7	3.9	1.150	0.928	0.032	0.190	80.7	2.8	16.5	4.5	640	20	0	0	7.4

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

tained equilibrium, he lost more than twice as much body nitrogen as in the previous period (II). Even assuming the intensity of the katabolic processes to have been no greater in Period II than in III—and it probably was greater—the additional carbohydrate of Period II (equivalent to about 30 cal. per kg.) appears to have accomplished a sparing of 4.3 gm. nitrogen per day.

During the next three days (Period IV), in the midst of a relapse, the protein intake was increased by the addition of "somatose" to between 21 and 23.5 gm. nitrogen, the total fuel value of the diet remaining at about 40 calories per kg. On account of the lag in excretion, the first two days of the period are excluded and the last day is taken to represent the period. On this day the loss of nitrogen was 7.9 gm., indicating no advantage from the increase of protein intake, though this conclusion is rendered somewhat uncertain by the relapse and the consequent probable further increase in the katabolism of body protein.

During at least the last nine of the twelve days of Period V the subject was in what would ordinarily be called a convalescent condition. His temperature was normal, and clinically his disease was at an end. But, in spite of diet of high caloric value (72 calories per kg.) and containing 17.1 gm. of nitrogen, there was a small loss of body nitrogen throughout the period. A loss of 0.2 gm. of nitrogen per day, of course, is not great and, if less than the estimated 15 per cent. of the food nitrogen was excreted in the feces, there may even have been an actual slight gain of nitrogen. But this difference is of little consequence; the significant thing is that the subject was not gaining three or four grams of nitrogen each day which, according to other experiments, he should have done on such a diet unless a pathologic increase in metabolism was persisting after the fall of temperature. We are inclined to interpret the result in this way: that in this period, as in Period III, the pathologic increase in katabolism continued after the temperature became normal and after the disease was apparently at an end, and that a considerable loss of body nitrogen was prevented by the large food-supply.

Patient 6.—L—d, male, aged 32, waiter, fairly well nourished. Moderately severe illness, with a relapse of thirteen days. Positive serum reaction with typhoid bacilli.

The experiment began on the seventeenth day of the disease, almost at the end of fever, and continued for forty-three days, including a relapse of thirteen days' duration. The detailed results are given in Tables 21, 22 and 23, and the averages of periods in Table 24.

During the first period of four days, representing the end of the fever, the patient received food equivalent to 24 calories per kg. and

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 21.—PATIENT 6, L—D: DAILY TEMPERATURE AND FOOD

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food Milk.	Cream.	Eggs.	Lactose.	Toast.	Protein.	Fat.	C. H.
					PERIOD I						
17	64.5	102.2	99.0	1770	...	..	...	..	58.5	88.5	88.5
18	....	101.4	99.4	1920	...	..	...	..	63.4	96.0	96.0
19	64.0	100.0	99.8	1920	...	..	...	..	63.4	96.0	96.0
20	....	99.4	98.2	1920	...	..	...	..	63.4	96.0	96.0
Average									62.2	94.0	94.0
					PERIOD II						
Normal Temperature.											
1	....	98.8	97.6	1660	90	..	90	..	57.3	111.0	176.0
2	63.0	99.4	97.8	1680	180	..	210	..	59.0	138.0	300.0
3	....	99.0	98.0	2000	230	..	285	..	70.6	169.0	392.0
4	....	98.6	98.2	1680	120	..	300	..	58.0	120.0	387.0
5	....	98.6	98.2	2000	285	..	285	..	71.7	185.0	393.0
6	62.3	99.2	98.2	1700	180	1	300	..	66.8	144.0	390.0
Average (excluding first day)									65.2	151.0	372.0
					PERIOD III						
7	....	99.6	97.8	1460	180	3	270	..	73.4	143.0	348.0
8	....	99.6	98.4	1210	165	3	225	..	65.0	126.0	290.0
Relapse.											
1	63.5	101.6	98.2	1910	285	3½	360	60	100.5	200.0	499.0
2	....	103.0	99.6	1680	225	3	315	60	88.0	167.0	442.0
3	64.0	103.2	100.6	1890	315	..	360	..	68.6	188.0	464.0
4	63.2	102.8	101.2	1950	180	2	360	..	82.3	162.0	464.0
Average (excluding first day)									80.9	169.0	432.0
					PERIOD IV						
5	....	103.4	100.4	1910	270	1	345	..	75.6	152.0	448.0
6	63.7	103.4	101.2	1760	295	..	295	..	64.0	176.0	393.0
7	....	104.2	101.6	1710	405	2	210	..	78.6	220.0	308.0
8	64.0	103.4	101.4	1160	600	2	105	..	64.7	248.0	180.0
9	....	102.0	100.4	830	630	2	225	..	54.4	240.0	285.0
Average									67.5	207.0	323.0
					PERIOD V						
10	64.0	101.6	100.0	960	600	6	365	..	87.0	260.0	430.0
11	....	101.5	99.6	1080	360	6	570	..	86.0	194.0	635.0
12	....	100.0	99.4	1080	360	6	690	..	86.0	194.0	755.0
13	....	99.8	98.8	1080	360	5.5	690	..	83.0	191.0	755.0
Convalescence.											
	....	99.4	99.0	1080	360	6	690	..	86.0	194.0	755.0
2	....	99.4	98.6	1080	360	6	540	..	86.0	194.0	605.0
3	....	99.2	98.6	1080	360	6	690	..	86.0	194.0	755.0
4	....	99.4	98.8	1120	300	6	690	..	86.0	178.0	755.0
Average (excluding last day. Urine lost)									86.0	203.0	670.0
					PERIOD VI						
5	64.5?	99.6	98.6	1080	360	6	...	..	86.0	194.0	65.0
6	....	99.8	98.4	1080	360	6	...	..	86.0	194.0	65.0
7	....	99.6	98.4	1190	250	6	...	..	87.0	166.0	67.0
8	65.1	99.8	98.0	1080	360	6	...	..	86.0	194.0	65.0
9	....	99.6	98.2	1080	360	6	...	..	86.0	194.0	65.0
Average									86.0	192.0	65.0
					PERIOD VII						
10	....	99.6	98.6	1080	360	6	540	..	86.0	194.0	605.0
11	66.7	99.6	98.2	1080	360	6	690	..	86.0	194.0	755.0
12	....	99.4	98.4	1080	360	6	660	..	86.0	194.0	725.0
13	68.1	99.6	98.6	930	350	6	690	..	81.0	184.0	746.0
14	....	100.0	97.8	1080	360	6	440	..	86.0	194.0	505.0
15	....	99.6	97.6	1080	360	6	360	..	86.0	194.0	425.0
16	....	99.6	98.2	1080	360	6	360	..	86.0	194.0	425.0
17	....	100.0	98.4	1080	360	6	360	..	86.0	194.0	425.0
18	....	100.4	98.2	900	360	6	360	..	80.0	185.0	416.0
19	....	99.2	98.4	1080	360	6	360	..	86.0	194.0	425.0
Average									84.9	192.0	545.0

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 22.—PATIENT 6, L—D: DAILY ANALYSES OF URINE

Day of Disease.	Volume c.c.	Urine Nitrogen as— Total	NH₃	Kreatinin.	Kreatin.	U. A.	"Rest."	—Per Cent. Total N.— Urea	NH₃	"Rest."
				PERIOD I						
17	1590	16.5	0.95	0.47	0.07	0.30	0.80	84.4	5.7	4.8
18	Urine lost.									
19	1520	18.1	1.08	0.47	0.10	0.27	0.60	86.2	6.0	3.3
20	1930	15.8	0.97	0.36	0.16	0.24	0.60	85.3	6.2	3.8
				PERIOD II						
Normal Temperature.										
1	1900	15.5	0.91	0.40	0.14	0.22	0.63	85.2	5.9	4.1
2	1200	11.6	0.76	0.35	0.07	0.18	0.43	84.7	6.6	3.7
3	1380	10.9	0.73	0.34	0.08	0.17	0.68	81.7	6.7	6.3
4	1590	10.2	0.60	0.40	0.00	0.13	0.66	82.5	5.9	6.5
5	1440	8.1	0.56	0.39	0.00	0.12	0.52	80.7	6.8	6.4
6	1480	9.1	0.59	0.42	0.01	0.11	0.40	82.9	6.5	4.4
				PERIOD III						
7	Urine lost.									
8	1040	9.0	0.62	0.44	0.00	0.13	0.56	80.7	6.8	6.2
Relapse.										
1	840	11.4	0.72	0.50	0.00	0.13	0.60	82.7	6.3	5.3
2	2040	10.9	0.82	0.52	0.08	0.12	0.55	80.7	7.5	5.0
3	2340	10.4	0.86	0.49	0.13	0.14	0.55	79.2	8.3	5.3
4	1540	10.5	0.84	0.52	0.02	0.16	0.64	79.2	8.0	6.1
				PERIOD IV						
5	1940	12.9	0.96	0.53	0.00	0.19	0.75	71.1	7.4	5.8
6	1450	12.5	0.92	0.51	0.03	0.19	0.87	80.1	7.3	7.0
7	1940	14.6	1.23	0.56	0.03	0.20	0.94	79.8	8.4	6.5
8	2290	13.7	....	0.48	0.02	....	....	....	...	..
9	1920	11.5	....	0.45	0.01	....	....	....	...	...
				PERIOD V						
10	1640	10.1	....	0.43	0.00	....	....	....	...	...
11	2450	8.2	....	0.43	0.00	....	....	....	...	...
12	1600	7.7	....	0.39	0.00	....	....	....	...	...
13	1900	7.7	....	0.40	0.00	....	....	....	...	...
1	1600	7.6	....	0.40	0.00	....	....	....	...	...
3	1740	7.4	....	0.40	0.04	....	....	....	...	...
3	1580	6.8	....	0.36	0.01	....	....	....	...	...
4	Urine lost.									
				PERIOD VI						
5	2330	9.6	....	0.41	....	....	....	....	...	...
6	1950	10.9	....	0.36	....	....	....	....	...	...
7	2060	13.0	....	0.46	....	....	....	....	...	...
8	1840	11.1	....	0.42	....	....	....	....	...	...
9	1770	10.3	....	0.41	....	....	....	....	...	...
				PERIOD VII						
10	2310	9.7	....	0.43	....	....	....	....	...	...
11	2220	7.3	....	0.41	....	....	....	....	...	...
12	3400	7.2	....	0.45	....	....	....	....	...	...
13	2370	5.4	....	0.50	....	....	....	....	...	...
14	2360	6.5	....	0.50	....	....	....	....	...	...
15	2010	6.9	....	0.41	....	....	....	....	...	...
16	3300	....	....	0.45	....	....	....	....	...	...
17	2630	7.7	....	0.42	....	....	....	....	...	...
18	3010	7.3	....	0.43	....	....	....	....	...	...
19	2750	7.5	....	0.46	....	....	....	....	...	...

