CCLXXXII. A STUDY OF THE EFFECT OF OVERFEEDING ON THE PROTEIN METABOLISM OF MAN

IV. THE EFFECT OF MUSCULAR WORK AT DIFFERENT LEVELS OF ENERGY INTAKE, WITH PARTICULAR REFERENCE TO THE TIMING OF THE WORK IN RELATION TO THE TAKING OF FOOD

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On a diet adequate in protein and energy value Tallqvist [1902] and more recently Silver [1937] have found that restriction of the carbohydrate content with an isocaloric increase in fat produces a rise in the urinary N excretion, and recent work has shown that the addition of extra carbohydrate to an adequate diet causes a decrease in the urinary N output of man [Cuthbertson & Munro, 1936; 1937] and of the dog [Larson & Chaikoff, 1937]. The former found that this protein-saving effect increased in proportion to the intake of additional carbohydrate, and it thus appears that there is a reciprocal relationship between the carbohydrate intake and the extent of the N elimination. It is presumed that during overfeeding with carbohydrate there is preferential combustion of this material since the storage capacity for carbohydrate as such is very limited. In the absence of a rise in metabolism sufficient to utilize the excess energy intake, storage results and in consequence N elimination falls. The work of Larson & Chaikoff [1937] and the *in vitro* experiments of Krebs [1935] support the belief that an abnormal rise in the concentration of carbohydrate in the tissues during absorption of the products of a mixed meal inhibits deamination.

To elucidate the problem further, it was decided to examine the effects of diminishing the fuel reserves of the body by muscular work, done:

1. (*a*) before and (*b*) after food, on certain days during a period of prolonged excess feeding with carbohydrate;
2. (*a*) before and (*b*) after food on a diet just adequate to cover the additional work performed;
3. (*a*) before and (*b*) after food, the diet being adequate for maintenance, but not covering the additional work done.

In this way it was hoped to examine the effect of increased carbohydrate oxidation when accumulation of products of digestion was at a minimum, for comparison with the periods in which both increased carbohydrate oxidation and absorption from the intestine were proceeding together.

Experimental

D. P. C. (37 years; height 184·4 cm.) and H. N. M. (21 years; height 164 cm.) were the subjects of these experiments and the basal diets selected were somewhat similar to those employed in the earlier studies. As the relationship of the work done to the time of taking of food is of importance the exact meals and times of consumption are given.

Table I

D. P. C.

	Breakfast 8.5 a.m.	Lunch 1 p.m.	Tea 5.10 p.m.	Supper 11 p.m.
Cheese	—	25 g.	25 g.	—
Brown bread	100 g.	60 g.	60 g.	30 g.
White bread	50 g.	150 g.	150 g.	50 g.
Jam	100 g.	per day, the distribution being governed by the total amount of bread per meal		
Butter	120 g.			
Tomatoes	200 g.			
Apples	1	—	—	1
Lettuce	+	+	+	—
Milk	25 ml.	250 ml.	25 ml.	200 ml.
Potato	—	50	—	—
Sugar (cane)	10 g.	—	10 g.	—
Water	310 ml. (As tea)	400 ml. + juice of one half lemon	310 ml. (As tea) 300 ml. + juice of one half lemon	100 ml.

H. N. M.

	Breakfast 9.30 a.m.	Lunch 12.45 p.m.	Tea 4.30 p.m.	Supper 8 p.m.
Cheese	—	15 g.	—	—
Brown bread	25 g.	60 g.	60 g.	25 g.
White bread	50 g.	150 g.	100 g.	25 g.
Jam	100 g.	per day, the distribution being governed by the total amount of bread per meal		
Butter	120 g.			
Bran	—	—	—	15 g.
Apples	—	1	—	1
Milk	—	—	250 ml.	250 ml.
Water	880 ml.	440 ml.	150 ml. (As tea)	240 ml. (As tea)

The calorie values of these diets as calculated from Plimmer's tables were 3533 and 2815 Cal. respectively, and the total N contents were found by analysis to be 16·32 and 12·21 g.

In the case of D. P. C. urine was collected from 7.45 a.m. to 7.45 a.m. the next day and from 9.30 a.m. to 9.30 a.m. in the case of H. N. M. It was preserved with 2% thymol in chloroform except on the few occasions when sugar was being estimated; toluene was then used. The experiments on D. P. C. were performed in one continuous period in May 1937, those on H. N. M. in two periods, one in April the other in July 1937. The body weights were measured at the same time each forenoon and in the same light clothes. In the graphical records the body weight has been correlated with the N etc. excretions of the previous 24 hr.

