[CONTRIBUTION FROM THE HAVEMEYER LABORATORIES OF COLUMBIA UNIVERSITY, NO. 90.]

ON THE INFLUENCE OF DIET, MUSCULAR EXERTION AND LOSS OF SLEEP UPON THE FORMATION OF URIC ACID IN MAN

BY H. C. SHERMAN.

Received September 11, 1903.

WITHIN the last few years much attention has been given to the behavior of the nucleins and purin bodies in the human organism, and the sources and significance of the uric acid eliminated. This work has been so fully discussed by recent writers,[1] that it is unnecessary to review it here. The principal workers are agreed that the uric acid eliminated comes, in part, from the activities within the body and, in part, from the purin bodies ingested, either as such or as constituents of the nucleins, the former being sometimes called the "endogenous," the latter the "exogenous" uric acid. No general agreement exists, however, in regard to the causes or limits of variation in either the endogenous or the exogenous portion. The daily elimination of uric acid by healthy men, on diets believed to be practically free from purin bodies, has been variously reported at from 0.20 to 0.60 gram. Burian and Schur hold that this variation in the endogenous uric acid is a matter of individual peculiarity, but that the exogenous portion bears quantitative relations to the different purin compounds of the ingested foods. Other investigators have failed to confirm the latter claim and hold that this exogenous portion is also influenced by other causes. Evidently these questions can only be settled by the accumulation of data regarding the influence of various conditions upon the elimination of uric acid by different healthy men.

Some years ago, in connection with a study belonging to the nutrition investigations of the United States Department of Agriculture,[2] the writer had opportunity to determine the uric acid eliminated by professional bicycle riders during a six-day race, involving such severe and long-continued exertion as would only be possible for well-trained athletes of unusual strength and en-

[1] Burian and Schur: *Archiv. für ges. Physiol.* (Pflüger), **80**, 241; **87**, 239; **94**, 273. Loewi: *Archiv. experimen. Path. and Pharm.*, **44**, 1; **45**, 157. Weiner's "Ergebnisse der Physiologie," 1902.

[2] U. S. Dept. of Agr., Office of Experiment Stations, Bull. 98. "The Effect of Severe and Prolonged Muscular Work upon Food Consumption, Digestion and Metabolism," by W. O. Atwater and H. C. Sherman.

durance. The subjects rode usually about twenty hours per day, sleeping only one or two hours in every twenty-four, and the food consumed was large in amount and, in some cases, contained large quantities of meat extract. As there was no opportunity to experiment with these subjects, except during the race, it was impossible to judge in how far the results of muscular exertion were complicated by those of diet and loss of sleep, and the figures for uric acid were, therefore, not published. Since that time it has been possible to experiment with another subject regarding the influence of loss of sleep, as well as with some of the foods used by the racers, and it is believed that the results can now be interpreted with sufficient accuracy to render them of value.

OBSERVATIONS UPON PROFESSIONAL BICYCLE RACERS.

A detailed description of the subjects and their work, diet and metabolism will be found in the bulletin cited above. The principal data bearing upon the present discussion, may be summarized as shown on pages 1161 and 1162.

It will be noted that large amounts of food were consumed and large quantities of nitrogen eliminated. The elimination of uric acid was not, as a rule, increased in proportion to the total nitrogen, but was in most cases somewhat and in some cases considerably above the normal. Before considering whether this increase of uric acid should be attributed to the diet or the work, the possible influence of loss of sleep may be noted.

INFLUENCE OF LOSS OF SLEEP.

In connection with certain experiments with another subject, "S," the details of which are described elsewhere,[1] the uric acid elimination was observed for a period of several days, the diet being kept constant and all the conditions as nearly uniform as possible, except that during three consecutive days the amount of sleep was materially reduced. The food of each day consisted of 300 grams bread (soda-crackers), 2,040 grams milk, and 40 grams butter. The principal results are given on page 1163.

[1] U. S. Dept. of Agr., Office of Experiment Stations, Bull. 121. "Experiments upon the Metabolism of Nitrogen, Sulphur and Phosphorus in the Human Organism.