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 23.—PATIENT 6, L—D: DAILY NITROGEN BALANCE

Day of Disease.	Food: Total Calories.	Food: Cal. Per Kg.: Total.	Food: Cal. Per Kg.: From C. H.	Food: Nitrogen.	Excretion N.	Nitrogen Balance.
			PERIOD I			
17	1425	22	6	9.3	17.9	— 8.6
18	1545	24	6	10.1	....	......
19	1545	24	6	10.1	19.6	— 9.5
20	1545	24	6	10.1	17.3	— 7.2
			PERIOD II			
Normal Temperature.						
1	1985	31	11	9.2	16.9	— 7.7
2	2750	44	20	9.4	13.0	— 3.6
3	3470	55	26	11.3	12.6	— 1.3
4	2940	47	25	9.3	11.6	— 2.3
5	3620	58	26	11.5	9.8	+ 1.7
6	3210	51	26	10.7	10.7	+ 0.0
			PERIOD III			
7	3060	48	23	11.7	....	......
8	2575	41	19	10.4	10.6	— 0.2
Relapse.						
1	4320	68	32	16.1	13.8	+ 2.3
2	3670	57	29	14.1	13.0	+ 1.1
3	3930	61	30	11.0	12.0	— 1.0
4	3750	59	30	13.2	12.5	+ 0.7
			PERIOD IV			
5	3560	56	29	12.1	14.7	— 2.6
6	3510	55	25	10.2	14.0	— 3.8
7	3620	57	20	12.6	16.5	— 3.9
8	3310	52	12	10.3	15.2	— 4.9
9	3620	57	18	8.7	14.8	— 6.1
			PERIOD V			
10	4540	71	28	13.9	12.2	+ 1.7
11	4750	74	41	13.7	10.3	+ 3.4
12	5250	82	48	13.7	9.8	+ 3.9
13	5230	82	48	13.2	9.7	+ 3.5
Convalescence.						
1	5250	82	48	13.7	9.7	+ 4.0
2	4630	72	39	13.7	9.5	+ 4.2
3	5250	82	48	13.7	8.9	+ 4.8
4	5100	79	48	13.7	....	......
			PERIOD VI			
5	2420	37	4	13.7	11.1	+ 2.6
6	2420	37	4	13.7	12.4	+ 1.3
7	2170	34	4	13.9	14.5	— 0.6
8	2420	37	4	13.7	12.6	+ 1.1
9	2420	37	4	13.7	11.8	+ 1.9
			PERIOD VII			
10	4630	70	38	13.7	11.7	+ 2.0
11	5250	79	46	13.7	9.3	+ 4.4
12	5120	76	44	13.7	9.2	+ 4.5
13	5100	76	45	13.0	7.3	+ 5.7
14	4220	62	30	13.7	8.5	+ 5.2
15	3900	58	26	13.7	8.9	+ 4.8
16	3900	58	26	13.7	....	......
17	3900	58	26	13.7	9.7	+ 4.0
18	3760	55	25	12.8	9.2	+ 3.6
19	3900	58	26	13.7	9.3	+ 4.4

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 24.—PATIENT 6, L—D: AVERAGES FROM PERIODS

Figures given are for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food: Cal. Per Kg. Total.	Food: Cal. Per Kg. Fat.	Food: Cal. Per Kg. C. H.	Food: Nitrogen. Gm.	Excretion N.	Balance N.	Urine: Kreatinin N.	Urine: Kreatin N.	Urine: NH_3 N. Gm.	Urine: NH_3 N. Per Cent. of Total N.	Urine: "Rest" N. Gm.	Urine: "Rest" N. Per Cent. of Total N.	Urine: Uric Acid. N.	Urine: Xanthin Bases Mg. Xanthin.	Kreatinin Coef.
							PERIOD I									
4	102.2- 99.4	24	13	6	10.0	18.3	—8.3	0.43	0.11	1.00	6.0	0.67	4.0	0.27	42‡	6.7
							PERIOD II									
6	Normal	51	22	24	10.4	11.5*	—1.1	0.38	0.03	0.65	6.5	0.54	5.4	0.14	48‡	6.0
							PERIOD II									
6	99.6-103.0	58	25	28	12.9	12.3	+0.6	0.51	0.06	0.81	7.8	0.58	5.6	0.14	..	8.0
							PERIOD IV									
5	103.4-102.0	55	30	21	10.8	14.6	—3.8	0.51	0.02	1.04†	7.7	0.85†	6.4	0.20	52‡	8.0
							PERIOD V									
8	101.6- 99.2	78	29	43	13.7	9.9	+3.8	0.40	0.00	....	...	....	...	0.16‡	..	6.2
							PERIOD VI									
5	Normal	37	27	4	13.7	12.5	+1.2	0.41	....	....	...	....	...	0.15‡	..	6.4
							PERIOD VII									
10	Normal	64	26	33	13.6	9.3	+4.3	0.45	....	....	...	....	...	0.13‡	..	6.7

* First day of period excluded from average.

† Average of first three days of period.

‡ Determination made in "composite" urines.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

containing 10 gm. of nitrogen. A daily minus balance of 8.3 gm. of nitrogen was found, and 0.11 gm. of kreatin-nitrogen was excreted. Both of these results are of very considerable interest, showing, as they do, that, with a somewhat inadequate food-supply, the protein katabolism was still very markedly increased, when the disease, as indicated by the temperature and clinical condition of the subject, had practically run its course. Attention is particularly called to the considerable excretion of kreatin at this time.

In the second period of six days, during which the temperature was normal, the energy value of the food was doubled (51 cal. per kg.), which was immediately followed by a sharp decline in the excretion of nitrogen and of kreatin as well.

Excluding the first day of the period, in which the effect of the high caloric diet is not seen, the averages for the period are: a minus balance of 1.1 gm. nitrogen (as compared with 8.3 gm. of the preceding period), and 0.03 gm. kreatin-nitrogen.

Four of the six days of Period III were the beginning of a relapse. The patient received food equivalent to 58 cal. per kg. and containing 12.9 gm. of nitrogen. Excluding the first day of the period, the urine of which was lost, there was an average plus balance of 0.6 gm. nitrogen and 0.06 gm. kreatin-nitrogen; the kreatin indicating a somewhat greater absorption of muscle protein, which was more than compensated for by the retention of other protein. The next five days, Period IV, representing the height of the relapse, the patient received food equal to 55 calories per kg. and 10.8 gm. nitrogen, nearly as much as in the preceding period, but this was not sufficient to counterbalance or prevent a marked increase in the protein katabolism, and the subject lost an average of 3.8 gm. nitrogen each day. This loss, however, quickly stopped when the food was increased to 78 calories per kg. and 13.7 gm. nitrogen, the average of the next period (V).

During each of the eight days of this period (V), on three of which the temperature was above normal, the subject showed a plus balance of nitrogen, the average being 3.8 gm. Practically no kreatin was excreted.

For the following five days of normal temperature the greater part of the carbohydrate was withdrawn from the food, which was otherwise the same as in Period V, and represented 13.7 gm. nitrogen and 37 calories per kg. The excessive endogenous katabolism of protein observed in earlier periods had ceased and this diet was more than sufficient for equilibrium, the subject gaining 1.2 gm. nitrogen per day.

In the last period (VII) much carbohydrate was again added and an average plus balance of 4.3 gm. nitrogen was found. Carbohydrate

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

equivalent to about 30 calories per kg. added to the food caused an increased retention of 3.1 gm. nitrogen (4.3-1.2) per day for ten days.

Patient 7.—G—t, male, aged 38, tinsmith, admitted on the twenty-first day of the disease, claimed to have lost 15 pounds, but looked well-nourished. Illness very severe. Duration of fever forty-seven days, followed by a relapse of twenty-seven days. Complicated by serofibrinous pleurisy, cholecystitis with jaundice, and several slight intestinal hemorrhages. Sputum bloody but no tubercle bacilli could be found.

The experiment with this patient is the longest of this series. Our observations began on the thirtieth day of the disease, which was twenty days before the temperature remained normal for the first time, and continued for seventy-two days, on forty-seven of which fever was present. In spite of this long and very severe illness, the patient weighed about 2 kg. more at the end than at the start of the experiment. According to the sum of the daily balances of nitrogen, there was during the experiment a total loss of about 150 gm. (allowing 20 gm. for the days on which the urine was lost) and a total gain of 243 gm., giving a net gain of about 93 gm. of nitrogen. This is the equivalent of about 2.9 kg. of muscle tissue.[33]

The seventy-two days of the experiment are divided into fifteen periods, the average results of which are given in Table 28. The daily data are given in Tables 25, 26 and 27.

During the time of Periods I to IV, and VII to XI, inclusive, the patient had a fever temperature, while in the remaining periods the temperature was practically normal. In Period I there was an average daily loss of 7.7 gm. nitrogen (excluding the first two days, when the protein intake was very low) with food of an average value of 32 cal. per kg. and 9.2 gm. nitrogen. During the next three days (II) the food was increased by the equivalent of 21 cal. per kg. in the form of carbohydrate, and the nitrogen loss was decreased by 5.5 gm. per day. This result is probably in part due to a lowered intensity of the katabolic processes coincident with the fall in temperature, because in the two following periods (III and IV) a slight plus balance was obtained, though the food was of less caloric value (but of higher protein value) than in Period II.

In Periods V and VI the temperature was about normal and the protein katabolism was not markedly abnormal; minus balances of 0.6 and 0.7 gm. nitrogen were obtained with food equivalent to 28 and 27 cal. per kg.