Work was done on the bicycle ergometer described by McCall & Smellie [1931] and, except for the first series of experiments, lasted for two periods of 55 min. on the two successive days in each period, the loads being 0·88 kg. (D. P. C.) and 1 kg. (H. N. M.), the pedalling being at constant rate controlled by metronome (120 beats per min.). Approximately 43,100 kg.m. (101 Cal.) work per day were done by D. P. C.; approximately 48,000 kg.m. (112 Cal.) work per day by H. N. M. At no time was sweating profuse or the work at all exhausting (H. N. M.'s first work period excepted). The metabolic cost of the additional work done was obtained by deducting from the total calories expended during the working period the calories expended when performing light laboratory work. These measurements were made indirectly by analysis of the expired air collected in a Douglas bag during the middle of the work periods or corresponding period of the basal days.

The analytical methods used were:

Total N—Kjeldahl.
Total S—Denis.
Cl—Volhard-Harvey [Harvey, 1910].
P (inorg.)—Fiske & Subbarow [1925].
Na—Butler & Tuthill [1931].
K—Kramer & Tisdall [1921].
Ca and Mg—Shohl & Pedley [1922].

First series (Preliminary)

Subject H. N. M. Table II, Fig. 1.

Table II. *Subject H. N. M. Metabolic data of first series of experiments*

Day of diet	Diet	Body wt. kg.	Urinary vol. ml.	Urinary total N g.	Faecal total N g.	Urinary total S g.	Extra muscular work (total period per day 1 hr.)
2	Basal	64·20	880	—	—	—	—
3	,,	64·05	2090	10·79	—	0·658	—
4	,,	63·70	2248	10·63	—	0·725	—
5	Basal + 210 g. glucose	64·00	1795	10·24	1·12/day	0·647	—
6	,,	64·30	1810	9·24		0·592	—
7	,,	64·50	1380	9·06		0·609	—
8	,,	64·35	2018	9·29		0·606	—
9	,,	64·15	1350	8·73		0·614	48,000 kg.m. per day performed shortly before food at a physiological cost of 522 Cal. (657 Cal. gross − 135 Cal. light work basal)
10	,,	64·60	825	9·50	—	0·734	
11	,,	65·10	1410	9·80	—	0·594	—
12	,,	64·90	2106	9·12	—	0·641	—
13	,,	64·65	1740	9·02	—	0·673	48,000 kg.m. per day performed shortly after food
14	,,	64·30	1305	10·06	—	0·722	
15	,,	64·70	1480	10·69	—	0·717	—
16	,,	64·45	1840	10·59	—	0·782	—
17	,,	—	680	9·62	—	0·750	—

N equilibrium was first established on an adequate diet; the energy value was then increased above requirement by the addition of 210 g. glucose (785 Cal.) taken in three equal lots of 70 g. each, at 3, 4 and 7 p.m. daily. As a result of this excess food a definite retention of N and S took place comparable with that noted in earlier experiments. The daily N output was depressed by about 1·5 g. As soon as the N excretion had come to a steady value muscular work was superimposed on 2 successive days, the work being 48,000 kg.m. (112 Cal.), and at a physiological cost of approximately 522 Cal. based on analysis of the expired air. From the gross value was deducted the cost of performing light laboratory duties.

In this particular period the extra work was all completed between 11.30 a.m. and 12.30 p.m. on each of the 2 days, i.e. immediately before lunch. On the first day of work there was a diminution in the N excretion and on the day following a slight rise which was continued into the first post-work day; the basal value was reached on the second post-work day. The S excretion behaved somewhat differently. No fall took place on the first work day. On the second work day there was a definite rise which did not continue like that of N into the post-work period.

On the next 2 days further periods of work were performed equivalent to 48,000 kg.m. per day but as the rate of working had proved somewhat exhausting in the first work period, on this occasion it was done in three 30 min. spells, after lunch, tea and supper and was equivalent to 22,880, 18,300 and 6860 kg.m. On these 2 days the additional glucose (210 g.) was divided so that at lunch, tea and supper the amounts consumed were 100, 80 and 30 g. The N and S excretions rose to much higher levels during this period; there was no rise in N on the first work day and the maximum excretion was again noted on the first post-work day, but even by the third post-work day the N and S excretions had not returned to normal.

Although unsatisfactory in many respects, this experiment was of interest in so far as it indicated the possibility that a time relationship between the work done and the period of absorption of food might play a part in determining the extent of the increased N excretion which many have observed to result from work, e.g. Cathcart & Burnett [1925], Wilson [1932].

