A NOTE ON THE EFFECT OF SOME ORGANIC ACIDS UPON THE URIC ACID EXCRETION OF MAN.

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Experiments by Lewis, Dunn, and Doisy (1918) seemed to indicate that the increased excretion of uric acid after the ingestion of amino-acids is not due either to specific dynamic action or to ammonia which has been split from the ingested amino-acid. Amino-acids (aspartic and glutamic) without specific dynamic action produce fully as great an increase in the uric acid eliminated as amino-acids which markedly stimulate the heat production. Neither ammonium chloride nor urea taken *per os* affect the excretion of uric acid. These possible explanations having been rendered unlikely, it occurred to us that the testing of the effect of the organic acids obtained by oxidative and by hydrolytic removal of the amino group might yield data of some interest.

The experiments were conducted on two normal men according to the same general scheme used by Lewis, Dunn, and Doisy. Most of the uric acid determinations in urine and all of those on blood and plasma were made by the Morris-Macleod (1922) method. We have found that this method yields very good results on plasma. To assure ourselves that our results were not due to interference with the colorimetric determination the uric acid has been isolated by the well known Kruger-Schmidt copper precipitation.[1] These values which agreed fairly well with the colorimetric values leave no doubt about the observations regarding the effects of the organic acids.

As the hydroxy- and keto-acids analogous to alanine are easily obtainable they were used in our experiments. It would have been

[1] We wish to express our thanks to Dr. Michael Somogyi for these determinations.

desirable to use other hydroxy- and keto-acids and with this in view we have performed two experiments with glycollic acid. Glyoxylic acid was not used because of the difficulty in obtaining it in a sufficiently pure condition and the very toxic effects of the substances which are frequently present as impurities. Approximately equimolecular quantities of the sodium salts of lactic acid and of pyruvic acid were ingested after the collection of two or three normal hourly specimens. The effects of both acids were very striking. Pyruvic acid increased the hourly excretion of uric acid from 17 to 25 mg. in one experiment and in the other from 16 to 28 mg. which was about the same increase as that produced by an equal amount of alanine. Both lactic and glycollic acids, on the contrary, caused an immediate depression in the quantity of uric acid excreted. In all of these experiments there was an abrupt fall to about one-half the quantity excreted prior to the ingestion of the acid. Data which are given in Tables I and II illustrate the contrast in the effects of these compounds on the excretion of uric acid.

The explanation of these experiments is very difficult and our data are insufficient to decide which of the various possibilities may be correct. Lewis, Dunn, and Doisy referred the increased excretion following amino-acids to an increased production (stimulation of endogenous metabolism) such as occurs when the subject passes from a low to a high protein diet. In so far as our data go this theory is not shaken. In Table III, we have collected the results of our various experiments on the uric acid of blood or plasma. It is evident that we have found some slight variations in two samples of blood drawn from the same normal fasting subject at a 2 or 3 hour interval. About the same variation prevails when a pyruvic or an amino-acid is ingested, but the variation after lactic acid seems somewhat more pronounced. There appears to be a slight rise in the uric acid in the plasma after the ingestion of lactic acid which, coupled with the decreased excretion, would lead one to think of an elevated threshold in the kidney.

The changes in plasma uric acid are, to be sure, very small and it is possible that even such minute changes as would escape detection by our analyses could cause decided alterations of hourly urinary uric acid. But granting this, it still seems that

TABLE I.

Uric Acid in Urine in Milligrams per Hour.

Normal human subject. Male instructor. Weight 63 kilos.

Hour.	Normal.	Alanine.	Pyruvic acid.	Lactic acid.	Glycollic acid.
a.m.					
7–8	20.8	18.6*	17.3	20.6	22.5
8–9	20.0	20.9	17.1†	21.0‡	23.6§
9–10	17.8	29.5	20.9	12.2	14.3
10–11	19.1	27.5	24.0	6.0	11.8
11–12	19.2	21.1	25.2	6.0	11.0
p.m.					
12–1	19.0	16.9	21.8	10.2	13.4
1–2	19.0	17.4	16.8	14.8	16.1
2–3	17.2		16.0	22.9	20.4
3–4	18.2		14.0	22.9	

* 21.5 gm. of alanine taken at 8.00 a.m.

† 16 gm. of pyruvic acid taken at 9.00 a.m.

‡ 12 gm. of lactic acid taken at 9.10 a.m.

§ 10 gm. of glycollic acid taken at 9.00 a.m.

No food after supper of previous evening until completion of experiment.

TABLE II.

Uric Acid in Urine in Milligrams per Hour.

Male. Medical student. Weight 59 kilos.