33. The loss of nitrogen during the first thirty days of the disease, before the experiment began, was of course great and probably more than offsets the above gain.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 25.—PATIENT 7, G—T: DAILY FOOD

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
						PERIOD I						
30	640	150	..	270	...	...	..	..	..	24.1	77	306
31	400	100	..	600	...	...	..	..	60	15.2	50	623
32	1500	...	..	330	...	...	..	..	50	49.5	75	405
33	1500	...	..	120	...	...	..	..	90	49.5	75	285
34	2000	...	..	...	...	...	..	..	90	66.0	100	100
35	1800	60	..	185	...	...	..	..	90	60.6	108	277
36	2000	...	..	...	...	...	..	..	90	66.0	100	100
37	2000	...	..	...	...	...	..	..	90	66.0	100	100
38	1230	120	..	345	...	...	..	..	75	43.0	97	410
Average (excluding first two days)										57.2	93	240
						PERIOD II						
39	1350	150	..	520	...	...	..	..	75	47.0	112	592
40	1435	60	..	505	...	...	..	..	90	48.5	90	578
41	1440	60	..	493	...	...	..	..	90	48.7	90	567
Average										48.0	97	579
						PERIOD III						
42	1350	60	..	455	...	...	..	60	90	94.0	85	526
43	1110	60	..	410	...	...	..	60	90	84.5	73	467
44	1110	60	..	290	...	...	..	60	90	84.5	73	347
Average										87.7	77	447
						PERIOD IV						
45	1470	60	1	345	...	...	..	..	90	57.0	97	420
46	1470	60	2	345	...	...	..	..	90	64.2	102	420
47	1410	60	2	305	...	...	..	..	90	62.0	99	377
48	1410	60	2	365	...	...	..	..	90	62.0	99	437
Average (excluding first day of period)										62.7	100	411
						PERIOD V						
49	2190	...	..	...	...	...	..	..	90	72.3	110	110
50	2190	...	..	...	...	...	..	..	90	72.3	110	110
51	2190	...	..	...	...	...	..	..	90	72.3	110	110
Average										72.3	110	110

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
					Period VI							
52	2400	...	..	...	...	...	60	..	..	79.2*	120	120
53	1920	...	..	...	...	...	60	..	..	63.3*	96	96
Average										71.2*	108	108
					Period VII							
54	795	390	4	195	...	...	..	..	..	62.8	178	246
55	1080	330	4	360	...	30	..	..	..	74.4	174	442
56	1320	270	4	320	30	60	..	..	..	84.4	194	427
57	1290	270	5	310	...	...	..	..	..	84.0	172	380
58	1140	270	4	280	...	...	..	..	..	71.8	159	345
Average (excluding first day of period)										78.6	175	398
					Period VIII							
59	1440	300	2	325	...	...	..	..	..	68.0	173	406
60	1380	600	2	190	...	...	..	..	..	72.0	260	277
61	1260	480	2	300	...	...	..	..	..	65.5	218	377
62	1260	480	2	240	...	...	..	..	..	65.5	218	377
Average										67.8	216	344
					Period IX							
63	520	240	1	180	...	...	..	..	..	29.0	103	213
64	480	240	..	...	...	...	51	..	..	20.6	96	171
65	1020	120	..	140	...	...	..	..	..	36.0	87	195
66	1590	90	..	160	...	...	..	..	..	54.3	107	242
67	1820	120	..	160	...	...	..	..	..	62.4	127	255
68	2160	...	..	180	...	...	..	..	..	71.4	108	288
69	2160	...	..	180	...	...	..	..	..	71.4	108	288
70	2160	...	..	180	...	...	..	..	..	71.4	108	288
Average (last three days of period)										71.4	108	288
					Period X							
71	2160	...	1	180	...	...	..	..	..	78.5	113	288
72	2160	...	2	155	...	...	..	..	..	85.7	119	263
73	2160	...	2	150	...	...	..	..	..	85.7	119	258
74	2160	...	2	180	...	...	..	..	..	85.7	119	288
75	2160	...	2	180	...	...	..	..	..	85.7	119	288
76	2160	...	2	315	...	...	..	..	..	85.7	119	421
Average										84.5	118	301

* Does not include nitrogen of beef extract

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 25.—(CONTINUED)

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
						PERIOD XI						
77	2160	180	3	405	8	30	..	..	..	99.8	190	536
78	2040	255	4.5	385	16	...	..	..	..	104.8	225	495
79	1920	240	4	360	16	...	..	..	..	97.0	210	463
80	2160	270	5	540	76	60	..	..	..	119.3	291	692
81	1920	240	4	480	61	60	..	..	..	103.6	249	619
82	2160	180	5	180	106	60	..	..	..	117.5	288	329
83	2160	210	5	540	106	105	..	..	..	123.1	297	717
84	2400	300	5	540	136	90	..	..	..	131.2	362	723
Average										112.0	264	572
						PERIOD XII						
85	2160	270	5	...	136	90	..	..	..	122.6	332	170
86	2400	300	5	...	135	120	..	..	..	134.4	352	201
87	2400	210	5	...	103	120	..	..	..	132.6	298	198
88	2400	300	5	...	111	120	..	..	..	134.4	332	191
89	1680	240	5	330	111	150	..	..	..	112.8	278	511
Average										127.4	318	254
						PERIOD XIII						
90	2400	330	5	520	111	150	..	60	..	183.0	320	740
91	2400	300	5	600	111	150	..	60	..	182.4	311	820
92	2400	300	5	600	111	150	..	60	..	182.4	311	820
93	2160	270	5	600	87	120	..	60	..	172.5	290	788
94	2160	270	5	600	111	150	..	60	..	176.0	310	806
Average										179.0	317	795
						PERIOD XIV						
95	2400	300	5	...	111	150	..	60	..	184.0	331	219
96	2400	300	5	...	111	150	..	60	..	184.0	331	219
97	2400	300	5	...	111	150	..	30	..	161.0	331	219
Average										176.0	331	219
						PERIOD XV						
98	2400	300	5	...	111	150	..	..	..	127.7	331	219
99	2400	300	5	...	111	150	..	..	..	127.7	331	219
100	2400	300	5	...	111	120	..	..	..	124.4	331	201
101	2160	300	5	...	120	165	..	..	..	131.4	327	216
Average										127.8	330	214

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 26.—PATIENT 7, G—T: DAILY ANALYSES OF URINE *

Day of Disease.	Volume c.c.	Nitrogen Total.	Kreatinin.	Kreatin.	Uric Acid.
		PERIOD I			
30	750	16.0	0.50	0.10	0.25
31	950	18.3	0.63	0.15	0.33
32	1570	12.0	0.51	0.01	0.28
33	2450	16.3	0.54	0.13	0.32
34	1970	16.3	0.50	0.19	0.23
35	1050	14.3	0.39	....	....
36	1590	15.5	0.37	0.17	0.24
37	1490	15.3	0.43	0.11	0.23
38	1490	15.3	0.43	0.11	0.23
		PERIOD II			
39	740	8.9	0.36	0.01	0.22
40	1000	9.0	0.50	0.09	....
41	800	8.4	0.45	0.04	....
		PERIOD III (Somatose)			
42	920	9.1	0.39	0.07	....
43	1860	10.5	0.46	0.04	....
44	1620	11.1	0.41	0.07	....
		PERIOD IV			
45	1920	11.0	0.43	0.05	....
46	1670	8.8	0.41	0.00	....
47	1740	8.3	0.41	0.02	....
48	1430	7.9	0.36	0.05	....
		PERIOD V			
49	2060	8.8	0.38	0.02	....
50	2060	10.2	0.39	0.03	....
51	1940	10.8	0.41	0.02	0.11
		PERIOD VI (Meat Extract)			
52	2135	12.3	0.72	0.21	0.30
53	2040	15.0	0.86	0.40	0.49
		PERIOD VII			
54	1580	10.4	0.40	0.01	0.19
55	1320	7.3	0.39	0.00	....
56	1900	7.4	0.43	0.00	....
57	1950	7.7	0.47	0.00	....
58	1880	7.7	0.47	....	....
		PERIOD VIII			
59	1360	5.8	0.36	0.06	....
60	2650	6.9	0.40	0.12	....
61	2040	6.9	0.48	....	....
62	2340	7.8	0.53	....	....
		PERIOD IX			
63	1870	8.4	0.58	....	....
64	2000	14.6	0.84	Meat Extract	....
65	1380	14.9	0.55	....	....
66	Urine lost.				
67	Urine lost.				
68	860	12.7	0.60	....	....
69	Urine lost.				
70	1160	13.7	0.52	....	....
		PERIOD X			
71	1330	12.5	0.50	....	....
72	1300	12.3	0.47	....	....
73	1320	11.8	0.56	....	....
74	1200	11.7	0.56	....	....
75	1400	10.1	0.53	....	....
76	1600	11.0	0.48	....	....

* During Period VI, and on second day of Period IX, subject was given meat extract. During Periods III, XIII and XIV, the food contained "somatose."

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 26.—(CONTINUED)

Day of Disease.	Nitrogen Volume c.c.	Total.	Kreatinin.	Kreatin.	Uric Acid.
		PERIOD XI			
77	1440	9.8	0.49	....	....
78	1660	8.4	0.41	....	....
79	1860	8.8	0.39	....	....
80	1560	8.0	0.39	....	....
81	1660	9.3	0.41	....	....
82	1580	7.3	0.36	....	....
83	1680	8.6	0.42	....	....
84	1830	8.4	0.36	0.02	....
		PERIOD XII			
85	2360	9.3	0.37	0.02	....
86	2140	10.7	0.36	0.02	....
87	2225	11.4	0.34	....	....
88	1860	11.2	0.35	....	....
89	1700	10.1	0.38	....	....
		PERIOD XIII (Somatose)			
90	1860	8.6	0.36	....	....
91	1600	8.3	0.37	....	....
92	2150	8.5	0.35	....	....
93	2700	8.3	0.35	....	....
94	2660	9.6	0.37	....	....
		PERIOD XIV (Somatose)			
95	3040	11.9	0.44	0.00	....
96	2410	14.7	0.41	0.00	....
97	2210	15.3	0.39	0.00	....
		PERIOD XV			
98	2140	14.0	0.35	0.00	....
99	2250	13.9	0.39	0.00	....
100	1620	11.5	0.33	0.03	....
101	2000	13.6	0.38	0.02	....