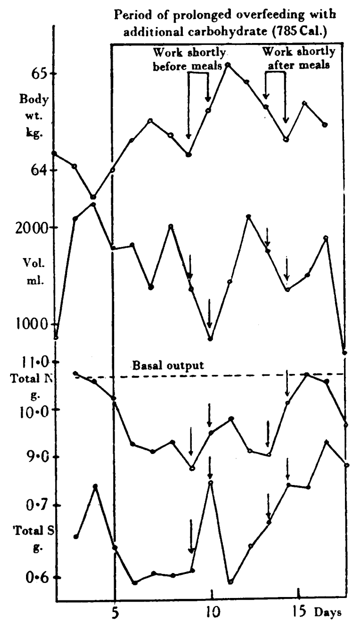

Fig. 1. Subject H. N. M. The effect of work performed shortly before and shortly after meals during a period of prolonged overfeeding with additional glucose equivalent to 785 Cal.

To elucidate this point further a second series of experiments was performed.

Second series

Subject D. P. C. Table III, Fig. 2.

N and weight equilibrium were first established on the basal diet. Muscular work was then performed on 2 successive days without any increment in energy intake. Lunch and tea were consumed at 1–1.30 and 5.30–6.0 p.m. respectively and the work, 43,100 kg.m. (101 Cal.), was performed at 2–2.55 and 6.30–7.25 p.m., that is during the maximum absorptive periods for carbohydrate. (The work of Christensen *et al.* [1934], Courtice & Douglas [1936] and Haldi & Bachmann [1937] indicates that freshly ingested carbohydrate is not used for muscle work. There is evidence to show that in moderate work both carbohydrate and fat are catabolized in proportions determined by the preceding diet.) The physiological cost of the work was approximately 476 Cal. as based on analyses of air taken during the middle of the work period.

After a slight fall in N output on the first day of work, the level then rose and reached its maximum on the first post-work day. It had practically reached the basal level on the next day. The total rise over basal during the 2 work days and the post-work day was 1·71 g. The urinary excretion of S rose on the first work day to its maximum value. The output on the second work day was practically the same and by the first post-work day basal values were reached.