Subject.	Day of race.	Sleep (about). Hrs. and min.	Distance ridden. Miles.	Food consumed.	Nitrogen in urine. Grams.	Uric acid in urine. Grams.[2]
"M"	1[1]	0:0	441.8	Eggs, 43 grams; milk and kumyss, 7828 grams; boiled rice, 360 grams; sugar, 72 grams; fruit, 480 grams.	35.1	1.00
	2	1:40	366.7	Meat extract, 127 grams; eggs, 173 grams; milk and kumyss, 3261 grams; boiled cereals, 643 grams; sugar, 92 grams; fruit, 999 grams.	42.7	1.07
	3	1:35	334.1	Meat extract, 311 grams; milk, 4937 grams; bread, 35 grams; boiled cereals, 877 grams; pastry, 142 grams; sugar, 53 grams; fruit, 2003 grams.	46.2	1.50
	4	1:10	316.5	Meat extract, 43 grams; milk and matzoon, 1057 grams; rice pudding, 737 grams; pastry, 71 grams; fruit, 1459 grams.	35.7	1.71
	5	1:5	327.8	Meat extract, 9 grams; eggs, 94 grams; milk, 823 grams; soup, 113 grams; boiled cereals, 386 grams; sugar, 25 grams; pastry, 1009 grams; fruit, 870 grams.	30.7	1.15
	6	2:30	220.5	Meat extract, 5 grams; milk, 1985 grams; boiled rice, 422 grams; pastry, 1189 grams; sugar, 19 grams; fruit, 2161 grams.	26.9	1.00
"P"	1[1]	?	863.2	Eggs, 79 grams; milk and kumyss, 6122 grams; boiled cereals, 1080 grams; sugar, 89 grams; fruit, 19 grams.	32.8	0.62
	2	?		Meat extract, 85 grams; eggs, 46 grams; milk and kumyss, 4729 grams; boiled cereals, 887 grams; sugar, 85 grams; fruit, 255 grams.	43.6	0.84
	3	?		Meat extract, 156 grams; butter, 28 grams; milk and kumyss, 4340 grams; bread, 307 grams; boiled cereals, 1118 grams; sugar, 80 grams; fruit, 235 grams.	40.3	1.06
"A"	1	0:0	402.0	Meat, 85 grams; beef tea, 440 grams; eggs, 241 grams; milk, 531 grams; malted milk, 91 grams; jelly, 42 grams; bread, 459 grams; boiled cereals, 935 grams; sugar, about 200 grams; fruit, 434 grams.	25.3	0.88

[1] Subjects "M" and "P" dined heartily upon beefsteak about two hours before the beginning of the race.

[2] Determined by the Ludwig-Salkowski method.

Subject.	Day of race.	Sleep (about). Hrs. and min.	Distance ridden. Miles.	Food consumed.	Nitrogen in urine. Grams.	Uric acid in urine. Grams.
"A"	2	1 : 30	371.3	Meat, 148 grams; broth, 170 grams; beef juice, 128 grams; butter, 64 grams; eggs, 57 grams; milk, 116 grams; malted milk, 82 grams; jelly, 99 grams; bread, 204 grams; boiled cereals, 347 grams; sugar, about 250 grams; fruit, 1195 grams.	32.8	0.90
	3	0 : 20	352.7	Meat, 149 grams; meat extract, 24 grams; broth, 283 grams; eggs, 369 grams; butter, 78 grams; milk, 142 grams; malted milk, 78 grams; jelly, 213 grams; soup, 191 grams; bread, 361 grams; boiled cereal, 532 grams; sugar about 400 grams; fruit, 933 grams; cocoa wine, 170 grams.	39.0	1.08
	4	2 : 0	285.3	Meat, 206 grams; meat extract, 43 grams; broth, 879 grams; eggs, 283 grams; butter, 198 grams; milk, 312 grams; malted milk, 36 grams; jelly, 269 grams; bread, 659 grams; sugar, about 300 grams; fruit, 928 grams; cocoa wine, 198 grams.	65.1	2.50
	5	3 : 40	229.4	Meat, 326 grams; broth, 305 grams; eggs, 56 grams; butter, 220 grams; milk, 149 grams; malted milk, 21 grams; jelly, 156 grams; bread, 709 grams; tapioca pudding, 170 grams; sugar, about 300 grams; fruit, 1495 grams; cocoa wine, 43 grams.		
	6	2 : 0	181.9	Meat, 220 grams; broth, 701 grams; eggs, 114 grams; butter, 92 grams; milk, 269 grams; malted milk, 7 grams; jelly, 220 grams; bread, 496 grams; tapioca pudding, 142 grams; sugar, about 330 grams; fruit, 673 grams; cocoa wine, 113 grams.	39.8	1.63