TABLE 27.—PATIENT 7, G—T: DAILY TEMPERATURE AND NITROGEN BALANCE *

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Total Cal.	Cal. Per Kg. Total.	Cal. Per Kg. C. H.	Nitrogen Balance Intake.	Nitrogen Balance Excretion.	Nitrogen Balance Balance.
				PERIOD I					
30	67.0	105.0	103.2	2065	31	19	3.8	16.6	—12.8
31	....	104.0	103.0	3085	46	38	2.4	18.7	—16.3
32	67.4	104.2	102.6	2570	38	25	7.8	13.2	— 5.4
33	....	104.0	103.2	2075	31	17	7.8	17.5	— 9.7
34	....	104.8	102.0	1610	24	6	10.5	17.9	— 7.4
35	65.6	104.0	103.2	2390	36	18	9.7	15.7	— 6.0
36	....	103.6	102.0	1610	24	6	10.5	17.1	— 6.6
37	....	103.4	102.2	1610	24	6	10.5	16.6	— 7.9
38	....	103.0	101.4	2760	42	26	6.9	16.6	— 7.9
				PERIOD II					
39	65.0	103.4	100.4	3660	56	37	7.5	10.0	— 2.5
40	....	103.2	100.4	3405	52	36	7.7	10.1	— 2.4
41	....	102.8	100.0	3350	52	36	7.8	9.6	— 1.8
				PERIOD III					
42	64.5	102.6	100.4	3330	52	33	15.0	(11.3)	(+ 3.7)
43	....	103.2	99.6	2950	46	30	13.5	12.5	+ 1.0
44	63.5	102.8	99.8	2450	38	22	13.5	13.1	+ 0.4
				PERIOD IV					
45	63.3	101.4	99.4	2860	45	27	9.1	(12.4)	(— 3.3)
46	....	102.2	98.8	2920	46	27	10.3	10.3	+ 0.0
47	63.5	101.2	98.8	2720	43	24	9.9	9.8	+ 0.1
48	....	100.6	98.6	2960	47	28	9.9	9.4	+ 0.5

* In Period VIII, the feces contained 1.8 gm. N. per day. In other periods "excretion"=total N. of urine + 15 per cent. of food N.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 27.—(CONTINUED)

Day of Disease.	Wt. Kg.	—Temp. F.— High.	Low.	Total Cal.	Cal. Per Kg. Total.	C. H.	—Nitrogen Balance.— Intake.	Excretion.	Balance.
				PERIOD V					
49	64.0	100.2	98.4	1765	28	7	11.5	(10.5)	(+ 1.0)
50	....	100.0	97.6	1765	28	7	11.5	11.9	— 0.4
51	62.5	100.4	98.4	1765	28	7	11.5	12.3	— 0.8
				PERIOD VI					
52	....	100.0	98.2	1930	31	8	18.0	(15.0)	(+ 3.0)
53	....	99.8	98.6	1540	24	6	15.4	17.3	— 1.9
				PERIOD VII					
54	....	100.4	98.8	2920	46	16	10.0	11.9	— 1.9
55	....	101.6	99.2	3740	60	29	11.9	9.1	+ 2.8
56	....	102.6	99.6	3900	62	28	13.5	9.6	+ 3.9
57	....	103.8	100.0	3500	55	25	13.4	9.9	+ 3.5
58	....	102.6	99.2	3190	50	22	11.5	9.4	+ 2.1
				PERIOD VIII					
59	....	101.8	98.8	3550	56	26	10.9	7.6	+ 3.3
60	....	101.8	99.4	3850	60	18	11.5	8.7	+ 2.8
61	....	102.6	99.8	3850	60	24	10.5	8.7	+ 1.8
62	....	103.4	100.6	3600	56	20	10.5	9.6	+ 0.9
				PERIOD IX					
63	....	104.4	102.4	1950	30	14	4.6	10.2	— 5.6
64	....	104.8	103.2	1680	26	11	8.1	16.4	— 8.3
65	....	104.6	103.6	1760	27	12	5.8	16.7	—10.9
66	....	104.8	103.4	2210	34	15	8.7	....	......
67	65.1	104.2	102.8	2480	38	16	10.0	....	......
68	....	104.8	102.8	2480	38	18	11.4	14.5	— 3.1
69	....	104.8	102.8	2480	38	18	11.4	....	......
70	64.2	104.2	102.8	2480	38	18	11.4	15.5	— 4.1
				PERIOD X					
71	....	103.6	101.8	2550	40	18	12.5	14.4	— 1.9
72	....	104.0	102.4	2530	39	17	13.7	14.4	— 0.7
73	....	103.2	101.2	2520	39	16	13.7	13.9	— 0.2
74	....	102.6	101.4	2740	43	18	13.7	13.8	— 0.1
75	....	102.6	101.4	2740	43	18	13.7	12.2	+ 1.5
76	....	102.5	100.2	3180	49	26	13.7	13.1	+ 0.6
				PERIOD XI					
77	....	102.4	100.4	4373	68	34	16.0	12.2	+ 3.8
78	....	102.0	99.5	4546	71	31	16.7	10.9	+ 5.8
79	....	101.0	99.0	4253	66	29	15.5	11.1	+ 4.4
80	....	100.8	98.6	6040	94	44	19.1	10.9	+ 8.2
81	....	101.4	98.4	5280	82	39	16.6	11.8	+ 4.8
82	....	100.0	98.6	4510	70	21	18.8	10.1	+ 8.7
83	....	100.4	98.4	6210	96	46	19.7	11.6	+ 8.1
84	....	100.2	98.6	6860	106	46	21.0	11.6	+ 9.4
				PERIOD XII					
85	....	99.8	98.6	4290	67	11	19.6	12.2	+ 7.4
86	....	99.8	98.4	4645	72	13	21.5	13.9	+ 7.6
87	....	99.6	98.4	4126	64	13	21.2	14.6	+ 6.6
88	....	99.6	98.4	4425	69	12	21.5	14.4	+ 7.1
87	64.6	100.2	98.6	5140	80	32	17.9	12.8	+ 5.1
				PERIOD XIII					
90	....	100.4	98.6	6760	104	47	29.3	13.0	+16.3
91	....	99.8	98.8	7000	107	52	29.2	12.7	+16.5
92	65.0	99.6	98.4	7000	107	52	29.2	12.9	+16.3
93	....	100.4	99.8	6640	102	50	27.6	12.4	+15.2
94	....	100.2	99.4	6900	106	51	28.2	13.8	+14.4
				PERIOD XIV					
95	....	100.6	99.0	4730	71	13	29.4	16.3	(+13.1)
96	....	100.4	99.0	4730	71	13	29.4	19.0	(+10.4)
97	68.2	100.2	98.6	4640	68	13	25.8	19.2	(+ 6.6)
				PERIOD XV					
98	68.7	99.8	98.2	4500	65	12	20.4	17.1	+ 3.3
99	....	99.8	98.4	4500	65	12	20.4	17.0	+ 3.4
100	....	99.4	98.4	4410	64	12	19.9	14.5	+ 5.4
101	68.8	100.0	98.4	4460	65	12	21.0	16.7	+ 4.3

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 28.—PATIENT 7, G—T: AVERAGES OF PERIODS

Figures given for 24 hours.

	No. of Days.	Range of Maximum Temp. During Period.	Food: Cal. Per Kg. Total.	Food: Cal. Per Kg. From Fat.	Food: Cal. Per Kg. From C. H.	Food: Nitrogen. Gm.	Excretion N.[13] Gm.	Nitrogen Balance. Gm.	Urine: Total Nitrogen.	Urine: Kreatinin N.	Urine: Kreatin N.	Urine: NH_3 N. Gm.[1]	Urine: NH_3 N. Per Cent. Total N.	Urine: Uric Acid N.	Urine: "Rest" N. Gm.[1]	Urine: "Rest" N. Per Cent. Total N.	Urine: Urea. Per Cent. Total N.[1]	Urine: Xanthin Bases. Gm. Xanthin.[1]	Kreatinin Coef.
Period I[1].....	9	105.0-103.0	32	13	15	9.2	16.9	— 7.7	15.5	0.48	0.12	1.13	7.1	0.25	1.46	9.2	77.9	0.040	7.3
Period II.....	3	103.4-102.8	54	14	36	7.7	9.9	— 2.2	8.8	0.44	0.04	0.82	9.6	0.24[1]	1.02	11.6	69.9	.....	6.8
Period III....	3	103.2-102.6	45	11	29	14.0	12.8[3]	(+ 0.4) + 1.2	10.8	0.42	0.06	....	....	0.26[1]	1.00	9.8	....	0.086	6.5
Period IV[4]....	4	102.2-100.6	45	15	27	10.0	9.8	+ 0.2	8.3	0.39	0.02	0.59	7.2	0.20[1]	0.88	10.7	74.5	0.063	6.1
Period V.....	3	100.4-100.0	28	16	7	11.5	12.2[3]	— 0.7	10.5	0.40	0.02	....	....	0.11	....	....	....	.....	6.3
Period VI[5]....	2	100.0- 99.8	27	16	7	16.7[6]	17.3[7]	— 0.6	15.0	0.86	0.40	....	....	0.49	Beef Extract.			0.064	...
Period VII[4]...	5	100.4-103.8	56	25	25	12.6	9.4	+ 3.2	7.5	0.44	0.00	0.58	7.2	0.17[1]	0.98	12.1	72.7	0.072	6.9
Period VIII...	4	101.8-103.4	58	31	22	10.8	8.7	+ 2.1	6.9	0.44	....	0.75	11.0	0.15[1]	0.64	9.4	70.0	0.079	6.9
Period IX....	8	104.2-104.8	38[8]	16[8]	18[8]	11.4[8]	15.0[9]	— 3.6[9]	12.9[10]	0.56[11]	....	1.02	8.0	0.33[1]	1.50	11.5	73.3	0.066	8.7
Period X.....	6	104.0-102.4	42	17	19	13.5	13.6	— 0.1	11.6	0.51	....	1.07	9.2	0.30[1]	0.96	8.5	72.4	0.071	8.0
Period XI....	8	102.4-100.0	82	38	37	17.9	11.3	+ 6.6	8.6	0.40	....	0.77	9.0	0.24[1]	1.07	12.4	72.5	0.055	6.2
Period XII...	5	99.6-100.2	70	46	16	20.4	13.6	+ 6.8	10.5	0.36	....	0.67	6.4	0.24[1]	0.79	7.5	80.4	0.050	5.6
Period XIII..	5	100.4- 99.6	105	45	50	28.7	13.0	+15.7	8.7	0.36	....	0.60	6.9	0.22[1]	0.72	8.3	78.1	0.042	5.5
Period XIV...	3	100.6-100.2	70	45	13	28.2	19.5[12]	+ 8.7	15.3	0.41	0.00	....	....	0.23[1]	....	....	....	.....	6.0
Period XV....	4	100.0- 99.2	65	45	12	20.4	16.3	+ 4.1	13.3	0.36	0.01	0.55	4.0	.... 0.24[1]	....	....	....	0.051	.. 5.2

1. Determined in "composite urines" representing periods.
2. First two days of period excluded from averages for nitrogen balance and food.
3. First day of period excluded from average for excretion.
4. First day of period excluded from averages for nitrogen balance and food.
5. Beef extract period. Note high kreatinin, kreatin and uric acid.
6. 5.3 gm. of this N. was in form of beef extract.
7. Excretion of last day of period. 60 gm. beef extract were given on each of the two days.
8. Average of last three days.
9. Average of two of the last three days—urine of other day lost. Patient at times incontinent.
10. Average of five days of period. Urine of other days lost.
11. Average of four days—beef extract day excluded.
12. Excretion of last day used for nitrogen balance. Total N. of urine (15.3 gm.) + 15 per cent. of food-nitrogen (4.2 gm.).
13. In Period VIII the feces were collected and found to contain 1.8 gm. N. per day. "Excretion" of other periods=total N. of urine + 15 per cent. of food-nitrogen.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

In Period VII, coincident with the beginning of a relapse, the carbohydrate food was again increased and, during the next nine days of fever (VII and VIII), the subject gained nitrogen each day, the diet equaling 56 and 58 cal. per kg. and 12.6-10.8 gm. nitrogen. Here, again, it seems very clear that we wholly prevented any febrile loss of body protein.