Table III. *Subject D. P. C. Metabolic data of second series of experiments*

Day of diet	Diet	Body wt. kg.	Urinary vol. ml.	Urinary total N g.	Urinary total S g.	Urinary Cl g.	Urinary inorg. P g.	Urinary Na g.	Urinary K g.	Urinary Ca g.	Urinary Mg g.	Extra muscular work (total period per day 110 min.)
3	Basal	86·40	—	—	—	—	—	—	—	—	—	—
4	,,	86·00	—	—	—	—	—	—	—	—	—	—
5	,,	86·00	1062	14·34	0·944	5·40	1·36	4·80	2·08	0·202	0·145	—
6	,,	86·12	1415	14·59	0·984	6·25	1·44	5·27	2·20	0·208	0·147	—
7	,,	85·60	1080	13·83	1·054	6·38	1·41	5·11	2·24	0·214	0·157	43,100 kg.m. work per day performed shortly after food at a physiological cost of 476 Cal. (747 Cal. gross − 271 Cal. light work basal). R.Q. during middle of work period = 0·947
8	,,	85·63	980	15·48	1·048	5·82	1·03	4·91	2·20	0·212	0·155	
9	,,	85·60	1230	15·78	0·984	5·40	1·15	4·84	2·19	0·208	0·150	—
10	,,	85·70	1850	14·69	0·964	7·12	1·28	5·47	2·32	0·220	0·162	—
11	,,	85·57	2250	14·55	0·978	7·00	1·39	5·27	2·14	0·212	0·157	—
12	Basal + 130 g. cane sugar with food	85·57	1200	14·18	1·033	5·68	1·25	4·99	2·10	0·214	0·150	43,100 kg.m. work per day performed shortly after food at a physiological cost of 466 Cal. (750 Cal. gross − 284 Cal. light work basal). R.Q. during middle of work period = 0·950
13	,,	85·59	1210	15·03	1·044	5·82	1·23	4·88	2·22	0·220	0·164	
14	Basal	85·57	1510	15·23	1·020	6·38	1·29	5·27	2·35	0·270	0·157	—
15	,,	85·71	1670	14·21	0·996	6·45	1·31	5·11	2·28	0·210	0·158	—
16	,,	85·46	2260	14·66	1·081	7·17	1·41	5·20	2·27	0·250	0·154	—
17	Basal + 130 g. cane sugar with food	85·66	1350	13·67	0·988	6·25	1·45	4·72	2·19	0·220	0·145	43,100 kg.m. work per day performed shortly before food
18	,,	85·46	1375	13·91	0·956	5·92	1·14	4·91	2·19	0·215	0·154	
19	Basal	85·71	1340	14·18	0·978	5·96	1·09	4·84	2·16	0·245	0·156	—
20	,,	85·31	1710	14·89	0·896	6·39	1·40	5·07	2·28	0·258	0·166	—
21	,,	85·57	1840	14·02	0·956	6·67	1·39	5·15	2·17	0·273	0·167	—
22	Basal + 130 g. cane sugar with food	85·70	1400	13·64	0·908	6·25	1·15	4·99	2·13	0·249	0·163	—
23	,,	85·82	1440	13·66	0·908	6·46	1·20	5·03	2·10	0·206	0·157	—
24	,,	85·81	1440	13·09	0·896	6·39	1·25	4·99	2·15	0·224	0·151	—
25	,,	85·81	1340	13·35	0·918	6·25	1·20	4·95	2·08	0·197	0·158	—
26	,,	86·06	1020	13·48	0·967	6·43	1·12	4·99	2·14	0·204	0·163	43,100 kg.m. work per day performed shortly before food
27	,,	85·99	1620	14·37	1·005	6·39	1·14	4·99	2·28	0·227	0·157	
28	,,	86·07	1465	14·28	1·000	6·25	1·12	4·91	2·19	0·232	0·154	—
29	,,	85·91	1820	13·49	0·906	7·00	1·25	5·27	2·26	0·224	0·161	—
30	,,	86·01	1820	13·51	0·934	7·14	1·29	5·30	2·34	0·218	0·154	—
31	,,	85·97	1265	13·08	1·028	6·39	1·12	4·97	2·15	0·236	0·159	43,100 kg.m. work per day performed shortly after food at a physiological cost of 439 Cal. (708 Cal. gross − 269 Cal. light work basal). R.Q. during middle of work period = 0·950
32	,,	85·63	1075	14·64	1·058	6·25	1·08	4·92	2·30	0·228	0·150	
33	,,	85·61	1815	14·55	0·978	6·94	1·22	5·31	2·38	0·240	0·149	—
34	,,	85·94	1320	14·18	0·972	6·54	1·21	5·24	2·34	0·231	0·153	—
35	,,	86·47	1400	13·58	0·984	6·27	1·36	5·08	2·22	0·238	0·144	—
36	Basal + 20 g. cane sugar with food	86·17	1850	14·25	1·014	6·50	1·30	5·14	2·30	0·227	0·147	—
37	,,	85·87	1720	14·25	0·945	6·34	1·20	5·16	2·32	0·240	0·155	—
38	Basal + 130 g. cane sugar with food	85·99	1730	13·90	0·992	6·42	1·24	5·20	2·24	0·242	0·159	—

This more rapid excretion of S was also noted in the subsequent work periods. Body weight fell during this period.

The work period was repeated but on this occasion the physiological cost of the work (466 Cal.) was made good by the addition of two lots of 65 g. cane sugar taken in lemon water at the close of lunch and tea. The rise and fall in N and S excretions had the same general trend as in the first work period but the rises were less pronounced. During the 2 work days and first post-work day 1·06 g. N were excreted over basal. There was naturally no further loss in weight when the cost of the work was covered.