Hour.	Normal.	Pyruvic acid.	Lactic acid.	Gycollic acid.
a.m.				
7–8	17.1	16.5		
8–9	17.3	18.5*	15.7	22.5
9–10	18.0	18.9	16.6	21.6
10–11	18.2	26.7	16.7†	22.8‡
11–12	17.7	28.3	15.1	12.4
p.m.				
12–1	14.3	26.7	8.4	8.8
1–2	13.6	20.3	8.4	10.0
2–3	13.3	15.1	11.2	10.5
3–4	11.5	12.5	14.4	11.2

* 16 gm. of pyruvic acid taken at 9.20 a.m.

† 14 gm. of lactic acid taken at 10.30 a.m.

‡ 10 gm. of glycollic acid taken at 10.45 a.m.

No food after supper of previous evening until completion of experiment.

lactic acid causes a slight rise in the plasma which is concomitant with the decrease in urinary uric acid and we are inclined to the view that these results are due to an increased threshold of the kidney for uric acid.

TABLE III.

Blood and Plasma Uric Acid in Milligrams of Uric Acid per 100 Cc.

	Normal.	Amino-acid.	Pyruvic acid.	Lactic acid.
Sample 1	3.6	3.4	3.8	3.7
" 2	3.5	3.4	3.8	3.9
Increase	−0.1	0.0	0.0	+0.2
Sample 1	4.2	3.3		4.2
" 2	4.2	3.3		4.6
Increase	0.0	0.0		+0.4
Sample 1	5.5			4.6
" 2	5.5			4.9
Increase	0.0			+0.3
Sample 1	3.8			
" 2	3.9			
Increase	+0.1			
Sample 1	4.6	4.8	4.8	4.5
" 2	5.0	4.8	4.8	4.8
Increase	+0.4	0.0	0.0	+0.3
Sample 1	4.5			
" 2	4.5			
Increase	0.0			
Sample 1	4.7			
" 2	4.9			
Increase	+0.2			
Average change	+0.1	±0.0	±0.0	+0.3

The first sample of blood was generally taken a few minutes before the organic acid and the second sample 2 or 3 hours later.

It seemed that the effect of lactic acid upon the well known increase of urinary uric acid which occurs after eating cottage-cheese or sweetbreads would be of some interest. The data of Table IV show that instead of the usual increase of uric acid

excretion which occurs after the ingestion of these protein foods a decreased output which is much below the normal is obtained. From these experiments we draw the inference that lactic acid affects the elimination of uric acid whether it be from exogenous or endogenous sources. Of course, our experiments do not exclude an alteration of the rate of conversion of purines to uric acid, but since we have found a slight rise in the plasma and have failed to find an increase of non-uric acid purine nitrogen in the

TABLE IV.

Effect of Lactic Acid upon Excretion of Endogenous and Exogenous Uric Acid.

Hour.	Cottage-cheese.	Cottage-cheese and lactic acid.	Thymus.	Thymus and lactic acid.
1st	15.6	15.9	**21.3***	**21.3***
2nd	**18.5**†	**17.7**‡	25.0	**17.0**§
3rd	26.5	19.4	36.9	6.7
4th	30.3	**22.4**	44.4	14.5
5th	33.3	21.3¶	44.4	32.4
6th	33.3	9.4	35.7	33.3
7th	30.3	6.9	34.8	32.0
8th	29.4	12.9	35.0	30.7
9th		18.2	25.5	30.6
10th			23.1	29.5

* 200 gm. of thymus.

† 480 gm. of cottage-cheese.

‡ 500 gm. of cottage-cheese.

§ 10 gm. of lactic acid as sodium salt.

¶ 14 gm. of lactic acid as sodium salt.

Several experiments of this type, in which 5 gm. of sodium benzoate were taken instead of the larger dose of sodium lactate, yielded results which were practically identical with these data. Sodium hippurate appeared to have no influence upon the quantity of uric acid eliminated.

urine we are inclined to view the phenomenon as an effect upon the kidney.

From the results of these experiments two logical questions arise: (1) May the elimination of uric acid during and following exercise (Kennaway, 1909) be influenced by the production of lactic acid? (2) May the opposite effects of lactic and pyruvic or amino-acids upon the uric acid excretion be taken as evidence against the hydrolytic deamination hypothesis? With regard

to the first question, we have conducted some preliminary experiments which we are extending before reporting their results. As to the second question, we may say that there is a rapid rise (unpublished observations) in the excretion of nitrogen after the ingestion of amino-acids which we consider to be due to deamination. The deaminized product is rapidly made available and if much of it were lactic acid it is probable that a decreased output of uric acid would result. Actually, an increase occurs so it may be considered probable that hydrolytic deamination is not the chief pathway of decomposition; oxidative deamination is not so excluded.

SUMMARY.

The ingestion of sodium salts of lactic acid causes a decrease, and of pyruvic acid an increase in the excretion of uric acid.

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