In Period IX the patient's condition became more serious and we were able to give only a moderate amount of food, 38 cal. per kg. and less. The consequent great disproportion between the decreased food-supply and the probably increased demand for energy or increased intensity of the katabolic processes resulted in very considerable losses of body nitrogen (3 to 10 gm. daily). That the loss was not even greater seems surprising, and is probably to be explained by the known tendency of the organism to react less violently to such a stimulus in the later stages of a long illness.

This same tendency probably explains the fact that during the next period (X), with the temperature still above normal, nitrogen equilibrium was attained on almost the same diet.

On further increasing the value of the food to 82 cal. per kg. (XI) there was an average plus balance of 6.6 gm. nitrogen per day, though the maximum temperature on four days was above 101 F.

During the remainder of the experiment the temperature was normal and the excessive katabolism observed during the febrile reaction had given place to the increased anabolism characteristic of convalescence. Food of high protein content and equivalent to *70 (XII), 105 (XII), 70 (XIV) and 65 (XV) cal. per kg. resulted in the large average daily plus balances of 6.8, 15.7, 8.7 and 4.1 gm. nitrogen.*

A comparison of Periods XIII and XIV shows the great value of carbohydrate in assisting the gain of protein in convalescence, which is not wholly in accord with the idea of Benedict and Surânyi, that the nitrogen retention in convalescence is largely independent of the fuel value of the food.

A comparison of Periods II and VIII again illustrates the importance of the intensity of the katabolic process in determining the degree of sparing of body protein to be accomplished by any diet. The intensity of the katabolism does not always go parallel to the temperature, as has been pointed out by Kraus and others. In both of the above periods the maximum temperature was about the same, and the food differed only slightly.

	Cal. Per Kg.				
Food.	Total.	Fat.	C. H.	N. Gm.	N. Bal.
Period II	54	14	36	7.7	– 2.2
Period VIII	58	31	22	10.8	+ 2.1

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 29.—PATIENT 8, P—S: DAILY FOOD AND ANALYSES OF URINE

Insufficient food-supply throughout. Great loss of body protein. Great emaciation.

Day of Disease.	Temp. F. High.	Temp. F. Low.	Urine Volume. c.c.	Urine Total N.	Urine NH_3 N.	Urine Kreatinin N.	Urine Kreatin N.	Urine Uric Acid N.	Urine "Rest" N.	Per Cent. of Total N. Urea.	Per Cent. of Total N. NH_3	Per Cent. of Total N. Rest.	Remarks.
12	104.0	103.0	1280	22.7	1.61	0.54	0.71	0.17	1.56	80.0	7.1	6.9	*
13	103.5	102.4	1280	22.7	1.61	0.54	0.71	0.17	1.56	80.0	7.1	6.9	*
14	103.4	102.0	1350	22.4	1.80	0.54	0.67	0.19	1.07	81.0	8.0	4.8	*
15	103.5	102.0	860	....	....	0.35	0.34	0.11	....	....	7.9	....	
16	103.4	102.0	1240	18.7	1.65	0.52	0.48	0.19	1.62	76.3	8.8	8.7	*
17	103.4	101.0	1040	14.8	1.38	0.43	0.31	0.13	1.29	76.1	9.3	8.7	
18	104.4	99.0	1300	20.8	1.84	0.54	0.57	0.21	1.72	76.7	8.9	8.3	*
19	103.0	102.0	....	....	....	....	....	....	....	....	....	....	
20	103.0	103.0	950	13.8	0.07	0.37	0.38	0.11	1.24	77.0	7.8	9.0	
21	103.6	101.0	1140	14.7	1.44	0.43	0.37	0.07	1.32	75.3	9.8	9.0	
22	104.0	102.4	1150	15.9	1.47	0.49	0.35	0.11	....	....	9.2	....	*
23	104.0	100.0	....	....	....	....	....	....	....	....	....	....	
24	105.6	102.8	920	10.2	1.10	0.35	0.22	0.08	0.94	73.7	10.8	9.2	
25	104.4	103.4	....	....	....	....	....	....	....	....	....	....	
26	103.6	101.0	....	11.7?	1.44	0.51	0.17	0.13	1.62	66.9	12.4	13.9	*
27	103.4	102.0	....	8.0?	....	0.50	0.18	0.12	1.62	61.2	14.1	16.5	*
28	102.6	101.0	....	....	....	....	....	....	....	....	....	....	
29	103.0	100.0	....	....	....	....	....	....	....	....	....	....	
30	103.0	100.6	900	15.4	1.17	0.31	0.26	0.08	0.87	82.5	7.6	5.6	
31	103.0	101.0	1380	18.5	1.36	0.42	0.38	0.14	1.36	80.2	7.4	7.4	*
32	102.6	99.6	....	....	....	....	....	....	....	....	....	....	
33	102.6	99.6	1500	13.9	1.30	0.26	0.20	0.13	0.75	81.4	9.3	5.4	
34	103.6	101.8	2180	13.7	....	....	....	....	....	....	....	....	
35	102.0	100.4	1800	12.7	1.02	0.18	0.12	0.10	1.09	80.4	8.0	8.6	
36	103.0	99.0	800	8.8	0.61	0.18	0.15	0.07	1.15	75.6	6.9	13.1	
37	103.0	100.0	1800	....	....	....	....	....	....	....	....	....	
38	102.4	99.0	1960	....	....	0.30	....	....	....	....	....	....	
39	102.4	99.0	....	....	....	....	....	....	....	....	6.0	11.0	
40	102.4	99.6	1400	14.8	0.84	0.37	0.02	0.12	1.66	....	5.7	11.2	*
41	103.0	99.6	1320	14.2	0.66	0.42	....	0.12	1.17	83.4	4.6	8.2	*
42	103.0	101.0	1580	12.3	0.80	....	....	0.07	....	....	....	....	
43	103.4	100.6	1260	10.9	0.68	0.25	0.03	0.09	0.89	81.6	6.2	8.2	
44	104.4	100.4	750	10.5	0.74	0.28	0.00	0.08	1.04	79.6	7.0	9.9	*
45	103.8	101.6	540	....	....	....	....	....	....	....	7.9	9.3	
46	102.4	100.4	630	8.5	0.60	0.23	0.07	0.06	0.72	80.1	7.0	8.5	
47	104.4	100.4	520	6.0	....	....	0.03	0.04	0.56	80.3	8.1	8.3	
48	104.0	102.0	1360	14.7	1.01	0.27	....	0.07	1.34	81.8	6.8	9.1	*
49	103.0	100.0	620	7.2	....	....	0.00	0.05	....	....	3.4	8.8	Wt. 42 Kg.
50	103.0	101.0	730	9.6	0.71	0.27	....	0.07	0.85	80.3	7.3	8.8	*
51	103.0	100.0	390	....	....	....	....	0.04	....	....	8.2	7.8	
52	104.4	101.0	570	....	....	....	....	0.09	....	....	7.4	8.9	
53	103.0	101.0	570	10.0	0.73	0.28	....	0.09	....	....	7.3	....	*
54	102.4	100.0	930	10.0	0.73	0.28	....	0.09	....	....	7.3	....	*
55	103.0	100.0	1180	12.7	....	0.22	....	....	....	....	....	....	*
56	102.4	100.0	670	6.8	....	0.22	....	0.06	....	....	....	....	
57	103.0	99.0	890	9.9	....	....	....	....	....	....	....	....	
58	100.8	98.4	....	....	....	....	....	....	....	....	....	....	

* Many of the urines of this patient were incomplete; those which are known to be complete are marked with a *.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

The difference in the nitrogen balance of these periods must be, in large part, due to the difference in intensity of the katabolic processes.

THE NITROGEN PARTITION OF THE URINE IN TYPHOID FEVER

In addition to the data on this topic contained in the experiments already described, results from the analyses of the urine in three other severe cases are given in Tables 29, 30 and 31.

Patient 8.—P—s, aged 31, admitted the tenth day of the disease. Positive blood-culture. Illness very severe. Duration of temperature sixty-seven days. Complicated by intestinal hemorrhage. Marked emaciation.

Patient 9.—O—y, laborer, aged 21, poorly nourished, admitted the sixth day of the disease. Blood culture positive. Illness severe. Duration of fever twenty-eight days. Complicated by cholecystitis, without jaundice, and furunculosis. Emaciation during the illness marked.

Patient 10.—E. K—r, lithographer, aged 15, admitted the eighth day of the disease. Positive blood culture. Illness moderately severe. Duration of fever twenty-one days, followed by a relapse. Complication, otitis media.

Kreatinin.—From the work of Folin[34] and others[35] we know that in health the amount of this substance excreted is independent of the total amount of protein katabolized, and is practically constant from day to day, and from hour to hour. It has been further shown that the amount excreted by different individuals bears a definite relation to the weight,[34] muscular development and strength[36] of those individuals. Kreatinin is essentially a product of endogenous metabolism,[34] but is not a measure of the total endogenous metabolism.[36] The truth of the latter statement is well shown by the kreatinin excretion by subjects of typhoid fever. With the increased katabolism of fever there is usually an increase in the amount of kreatinin excreted, as has already been shown by Leathes,[37] but by no means in proportion to the total amount of the body protein katabolized. In considering the question of an increase or decrease of kreatinin excretion we must not base any conclusion on the absolute amount excreted, because of the great normal variations in different individuals; but must consider the relative amount per kg. of body weight. The highest relative excretion of kreatinin observed during these experiments is 10.6 mg. kreatinin-nitrogen per kg., the "kreatinin-coefficient" of U-h (Experiment 2, Period I, see Table 8), at which time the subject was losing about 9 gm. of nitrogen per day, and his total

34. Folin: Am. Jour. Physiol., 1905, xiii, 83.
35. Klercker: Biochem. Ztschr., 1907, iii, 46. Hoogenhuyze and Verploegh: Ztschr. f. physiol. Chem., 1905, xlvi, 415. Shaffer: Am. Jour. Physiol., 1908, xxii, 445.
36. Shaffer: Am. Jour. Physiol., 1908, xxiii, 1.
37. Leathes: Jour. Physiol., 1907, xxxv, 205.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 30.—PATIENT 9, O—Y: DAILY FOOD AND ANALYSES OF URINE

Weight about 50 Kg.