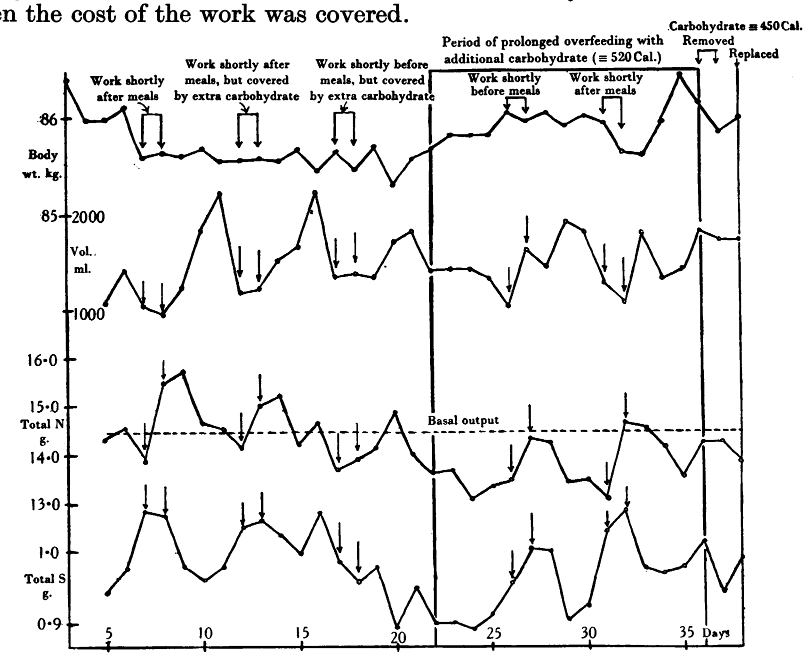

Fig. 2. Subject D. P. C. The effect of work performed shortly before and shortly after meals on (a) basal diet, (b) basal diet + sufficient cane sugar to cover cost of work, and (c) during period of prolonged surfeit with cane sugar.

When N equilibrium had again been restored the same amount of work was repeated on 2 successive days, the cost of the work again being made good by the same additions of cane sugar taken at the same times, but the work, instead of following the ingestion of food, was performed between 11.30 a.m. and 12.25 p.m. and between 4.15 and 5.10 p.m. Instead of rises in N and S excretions there occurred falls which persisted during the second work day. This confirmed the previous suspicion that the effect of work on protein metabolism was influenced by the time relationship of the working period to the taking of food. It was then decided to repeat the experiments of the first series and to this end the N and S excretions were first depressed by taking 130 g. cane sugar in lemon water daily in two equal lots at the conclusion of lunch and tea. A slight alimentary glycosuria amounting to 3·5 g. per day occurred. Body weight immediately commenced to rise, the N and S excretions to fall. Eventually the N excretion remained fairly stable, about 1 g. below basal level. As in the preceding experiment work was now performed before lunch and tea on 2 successive days. The additional daily work (43,100 kg.m.) was calculated to require an energy expenditure approximately equal to the calorie value of the daily extra intake of carbohydrate, so that a rise in N excretion to the original value was anticipated. Instead of a fall in N and S excretion as in the last work period, a rise occurred, confirming the findings on H. N. M. in the first experimental series. The maximum excretions took place on the second work day and practically reached the original basal value. For the 2 work days and the first post-work day the total rise over the depressed basal was 1·63 g.

The procedure was then repeated, the work (physiological cost 439 Cal.) however being done shortly after lunch and tea, as in the first two work periods of this series. The rise in N excretion was much more marked than in the preceding experiment and even on the second post-work day the N excretion was above normal. This was in accordance with what had been found in the case of H. N. M. The total rise over the depressed basal level was approximately 2·45 g.

For purposes of comparison with these last two work periods, carbohydrate (cane sugar) equivalent to 450 Cal. was omitted in two equal lots at lunch and tea, on 2 successive days. The result was an immediate rise in N excretion lasting for 2 days and amounting in all to approximately 1·54 g. above the depressed basal; an amount not far short of that observed when the work was done before food during the period of excess feeding, with the distinct difference that (1) on the first day of work there was virtually no rise in N excretion, whereas the direct removal of carbohydrate caused an immediate response, and (2) the rise in N following the work was continued into the first post-work day, whereas no such delay resulted from the direct removal of carbohydrate. The S excretion behaved in a somewhat analogous fashion. Apart from a slight elevation during the period of surfeit feeding, the creatinine excretion remained very constant.

Third series

H. N. M. Table IV, Fig. 3.

These experiments were instituted to confirm the previous findings on D. P. C.

Having first established N and weight equilibria on an adequate diet (30 g. less butter than the basal diet of April series), work was performed on 2 successive days between 11.30 a.m. and 12.30 p.m., lunch and tea being consumed at 12.45 and 4.30 p.m. respectively. In this period no attempt was made to cover the cost of the work. The increase in N and S excretions was slight and the maximum N output occurred on the first post-work day. These changes, when compared with those found during the third work period in this series, indicate that when the work is not covered by increasing the fuel value of the diet, there is a much more marked excretion of N and S if the work is done shortly after the taking of food than is the case if the work is performed shortly before meals.