Days.	Sleep (about). Hours.	Amount of urine. Grams.	Nitrogen in urine. Grams.	P_2O_5 in urine. Grams.	Uric acid in urine.[1] Gram.
1	7	817	15.38	2.98	....
2	7	902	13.89	3.07	....
3	7	993	14.28	3.21	0.37
4	7	838	13.68	3.23	0.32
5	2½	852	13.96	2.94	0.36
6	4	782	14.04	3.07	0.34
7	0	851	15.63	3.28	0.34
8	7½	966	15.06	3.80	0.30
9	7½	1160	15.65	3.46	0.31
10	7	978	13.67	3.07	0.34
11	7	952	13.51	2.89	0.32
12	7	1001	13.82	3.21	0.30

From this it would appear that the loss of sleep had little, if any, influence upon the elimination of uric acid.

INFLUENCE OF DIET AND MUSCULAR WORK.

While there is no question that the different nitrogenous bodies of the food differ greatly in their effect upon uric acid formation and that very little uric acid is formed on a diet of such foods as bread, milk, butter and eggs, it is still uncertain whether the uric acid output is entirely independent of the quantity of such foods consumed. The results of two series of observations upon subject "S," bearing upon this point, may be summarized as follows:

INFLUENCE OF VARYING AMOUNTS OF BREAD AND MILK.

Days.	Amount of urine. Grams.	Nitrogen in urine. Grams.	P_2O_5 in urine. Grams.	Uric acid in urine. Gram.	Food per day.
1	681	11.65	1.92	0.42	Bread ("soda-crackers"), 150 grams; milk, 1500 grams.
2	605	11.12	2.02	0.35	
3	620	11.35	2.27	0.37	
4	566	11.66	2.33	0.38	
5	555	11.75	2.29	0.38	
6	687	14.83	2.73	0.44	Bread ("soda-crackers"), 300 grams; milk, 3000 grams.
7	874	15.81	3.28	0.41	
1	...[2]	....	....	....	Bread ("soda-crackers"), 405 grams; milk, 1000 grams; butter, 60 grams.
2	609	10.19	2.15	0.32	
3	711	10.92	2.43	0.37	
4	670	10.17	2.34	0.33	
5	2180	15.12	3.39	0.33	Bread ("soda-crackers"), 120 grams; milk, 3060 grams.
6	2130	16.07	3.94	0.34	
7	1859	16.98	4.10	0.34	

[1] The figures for uric acid given in this and the following table were determined by Folin's modification of the Hopkins method.

[2] Sample lost.

In the first series, where the change consisted in doubling the amounts of bread and milk consumed, the relative proportions remaining the same, there appears to be a slight increase in the uric acid elimination. In the second series, where the diet was changed by omitting the butter, reducing the bread and greatly increasing the milk consumed, thus giving a large increase in the protein of the diet with but little change in the fuel value, the amount of uric acid eliminated remained practically unchanged.

The fact that the slight increase found in the first series does not appear in the second, may be taken as an indication either that the increase was due to the superabundance of the diet as a whole, rather than to the increased consumption of protein alone, or that the purin bodies, while occurring only in very small quantities in either, were relatively more abundant in the bread than in the milk. The latter seems probable, inasmuch as the quality of flour used in making "soda-crackers" might easily contain some of the germ of the wheat. In either case it would appear that even a diet of bread and milk introduces a certain amount of "exogenous" purin bodies, though this amount is doubtless quite small.

The large quantities of uric acid eliminated by the professional bicycle racers may, therefore, to some extent, be attributed to the mere abundance of the diet. To a much greater extent, however, it is doubtless due to the quantities of meat extract consumed. During a two days' experiment, the attempt was made by subject "S" to consume such quantities of meat, meat extract and fruit (together with bread and milk) as would be comparable with those found in the dietaries of two of the racers.[1] The food consumed by "S" during the two days was about as follows: Meat, 400 grams; meat extract, 100 grams; milk, 2000 grams; bread, 350 grams; fruit, 800 grams. Except as regards the quantities of cereal and milk products, this dietary is not greatly different from the average for subjects "M" and "P" during the first two days of the bicycle race, including the meat consumed by these subjects just before the beginning of the observations.