Average Daily Food and Nitrogen Balance.	Day of Disease.	Temp. F. High.	Temp. F. Low.	Urine Volume. c.c.	Urine Total N.	Urine NH_3 N.	Urine Kreatinin N.	Urine Kreatin N.	Urine Uric Acid N.	Urine "Rest" N.	Per Cent. of Total N. Urea.	Per Cent. of Total N. NH_3	Per Cent. of Total N. Rest.
					PERIOD I								
34 Cal. per kg. 11.1 gm. N. Bal. = — 6.7	9	105.0	103.0	2170	13.9	11.3	0.45	....	0.18	1.04	79.1	8.2	7.5
	10	104.6	102.0	3110	28.4	....	0.73	0.28	0.14	2.07	....	...	9.5
	11	104.0	102.4	1200	13.1	0.76	0.36	0.14	0.14	0.77	83.5	5.6	5.9
	12	104.4	102.6	1080	9.1	0.58	0.28	0.11	0.10	....	....	6.3	...
					PERIOD II								
39 Cal. per kg. 6.8 gm. N. N. Bal. = — 10.3	13	105.0	102.4	1200	17.1	0.87	0.47	0.22	0.20	0.88	84.5	5.1	5.1
	14	104.2	103.0	1960	16.1	1.03	0.46	0.19	0.21	0.50	85.1	6.4	3.1
	15	104.3	102.0	1320	15.0	0.81	0.47	0.22	0.22	0.89	82.7	5.4	5.9
	16	104.4	103.0	1170	16.0	0.79	0.47	0.27	0.25	0.49	86.0	5.0	3.1
					PERIOD III								
46 Cal. per kg. 4.4 gm. N. N. Bal. = — 5.4	17	104.2	102.0	1050	9.6	0.47	0.29	0.18	0.15	0.38	84.7	4.9	4.0
	18	104.8	102.6	....	....	....	....	....	....	....	....	...	...
	19	104.8	101.0	1500	9.6	0.49	0.31	0.16	0.16	0.63	81.9	5.1	6.5
	20	103.6	99.0	1340	8.3	0.49	0.26	0.12	0.13	0.46	82.3	6.0	5.5
					PERIOD IV								
47 Cal. per kg. 9.8 gm. N. N. Bal. = — 4.6	21	103.4	99.0	700	8.8	0.34	0.31	0.10	0.16	0.55	83.7	3.8	6.2
	22	103.8	99.0	400	....	....	....	....	....	....	83.3	5.4	5.4
	23	101.8	99.0	620	13.0	0.54	0.36	0.18	0.13	0.59	87.3	4.2	4.5
	24	102.0	98.2	1000	12.7	0.59	0.36	0.19	0.13	1.03	83.0	4.7	8.1
					PERIOD V								
40 Cal. per kg. 10.1 gm. N. N. Bal. = — 1.5	25	101.4	98.4	1080	10.8	0.52	0.34	0.15	0.11	0.92	81.2	4.9	8.5
	26	102.0	98.0	740	....	....	....	....	....	....	84.8	4.5	5.6
	27	101.4	98.4	950	9.4	0.40	0.30	0.14	0.08	0.57	84.2	4.3	6.0
	28	100.2	99.0	800	9.9	0.40	0.30	0.11	0.08	0.41	86.9	4.0	4.1

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 31.—PATIENT 10, K—R: DAILY FOOD AND ANALYSES OF URINE

Weight about 50 Kg.

Average Daily Food and Nitrogen Balance.	Day of Disease.	Temp. F. High.	Temp. F. Low.	Urine Volume. c.c.	Urine Total N.	Urine NH_3 N.	Urine Kreatinin N.	Urine Kreatin N.	Urine Uric Acid N.	Urine "Rest" N.	Per Cent. of Total N. Urea.	Per Cent. of Total N. NH_3	Per Cent. of Total N. Rest.
					Period I								
	13	104.0	102.0	1020	17.4	0.88	0.47	0.11	0.10	1.17	84.5	5.1	6.8
97 gm. Fat	14	103.4	101.4	....	....	....	....	....	....	....	....	....	....
468 gm. C. H.	15	102.0	99.0	1060	15.2	1.14	0.44	0.02	0.13	1.35	79.8	7.5	8.9
8.5 gm. N.	16	103.0	99.0	420	....	....	....	....	....	....	....	....	....
60 Cal. per kg.	17	102.4	99.4	840	12.0	1.06	0.46	0.10	0.13	0.98	77.3	8.8	8.2
N. Bal. = — 6.4	18	103.4	100.0	900	10.0	0.93	0.45	0.11	0.13	1.28	71.0	9.3	12.8
per day.	19	102.4	99.0	1800	....	....	....	....	....	....	....	....	....
	20	100.0	99.0	....	....	....	....	....	....	....	76.1	7.3	11.7
Normal Temperature.					Period II								
	1	99.4	98.4	1360	12.2	0.71	0.45	0.18	0.12	1.14	78.7	5.8	9.3
118 gm. Fat	2	99.4	98.4	....	....	....	....	....	....	....	....	....	....
463 gm. C. H.	3	98.8	98.4	975	10.8	0.72	0.36	0.19	0.10	1.12	77.0	6.7	10.4
9.3 gm. N.	4	99.8	98.0	1350	9.4	0.57	0.33	0.17	0.05	0.97	77.9	6.1	10.4
65 Cal. per kg.	5	100.0	98.0	1100	9.1	0.50	0.34	0.14	0.09	0.85	79.1	5.5	9.3
N. Bal. = — 1.9	6	100.4	98.0	1110	8.6	0.45	0.34	0.13	0.08	0.66	80.2	5.3	7.7
	7	100.0	98.0	1110	8.6	0.45	0.34	0.13	0.08	0.66	80.2	5.3	7.7
	8	99.2	98.2	....	....	....	....	....	....	....	....	4.6	9.5
Relapse.					Period III								
	1	101.4	99.0	1650	9.7	0.48	0.35	0.14	0.07	0.90	80.0	5.0	9.3
128 gm. Fat	2	103.4	100.0	1300	9.5	0.50	0.37	0.13	0.09	1.00	78.3	5.2	10.5
510 gm. C. H.	3	104.0	99.2	930	7.2	0.74	0.27	0.06	0.07	0.85	72.3	10.3	11.8
8.9 gm. N.	4	104.6	102.0	1125	10.2	0.46	0.43	....	0.10	0.83	82.3	4.5	8.2
70 Cal. per kg.	5	104.4	102.0	910	11.7	0.57	0.51	....	0.12	1.35	78.1	4.9	11.6
N. Bal. = — 2.0	6	102.0	100.4	1480	8.0	0.62	0.37	0.00	0.08	1.34	69.9	7.8	16.8
	7	100.6	98.6	1220	10.5	0.81	0.40	0.00	0.12	....	....	7.7	....
Convalescence.					Period IV								
	1	99.6	98.4	960	12.3	0.98	0.44	....	0.13	....	....	....	....
156 gm. Fat	2	99.0	98.4	1230	8.0	0.72	0.32	....	0.10	....	....	....	....
540 gm. C. H.	3	99.6	98.4	1390	7.3	....	0.32	....	....	....	....	....	....
13.2 gm. N.	4	99.0	98.4	1675	....	....	....	....	....	....	....	....	....
80 Cal. per kg.	5	100.0	97.9	1640	11.4	....	0.34	....	0.11	....	....	....	....
N. Bal. = + 1.4	6	100.0	97.4	860	....	....	....	....	....	....	....	....	....

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

endogenous katabolism was therefore greatly increased. The normal kreatinin-coefficient of this subject, a laborer, was certainly not less than 9, which gives a probable increase of less than 20 per cent. in the kreatinin excretion at the height of the fever. The other experiments show in general the same rule: a marked, though relatively rather slight, increase during the height of the fever. This increase is very clearly shown by those patients who suffered a relapse (see Tables 15, 24 and 28). With, or even before the fall in the temperature, there is a progressive decline in the kreatinin excretion, this decrease apparently going somewhat parallel with the lowered muscular strength of the individual, although the kreatinin-coefficient does not usually fall so low as is often seen in subjects of chronic diseases.[38]

The lowest relative kreatinin excretion observed in these subjects were about 4 and 5 mg. kreatinin-nitrogen per kg., found late in the disease with P——s (Table 29) and G——t (Table 28) respectively; and these were the patients who suffered the longest and most severe illnesses of the series.

In order to gather more accurate data from these patients regarding the relation between muscular strength and the amount of kreatinin excreted, a few measurements with a hand dynamometer were made on seven days early in convalescence on W——d, G——t, and B——t.

Five tests with two-minute intervals were made with each hand on each day. These tests were made after the end of the experiments and the kreatinin excretion at the time is not known, but the latter had probably not greatly changed from the values found in the last period of the respective experiments, and these values are therefore used in the accompanying comparison. The readings of the dynamometer are given in kilos.

While the tests with such an instrument are not very exact, and allow us to judge the strength of only one set of muscles, the results are fairly satisfactory and show very strikingly that the strongest subject excreted relatively the most kreatinin.[39]

The increase of kreatinin excretion during the height of the fever, as has already been pointed out by one of us,[40] is an exception in the relationship of kreatinin to muscular development; but, aside from this exception, the amount of kreatinin excreted per kg. of body weight runs parallel with the "muscular efficiency" of the individual.

38. Shaffer: Am. Jour. Physiol., 1908, xxiii, 1.

39. For making the tests with the dynamometer we are indebted to Dr. E. S. Bishop, Junior Physician on the second Medical Division of Bellevue Hospital.