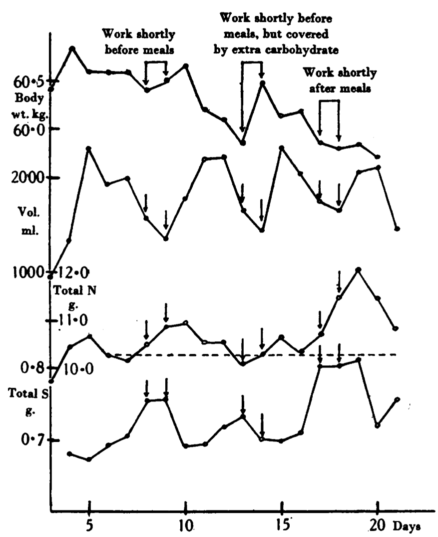

Fig. 3. Subject H. N. M. The effect of work performed shortly before and shortly after meals.

During the second work period in this series more than sufficient carbohydrate was taken at lunch and at tea to cover the extra work done (135 g.

Table IV. *Subject H. N. M. Metabolic data of third series of experiments*

Day of diet	Diet	Body wt. kg.	Urinary vol. ml.	Urinary total N g.	Urinary total S g.	Urinary Cl g.	Urinary inorg. P g.	Urinary Na g	Urinary K g.	Extra muscular work (total period per day 110 min.)
1	Basal	60·40	975	9·69	—	4·43	0·91	4·10	1·72	—
2	,,	60·85	1325	10·23	0·680	4·58	0·95	4·15	1·65	—
3	,,	60·60	2310	10·63	0·669	7·07	1·10	4·92	1·84	—
4	,,	60·60	1945	10·26	0·691	5·72	1·04	4·47	1·80	—
5	,,	60·60	1980	10·18	0·712	5·40	0·98	4·23	1·71	—
6	,,	60·40	1590	10·51	0·752	4·40	1·15	4·25	1·74	48,000 kg.m. work per day performed shortly before food
7	,,	60·50	1370	10·86	0·753	4·26	1·18	4·20	1·67	
8	,,	60·65	1790	10·95	0·690	4·97	1·02	4·26	1·74	—
9	,,	60·20	2205	10·53	0·698	6·28	0·94	4·35	1·78	—
10	,,	60·10	2242	10·56	0·721	6·50	0·90	4·50	1·81	—
11	Basal + 135 g. glucose with food	59·85	1638	10·16	0·733	5·40	0·98	4·32	1·72	48,000 kg.m. work per day performed shortly before food
12	,,	60·50	1442	10·27	0·707	3·55	1·23	4·03	1·66	
13	Basal	60·15	2310	10·63	0·706	6·56	1·02	4·67	1·75	—
14	,,	60·20	2022	10·38	0·711	5·45	1·05	4·58	1·74	—
15	,,	59·85	1767	10·72	0·805	5·68	0·98	4·27	1·77	48,000 kg.m. work per day performed shortly after food
16	,,	59·80	1640	11·52	0·805	4·40	0·95	3·91	1·73	
17	,,	59·85	2060	12·06	0·808	5·85	0·91	4·25	1·79	—
18	,,	59·70	2122	11·50	0·722	6·05	1·02	4·20	1·79	—
19	,,	—	1480	10·82	0·755	5·00	1·10	4·35	1·77	—

glucose = 505 Cal.). The work was performed before taking the food. A depression of N and S excretion took place just as in the similar experiment on D. P. C. There exists therefore a distinct difference between the effects of work on protein metabolism when the work is covered and when it is uncovered by extra available energy, the time relationship being unchanged.

Discussion

Analysis of the results of these experiments in accordance with the scheme outlined in the introduction demonstrates that:

(1) If work is done on certain days during a prolonged period of surfeit feeding with carbohydrate, such surfeit providing energy in slight excess of the extra expenditure on the selected work days, there occurs a rise in N and S excretion over the depressed basal values. The rise is exhibited even when the work is done shortly before food and is such as to bring the output of these catabolites up to their level on the basal maintenance diet. When the work is done shortly after meals (absorptive state) the rise in N and S excretion is more marked and of longer duration than when the work is performed before meals.

(2) When work is superimposed on a basal diet just adequate for maintenance a definite rise in N and S excretion is noted if the work is performed shortly after the meals. There is only a very small rise when the work is performed shortly before the taking of food.

(3) If the additional work be covered by extra carbohydrate, taken at lunch and tea, then no rise in N and S excretion takes place if the work be done shortly before these meals; indeed a fall may be noted, whereas if performed shortly after food, a definite rise occurs.