The principal source of purin bodies was, of course, the meat extract, a concentrated commercial preparation called "Vigoral."

[1] On account of the great variety of foods consumed by subject "A" and the fact that he took cocoa wine and, during the last days, small quantities of strychnine, no direct comparison with this subject was attempted.

"M" and "P" consumed respectively 127 and 85 grams (average 106 grams), while "S" consumed 100 grams of the same preparation. "S" eliminated, during the two days, 1.66 grams of uric acid, or 0.83 gram per day; "M" and "P" together 3.53 grams, or an average of 0.88 gram per day. This difference is hardly greater than would be expected from the large quantities of cereals and milk consumed by the latter subjects. Hence, in so far as this method of comparison is applicable, it would indicate that, at least during the early days of the race, the uric acid elimination of these athletes was only such as would naturally result from the food consumed and was not appreciably increased by the muscular work performed.

In another experiment, "S," who at this time was living upon a diet of cereals and milk, and had taken but little exercise for three or four weeks, walked two and one-half hours over country roads at the rate of four and one-half miles per hour and during the following two and one-half hours practiced, at intervals, an exercise consisting in raising and lowering the body by means of the arms. Nearly all of the muscles were thus exercised, and while the work performed was not large in actual amount, the exertion was sufficient to keep the pulse rate at 100 to 125 for about five hours and to cause a feeling of fatigue during the remainder of the day. The exercise was followed by an increase in the uric acid output of about 0.15 gram during the day of exercise and the day following. This result is in harmony with that reached by Dunlop, Paton, *et. al.*,[1] who found an increased elimination of uric acid after muscular exercise when the subject was in poor, but not when it was in good, training.

SUMMARY.

Without attempting a full discussion of the data here given, which would involve a review of the recent extensive investigations already mentioned, the principal points of interest may be summarized as follows:

Both with professional athletes and with the subject of sedentary habits, the elimination of uric acid was primarily dependent upon the food consumed.

While very small changes, apparently, resulted from large variations in the amount of a bread-and-milk diet, the elimination

[1] *J. Physiol.*, **22**, 68.

of uric acid was mainly determined by the quantities of meat products consumed.

In the case of well-trained professional athletes, very severe and prolonged muscular exertion had little influence upon the formation and elimination of uric acid, except indirectly, by inducing an appetite for stimulating foods such as meat extracts.

Marked loss of sleep had no apparent influence upon the amount of uric acid eliminated.

The writer desires to express his indebtedness to Professor W. O. Atwater, of Wesleyan University, in whose laboratory a large part of the work, here described, was performed.

NEW YORK CITY,
September, 1903.

[CONTRIBUTIONS FROM THE UNIVERSITY OF ILLINOIS, AGRICULTURAL EXPERIMENT STATION, NO. 10.]

THE CHEMICAL COMPOSITION OF DIFFERENT PARTS OF THE CORN[1] KERNEL.[2]

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Received September 8, 1903.

THE possibility of selecting seed corn for improved chemical composition by a simple mechanical examination of sections of kernels has been clearly established by experiments previously reported;[3] and the practical value of this method of selecting seed corn for high protein, high oil, and other desirable qualities, has been fully confirmed by subsequent investigations.[4]

A considerable amount of additional data relating to this matter has been accumulating with the progress of our experiments in corn-breeding, and because of the very great importance of this subject to agriculture, and also because of the marked interest which is manifested both by progressive, practical agriculturists and by scientific investigators, it has seemed advisable to publish, in somewhat greater detail, the results of our investigations along this line.

[1] "Corn" is, of course, used with the American meaning of Indian corn or maize.

[2] From advance sheets of Bulletin No. 87 of the University of Illinois Agricultural Experiment Station.

[3] This Journal **21**, 1039 (1899); Univ. of Ill. Agr. Expt. Station Bulletin **55** (1899).

[4] Univ. of Ill. Agr. Expt. Station Bulletin **82** (1902); U. S. Dept. of Agr., Office of Expt. Stations, Bulletin **123**, 91 (1903); West Indian Bulletin **4**, 9 (1903).