40. Shaffer: Am. Jour. Physiol., 1908, xxiii, 10.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

TABLE 32.—PATIENT 7, G—T: MEASUREMENTS WITH HAND DYNAMOMETER *

Day of Convalescence						
27	29	31	32	33	34	35
			RIGHT HAND			
Kg.	Kg.	Kg.	Kg.	Kg.	Kg.	Kg.
18	21	20	22	20	22	25
19	18	20	20	22	23	22
18	20	21	20	21	21	20
18	20	18	20	21	23	23
18	20	21	22	22	23	23
			LEFT HAND			
18	20	19	18	18	18	20
17	17	20	18	18	19	18
18	20	17	18	19	21	18
15	18	18	19	21	18	20
17	20	19	20	21	21	20
			Average			
17.6	19.4	19.3	19.7	20.3	20.9	20.9
			Average of all Readings			
..	..	..	19.7	..	..	..
			Kreatinin Coef.			
..	..	..	5.2	..	..	..

* Test began ten days after the end of experiment.

TABLE 33.—PATIENT 4, W—D: MEASUREMENTS WITH HAND DYNAMOMETER *

Day of Convalescence						
11	13	15	16	17	18	19
			RIGHT HAND			
Kg.	Kg.	Kg.	Kg.	Kg.	Kg.	Kg.
25	20	25	27	30	30	30
27	23	27	27	32	32	34
27	27	27	28	31	31	34
25	25	29	26	28	30	32
23	27	23	29	31	30	32
			LEFT HAND			
23	15	23	21	28	27	28
23	17	21	24	29	28	27
24	16	24	25	27	27	26
22	21	25	21	28	24	25
18	18	23	25	23	24	25
			Average			
23.7	20.9	24.7	25.3	28.7	28.3	29.3
			Average of all Readings			
..	..	..	25.8	..	..	..
			Kreatinin Coef.			
..	..	..	7.0	..	..	..

* Tests began three days after end of experiment.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

Kreatin.—The behavior of this substance in typhoid fever has already been referred to. It is excreted in large amounts at the height of the disease if the subject is losing large quantities of body protein (see Table 29, the subject of which lost much body nitrogen throughout the greater part of the experiment). We believe that the kreatin excreted under such circumstances is directly derived from muscle tissues, and that its appearance in the urine indicates that muscle tissues are being destroyed.

TABLE 34.—PATIENT 5, B—T: MEASUREMENTS WITH HAND DYNAMOMETER

Day of Convalescence				
11	13	15	16	17
		Right Hand		
(28)	39	41	35	41
37	37	36	40	43
36	40	40	43	44
41	35	39	39	44
37	33	40	42	40
		Left Hand		
36	35	37	36	41
35	28	34	40	38
38	30	35	37	37
36	31	35	38	38
34	30	37	36	39
		Average		
36.7	33.8	37.4	38.6	40.5
		Average of all Readings		
..	..	37.4	..	..
		Kreatinin Coeficient *		
..	..	8.3	..	..

* Average of last ten days of Period V=0.615 gm. Kreatinin—N. Divided by 74 Kg.=8.3

Uric Acid.—Except for a few instances, the diets used contained no purins, and we are therefore concerned only with endogenous uric acid. Our results show as a rule a marked increase in the excretion of this substance during the height of the fever, followed usually by a decline with the fall of the temperature. The amount excreted varies with different individuals and each experiment should be considered by itself. With some of the subjects the uric acid remained high well into convalescence (Tables 28 and 29), while with others it fell in convalescence to probably below the normal (Tables 8, 29 and 30). The high uric acid excretion during the fever is in accord with the observations of Leathes[37] and others.

Xanthin Bases.—A. R. Mandel[41] has determined the amount of xanthin bases excreted by three subject of surgical fevers and by one subject

41. Mandel: Am. Jour. Physiol., 1904, x, 452; ibid, 1907, xx, 439.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

of pneumonia, and finds a maximum of about 60 mg., calculated as xanthin, in twenty-four hours, as compared with the probable normal of about 20 or 30 mg. On the basis of these results, together with the fact that a rise in temperature follows the injection or ingestion of xanthin bases, Mandel apparently concludes that substances of this nature are primarily responsible for the febrile temperature. We can scarcely agree with this view. According to our results the excretion of xanthin bases bears no constant relation to the height of the temperature. With Z——o, for instance (Table 12), the xanthin increases with the slow fall in the temperature, the reverse of Mandel's finding. With B——t (Table 20) the same is true except that the highest amount (81 mg.) was excreted during the relapse. With L——d (Table 24) there is little difference between the periods of fever and of normal temperature. With W——d (Table 16) the highest amount, 91 mg. xanthin, is found at the height of the disease, but the lowest, 30 mg., appears during a relapse when the temperature was moderately high.

Most of our results are abnormally high, according to Mandel's standard,[42] but are not high when compared with the results of Camerer.[43]

We find no evidence in our experiments that the xanthin bases are increased in typhoid fever or that the amount excreted bears any constant relation to the febrile temperature, thus failing to confirm either Erben[44] or Mandel.

Urea, Ammonia and "Rest" Nitrogen.—Folin[45] has shown that for the judgment of the normality or abnormality in the excretion of these substances, or "fraction" in the case of the "rest nitrogen," it is necessary to consider the amount of total nitrogen excreted. Table 35 contains the normal limits, compiled from the results of Folin and of one of us, for the excretion of these substances. The figures are based on the analyses of about 200 urines from a large number of normal persons. On the basis of these standards it is rather surprising that we do not find any very marked deviations from the normal in these subjects of typhoid fever. There are many instances in each experiment of increased excretion of ammonia and "rest" nitrogen, but the increase is rarely great, and not at all comparable to the figures obtained by Ewing and Wolf in the toxemias of pregnancy and allied conditions. On the whole our results justify the conclusion that during the height of the disease or during a relapse there is usually a slightly higher "rest" nitrogen and

42. Morganbesser: Cited by Mandel.
43. Camerer: Ztschr. f. Biol., 1891, xxviii, 72.
44. Erben: Ztschr. f. Heilk., 1904, xxv, 33.
45. Folin: Am. Jour. Physiol., 1905, xiii, 66.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

ammonia excretion than is found either normally or in the less active stages of the disease, but that the differences are usually not great enough to warrant the belief that the urea-forming process is necessarily seriously interfered with in uncomplicated typhoid fever.

The almost, if not quite, normal urea and "rest" percentages at times when the subjects were losing much body protein-nitrogen are especially instructive in showing that the protein of body tissue is at least under these conditions katabolized in the same way as food protein.[46] (See Table 8, Periods I and III; Table 12, Period III; Table 20, Periods I, II, etc.).

TABLE 35.—PROBABLE NORMAL LIMITS IN THE EXCRETION OF UREA, AMMONIA AND "REST" N.

Gms. of Total Nitrogen.	Per Cent of Total Nitrogen — Urea Low.	Urea High.	Ammonia Low.	Ammonia High.	"Rest" Low.	"Rest" High.
3 to 5.9	56	79	4	13	4	15
6 to 9.9	72	85	2	7	5	10
10 to 14.9	80	89	2	6	4	9
15 to 22	85	90	2	5	2	7

We should, of course, not conclude from our results that one never finds in typhoid fever very marked abnormalities in the excretion of urea and rest nitrogen. Ewing and Wolf[47] have found low urea and high "rest" nitrogen percentages in fatal cases. We have had no fatal cases in this series, though many of the subjects were severely ill. From the fact that most of our subjects did not show a very marked increase in "rest" nitrogen or decrease of urea percentage we are led to the conclusion that a serious interference with the urea-forming function is not an essential part of the process of typhoid fever, and that, when such marked abnormalities of this function appear in this disease, as found by Ewing and Wolf, they are the result of factors complicating the disease. And by such complicating factors we mean not the common accidents, like intestinal perforation, but rather a serious damage to the liver or other

46. The truth of the above statement depends, of course, on the reliability of the methods for the determination of urea. The Folin method, which we believe is superior to other methods at present used, has been employed in these experiments and in all other recent work in this laboratory. This, like other urea methods, is, however, an indirect one, and is based on the assumption, proved by Folin for normal urines, that no substance other than urea is present which may be decomposed, with the formation of ammonia, under the conditions of the determination; and we should not overlook the possibility that in fever or other pathological urines such substances may be excreted.

47. Ewing, J., and Wolf, C. G. L.: The Clinical Significance of the Urinary Nitrogen: III. Nitrogenous Metabolism in Typhoid Fever, The Archives Int. Med., 1909, iv, 330.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

important organs, perhaps involving cellular degenerations, and thus interfering with the functions of those organs.

The ammonia excretion in these experiments was usually somewhat increased during the active stages of the disease, this increase being on the whole greater than the increase of "rest" nitrogen. The high ammonia is probably coincident with an increased excretion of organic acids; diacetic and oxybutyric acids were never found, even at those times when the subjects were not receiving much carbohydrate. The amount of ammonia was moreover never large enough to indicate any considerable acidosis. The ammonia excretion in these subjects does not appear to have been affected by the intake of carbohydrate, as it would be in the presence of an oxybutyric acid acidosis.

THE SULPHUR PARTITION OF THE URINE IN TYPHOID FEVER

Total Sulphur.—Since the sulphur of the urine is derived chiefly from food or tissue protein the amount of total sulphur excreted usually bears a fairly constant relation to the amount of total nitrogen of the urine. As might be expected this relation varied somewhat with different diets. With a milk-egg diet, with or without meat, between 7 and 8 parts of total sulphur are excreted for each 100 parts of total nitrogen.[48] The same relationship was found in the urine of these subjects of typhoid fever, whether they were losing body protein or retaining food protein. The ratio between total sulphur and total nitrogen was with W——d (Table 16) 7.5 when he was losing 11.3 gm. of body-protein nitrogen per day and 7.3 when he was gaining 3.7 gm. nitrogen per day. Much the same thing is seen with Z——o and B——t (Tables 12 and 20). The ratios are in several instances below 7, but are, on the whole, remarkably constant.

The fact that an equivalent amount of sulphur is excreted with the nitrogen, even when the subject is losing body protein, is of interest in showing that the effect of carbohydrate in decreasing the nitrogen excretion in fever is not to be explained by a mere temporary retention of amino-acids of the food protein in the form of amino-sugars (Lüthje[49]). Were this the case we should expect, on withdrawing the protecting carbohydrate, a sudden excretion of the retained nitrogen without an accompanying amount of sulphur.[50] On withdrawing the carbohydrate from Z——o (Tables 11 and 12) in Period III the nitrogen excretion

48. Folin and Shaffer: Am. Jour. Physiol., 1902, vii, 145. Folin: Am. Jour. Insanity, 1904, lx, 729. Shaffer: Am. Jour. Physiol., 1908, xxii, 449.