It is difficult to put forward a satisfactory hypothesis to account for these phenomena. These varied time relationships do, however, offer a possible explanation for the diversity of experimental results which have appeared in the literature concerning the effect of work on protein metabolism. The literature on the relation between protein metabolism and muscular work has been reviewed by Cathcart [1925], Mitchell & Hamilton [1929], Lusk [1931], Wilson [1932] and Mezincesco [1937]. The presence or absence of a rise in N excretion appears to be dependent on the time relationship of the work done to the absorption of the food, and on the relationship between the energy intake of the basal diet and that of the work period. Many experiments on muscular work can be criticized on the grounds either that the cost of the work was not covered by a sufficient intake or that the diet of the pre-work period was excessive.

When the adequately fed organism is confronted with the necessity of disposing of ingested food in excess of its energy requirement, it burns what it can and stores what it cannot. An alimentary glycosuria may also result if a large excess of carbohydrate is given. When the organism is flooded with carbohydrate the glycogen stores of the liver, muscle and other tissues are soon filled up, for the capacity to store this substance is limited. With a continued excess of glucose in the system, the proportion of carbohydrate burned is raised more and more. It is at this point in all probability that fat formation must result in order to dispose of the continued supply of carbohydrate. Coincidently with this increase in carbohydrate oxidation and the necessity for its disposal in some fashion, there occur N and also S retention [Cuthbertson & Munro, 1937]. Deamination is diminished, for the non-nitrogenous moiety of the amino-acids is no longer required for fuel purposes, the surplus amino-acids being stored as new protein or attached as Roche [1934] suggests to already existing protein.

The rise in N and S elimination which takes place when work is superimposed during a period of overfeeding is understandable on these grounds. The increased expenditure of energy, by reducing the plethora of readily oxidizable material in the organism, permits an increase in deamination. The extent of the rise depends on the relationship of the extra work done to the excess energy intake. The direct removal of excess carbohydrate causes a similar but more rapid effect.

To account for the more marked rise in N and S excretion when the work is performed shortly after food it is necessary to assume some additional metabolic process. This process must also account for the failure of N excretion to rise in those experiments in which the work was performed shortly before meals and for the presence of a rise when the work was done during the absorptive period, the cost of the work in each instance being fully met by additional carbohydrate. The nature of this effect may be acceleration of absorption and/or subsequent metabolism of the freshly ingested food protein, thus diminishing the normal time-lag between ingestion of protein and excretion of its catabolic end-products. On the other hand it may be that the anabolic phase of cellular metabolism, in particular of protein, is reduced and generally inhibited by the excessive catabolism. If this were so, it might be anticipated that the fraction of the ingested amino-acids which would normally make good the wear and tear of tissue protein would be partly deaminated and thus give a rise in N excretion.

A further possibility may be envisaged. The organism is never in continuous equilibrium but oscillates between slightly over- and under-charged states as regards its content of readily combustible substances. After a mixed meal there is a temporary plethora of readily oxidizable material in the tissues, and during this period it is possible that there is normally a partial retention of the food N owing to preferential oxidation of carbohydrate (not necessarily the freshly ingested carbohydrate). In the course of 24 hr. this particular metabolic phase is compensated by a period when an equivalent amount of the stored N is catabolized. This probably occurs during the night when post-absorptive conditions predominate. The superimposition of work reduces the plethora of readily oxidizable substances and, from considerations already discussed, the N excretion rises. This occurs even when the cost of the work is made good by ingesting sufficient carbohydrate just before its performance, probably because it is not the freshly ingested carbohydrate which is oxidized but the preformed carbohydrate stores. The rise in N over the 24 hr. is naturally greater if no attempt is made to cover the cost of the work. One would anticipate that a period of restitution would set in, and that the period of N loss would be followed by a period of N gain within the 24 hr. The biological pendulum swings slowly: the organism must be protected from violent changes in its internal environment.

Krebs [1935] has shown that deamination of amino-acids by kidney slices is inhibited by substances such as lactate, pyruvate, succinic acid and α-keto-acids (but not by glucose). Some such mechanism may inhibit deamination in the intact organism subjected to a plethora of readily oxidizable material. Larson & Chaikoff's work [1937] indicates that the N-saving effect of a plethora of carbohydrate is only apparent when this falls within 4 hr. of the ingestion of a mixed meal (i.e. in the dog).

The slight difference in reaction of the organism to work performed just before food when the energy expenditure was (*a*) covered and (*b*) not covered, is probably best explained on the grounds that the additional carbohydrate taken at the conclusion of the work period exercised a N-saving effect which dwarfed the slight rise caused by the negative energy balance and/or the accelerated metabolism.