49. Lüthje: Verhandl. d. Kongress f. inn. Med., 1906, xxiii, 440.

50. Unless the nitrogen were retained in some form of thio-amino-sugar.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

increased over 50 per cent., and the total sulphur increased practically in proportion. In Periods I and II, when there was great protection from the febrile loss of body nitrogen, the nitrogen-sulphur ratios were normal, again indicating that the body protein was actually protected from taking part prominently in the febrile katabolism. Had the carbohydrate caused merely a retention of amino-acids this ratio might well be abnormally high.

Ethereal Sulphur.—This fraction of the sulphur excretion by our subjects was within the normal limits, usually between 0.02 and 0.07 gm. This fact and the usual absence of a large excretion of indican gave no indication of excessive intestinal putrefaction.

Neutral Sulphur.—This fraction of the sulphur partition was uniformly much increased above the accepted normal values of 0.10 to 0.15 gm.[51] The highest amounts were excreted during the height of the fever, and fell to within normal limits with the decline of the temperature. The amount of neutral sulphur excreted in this disease bears no constant relation to the total sulphur, to total nitrogen, or to the loss of body-protein-nitrogen, and the significance of the febrile increase in this fraction is not at present clear.

Subjects of fever are supposed to be especially prone to alimentary glycosuria; and we rather expected to find a considerable excretion of sugar during the times when our patients were taking large quantities of lactose and other carbohydrates. Small quantities of sugar, rarely more than traces, were occasionally found in the urines during these experiments. The amounts were not large enough for accurate determination by titration with Fehling's or Pavy's solutions, and probably never exceeded 0.2 per cent., or a maximum of about 6 gm. in twenty-four hours.

THEORETIC CONSIDERATIONS

We have seen on a number of occasions in the preceding pages that, during the active stages of the disease, *a loss of body protein may be wholly prevented* by the intake of food of sufficient caloric value. These instances show very conclusively that the febrile destruction of body protein, including *both the effect of pyrexia and of toxins,* in the human subject of typhoid fever, may be either prevented altogether *or* may be compensated for by a large retention of body protein. As stated earlier in this paper, other experiments have indicated that the effect of pyrexia in causing an increased katabolism of protein may be prevented, but so far as we know the experiments here recorded are the first to show satis-

51. Shaffer: Am. Jour. Physiol., 1906, xvii, 369-375; ibid, 1908, xxii, 449.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

factorily in the human subject that the action of toxins, as well as of the pyrexia, may be prevented from causing a loss of body protein by the addition to the food of a sufficient quantity of carbohydrate.

What is the probable explanation of this sparing of protein by carbohydrate in fever? Do we, by food of high caloric value, actually retard or prevent the febrile destruction of the body protein, or do we cause an increased retention of food protein which masks the destruction of body protein?

This very important question we, of course, do not hope to answer conclusively in this paper, but certain of our results have a very direct bearing on this consideration.

Results based wholly on the comparison of the intake and excretion of nitrogen, the nitrogen balance, show merely the final gain or loss of nitrogen to the body; they do not show variations in the extent of the endogenous metabolism; they do not tell us the amount of body protein destroyed in fever any more than they tell us the amount of protein destroyed in the normal endogenous katabolism. The nitrogen balance in our experiments shows that the loss of protein in fever becomes less or may be prevented by food of high carbohydrate value. We might interpret this in at least two ways: that the large food-supply causes merely a retention of food protein or other nitrogenous substances, thus masking the destruction of body protein; or that the large food-supply has furnished all of the required energy and in available form to maintain equilibrium, and that the body found it no longer necessary to use its own material for that purpose.

Should we accept the idea of Krehl of an actual destruction of the protein of body cells by bacterial toxins we must also accept the first explanation of our result, because it is improbable that such a toxic destruction can be prevented by any form or amount of food. But Krehl's idea of the toxic destruction has by no means been proved to be correct, and there is one point brought out in our experiments and already referred to which we think distinctly favors the other interpretation—i. e., that the chief effect of the large carbohydrate intake is actually to protect the body protein from taking part in the excessive katabolism. This point is the behavior of the kreatin excretion. We have already considered this matter in some detail and need not repeat it here further than to say that endogenous kreatin, so far as we know, is excreted only when there is an abnormal absorption of muscle protein; that we have found it excreted in large amounts by the subjects of our experiments when they were at the same time losing much body protein; *and that it was not excreted,* or at any rate in but small amounts, *when*

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

the same subjects were being protected from the loss of body protein by food of high caloric value and rich in carbohydrates. It therefore seems very probable that such food in some way greatly retards and, if sufficient, may even prevent the "toxic" or other destruction of muscle protein.

The relative constancy of the relationship between total nitrogen and total sulphur, which has already been referred to, is another indication of the same character.

Whether the above conclusion is wholly sound, further work will have to determine. It may well be that there remains a relatively small effect of toxins on the protein katabolism which may not be influenced by food, for, as we have seen, small amounts of kreatin were often excreted when the subjects received a very large supply of food and when they were even gaining nitrogen. Kreatinin, uric acid, and neutral sulphur are usually high during the active stages of the disease, whether or not the food value is high, and the endogenous katabolism concerned with these substances may be independent of the food supply. But we believe our results show that *quantitatively the most important part of the febrile destruction of body protein (in typhoid) may be retarded or prevented by food containing a moderate amount of protein and very rich in carbohydrate.*

The total caloric value of the diets used in the periods of great protection of body protein is very high, 60 to 90 cal. per kg. Whether such large amounts of food were actually utilized within the organism it is impossible to learn from our data. We have had no facilities for determining the total energy exchange, but, from the few such determinations which have been made on fever subjects, it is perhaps improbable that the total heat production of our patients reached the values represented by the larger amounts of food.

It seems to us more probable that the carbohydrate is the essential constituent of the food, and that the same sparing of body protein might have been accomplished had the fat been withdrawn from the various diets. The basis for this opinion is, however, not wholly satisfactory, for the data in our experiments regarding the relative value of fat in sparing body protein are not clear. This point awaits further investigation.

If fat does not assist in the protection of body protein from the febrile destruction the sparing observed during these experiments is to be referred to carbohydrate alone. The carbohydrate value of the diets used during the most favorable periods was between 40 and 50 carbohydrate calories per kg., and this amount, or even more, is necessary to pre-

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

vent wholly a febrile loss of body protein. It may be that in carbohydrate alone we must supply more energy than equals the total heat production; and, if so, the situation is similar to that of the experiment by Murlin,[52] who found that 125 per cent. of the maintenance requirement in the form of carbohydrate, when given to a dog, spared 49 per cent of the starvation excretion of nitrogen, while 100 per cent. of the requirement spared only 23 per cent. of the starvation excretion.

The typhoid subject who is losing body protein (62.5 gm.) equivalent to 10 gm. of nitrogen per day derives from this protein only 250 cal., and it seems very remarkable that, to prevent this loss, we must give him additional carbohydrate equivalent to 2,000 cal. or more. The same is true in simple starvation. In neither instance have we at present any explanation of this apparent anomaly. In both cases it is evident that the use of the carbohydrate is not a mere replacement of isodynamic quantities of protein. Some insight into these questions will doubtless follow investigations of the total energy exchange in fever subjects receiving diets containing varying quantities of carbohydrate. At the present time an adequate explanation of this action of carbohydrate is not possible.

PRACTICAL THERAPEUTIC CONSIDERATIONS

We have so far avoided any discussion of the therapeutic value in typhoid or other acute infectious fevers of the protection from the katabolism of body protein afforded by diets rich in carbohydrates, for the reason that we have not accumulated sufficient data to judge this question. It seems to us obvious that unless there are distinct and forceful objections to such dietetic treatment the subject of the disease will be better off if he is not permitted to use up his body material. Unless we gratuitiously assume the febrile destruction and loss of body protein to be a beneficial process, it is difficult to avoid the conclusion that we are ministering to the welfare of the patient by preventing that destruction or loss. We have so far encountered clinically no valid objection to the use of such diets as those of the experiments here described, and, unless future experience proves such objection, we believe it highly desirable to retard and, if possible, prevent the febrile loss of body protein.

The general nutrition of the subjects of our experiments was exceptionally good at the end of the disease, many weighing more at the time of discharge than when they entered the hospital.

A more detailed discussion of the strictly clinical aspects of this question will be attempted in a future paper.

52. Murlin: Am. Jour. Physiol., 1907, xxi, 254.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015

CONCLUSIONS

As a result of our experiments the following conclusions may be drawn regarding the protein metabolism in typhoid fever:

1. By the use of diets of high caloric value and especially rich in carbohydrate it is possible to retard and, if the carbohydrate supply be sufficient, to prevent the febrile *loss* of body-protein-nitrogen in subjects of typhoid fever.

2. By such dietetic treatment the "toxic" destruction of body protein as well as the destruction due to simple pyrexia in this disease may therefore be *either prevented or compensated for.*

3. The behavior of kreatin and of total sulphur in our experiments appear to show that the febrile destruction of body protein, including the action of pyrexia and of toxins, is actually retarded or even wholly prevented by the intake of sufficient carbohydrate.

The prevention of the febrile loss of body protein is therefore probably not to be explained by a mere compensatory retention of food protein.

4. The results support the belief that in fever there is a greater need for carbohydrate; that if the food does not contain sufficient carbohydrate the body protein is drawn on perhaps to supply energy in an available form; but that, if sufficient carbohydrate be available from the food, the body protein is protected from the febrile destruction.

5. If, as seems probable from our results, the "toxic" destruction of body protein may be prevented by large carbohydrate intake, the mechanism of this "toxic" destruction cannot be a direct (poisonous) injury to body cells and proteins.

6. To maintain nitrogen equilibrium in typhoid fever the food must contain 10 to 15 gm. nitrogen in addition to much carbohydrate. Our experiments show no advantage from a further increase of food-protein

We take pleasure in expressing our obligations to Dr. Armstrong, to Miss Goodrich, to Drs. W. M. Kerr, T. S. Kearns, members of the resident staff of the second division of Bellevue Hospital, for many courtesies and assistance during the work; to Mr. M. I. Smith and Dr. G. H. Bentz for assistance in the laboratory, and to Dr. C. L. Dana for the privilege of continuing the work during his service in the hospital.

414 East Twenty-sixth Street—58 West Fifty-fifth Street.

Downloaded From: http://archinte.jamanetwork.com/ by a Monash University Library User on 06/04/2015