The maximum N excretions in these experiments have generally been observed on the first or second post-work days. This delay appears to indicate a time-lag between deamination and excretion of the end products (mainly urea) of this increased protein catabolism. When the body is accustomed to a certain rate of protein metabolism there is a time-lag in adjusting itself to a materially higher or lower level. This time-lag relates only to the N fractions for in general the appearance in the urine of the S moiety of the catabolized protein precedes the N fraction (*vide* Figs. 1–3, Table V). In the first series of experiments the

Table V. *S:N ratios*

	First series of exps.	Second series of exps.	Third series of exps.
Basal output	1 : 15·5	1 : 15·0	1 : 14·7
Depressed basal output	1 : 15·3	1 : 14·8	—
Material retained during prolonged surfeit with carbohydrate	1 : 16·1	1 : 19·0	—
Excess output when work performed shortly before food during surfeit feeding	1 : 6·8	1 : 7·9	—
Excess output when work performed shortly after food during surfeit feeding	1 : 6·6	1 : 6·9	—
Excess output when work performed shortly before food, the cost of the work not being met by extra intake	—	—	1 : 13·3
Excess output when work done shortly after food, the cost of the work not being met by extra intake	—	1 : 12·7	—
Excess output when work done shortly after food, the cost of the work being met by extra intake	—	1 : 6·3	1 : 14·3

S : N ratio of the material retained during the period of extra carbohydrate feeding was 1 : 16·1, whereas that of the excess outputs during the two work periods was much higher, *ca.* 1 : 7. In the second series the S : N ratio of the material retained during surfeit feeding was 1 : 19 and that of the excess output resulting from work was also high, viz. 1 : 7·9–1 : 6·9. When the work was performed on the basal diet after food the ratio of the rejected material was 1 : 12·7, but when the cost of the work was covered by previously ingested carbohydrate the ratio was 1 : 6·3. In the third series of experiments the S : N ratios of the excess outputs of the first and last work periods were 1 : 13·3 and 1 : 14·3. In the latter instance the food included an addition equivalent to the cost of the work. Too much stress cannot be laid on these values since they vary somewhat according to the method of computation, but the differences between the high and low values are worthy of record.

Note on the mineral metabolism during the foregoing experiments

In the second series of experiments the various work periods caused slight depressions in urinary volume paralleled by similar changes in Cl, inorganic P and Na excretions. The depressions were followed by more marked post-work rises. Addition and removal of excess carbohydrate had no effect. To a less extent the excretion of K reflected the changes in urinary volume. Its output was slightly depressed during the period of overfeeding but rose with the performance of work. Work in the earlier periods had no consistent effect upon the excretion of K. The Ca and Mg outputs generally fluctuated in parallel but here also no consistent effect of the work could be traced. The excretion was mainly influenced by the changes in urinary volume.

In the third series of experiments the three work periods resulted in depressions of the urinary volume, Cl and Na excretions. In place of similar depressions in the phosphate excretion there occurred definite increments in the first two work periods. The rise in sulphate excretion in the first period was not very marked and scarcely any rise occurred in the second period. It may be that some kind of reciprocal relationship exists between sulphate on the one hand and phosphate and to less extent chloride on the other: the alteration in chloride excretion being mainly due to sweat loss. The data are too scanty to establish this with any certainty. The main determining factor in the excretion of these inorganic metabolites, sulphate excepted, is the urinary volume. The excretion of K appears to bear some slight relationship to the intensity of the protein catabolism.

Summary

1. When work equivalent to 43,000–48,000 kg.m. per day is superimposed on a basal diet just adequate for maintenance a quite definite rise in N and S excretion is noted if the extra work is performed shortly after meals. There is only a small rise if the work is done shortly before taking food.

2. If the additional work be covered by extra carbohydrate taken at lunch and tea, then no rise in N and S excretion takes place if the work be performed before these meals; whereas if performed shortly after food a definite rise occurs.

3. When the work is performed on certain days during a prolonged period of surfeit feeding with carbohydrate, such surfeit providing energy in slight excess of the extra expenditure on the selected work days, there occurs a definite rise in N and S excretion over the depressed basal values caused by the ingestion of the excess food. When the work is done shortly after meals these increments are more marked and of longer duration than when the work is performed shortly before meals. Even in the latter case the rise is such as to bring the output of these excretory products up to their level on the basal maintenance diet. The effect is somewhat comparable with that which follows the removal of the surfeit carbohydrate from the diet.

4. The urinary excretion of N lagged behind that of S. The S : N ratio of the excess outputs of the work periods over the depressed basal values during the period of surfeit was high, irrespective of when the work was done; whereas when the work was done on the maintenance ration the ratio was generally lower.

5. The changes in certain of the other inorganic metabolites are discussed.

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