XLVII. ON THE PURINE METABOLISM OF RATS.

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Folin and Morris [1913] make the statement that "The purine metabolism of rats is like that of man and unlike that of other mammals hitherto investigated." If this were true the rat would be a most valuable animal on which to investigate the problems of gout.

This statement rests on the following evidence :

1. Rats excrete about 0.5 mg. of uric acid nitrogen a day. This *in proportion to body weight* is about as much as is found in human urine.
2. 100 g. of rat's blood contains 2.4-2.5 mg. of uric acid, "substantially the same figures as Folin and Denis found for human blood."
3. From 50 cc. of rat's urine enough uric acid was isolated for complete identification.

No attempt was made to estimate the allantoin in rat's urine or to observe the effect on the purine and allantoin excretion of adding purine substances to a purine free diet.

The essential difference between the purine metabolism of man and other mammals, except perhaps the chimpanzee, is not in the amount of uric acid excreted in proportion to body weight or the percentage of it contained in the blood, but rather in the fact that in man the purines are not further converted to allantoin as an end product while in other mammals this is the case. The observations recorded in the experimental part of this paper show that the relatively large amount of uric acid excreted by rats is an expression of a very high rate of purine metabolism, the main end product of which is allantoin, this latter representing about 15 times as much nitrogen as that of the total purine bases and uric acid.

Moreover when hypoxanthine is given by the mouth to rats about 60 per cent. of its nitrogen is excreted in the form of allantoin while only about 3 per cent. is excreted as purine base + uric acid nitrogen. This latter observation is also of interest from the fact that Jones and Rhodé [1909] were unable to demonstrate the existence in rat's organs of a ferment capable of destroying hypoxanthine.

EXPERIMENTAL PART.

The rats were kept in pairs in a modified form of the cage described by Völtz [1912]; the urine and faeces were separated by the ball method originally used at the Cancer Hospital, Fulham.

The cages were washed down daily and the urine + washings from each pair of rats preserved with toluene for seven days. The toluene was driven off on the water bath and the seven days' urine made up to 500 cc.

5 cc. were used for total nitrogen by Kjeldahl's method, 275 cc. for purine base + uric acid nitrogen by the Camerer-Arnstein method and 200 cc. for allantoin by Wiechowski's method. In this latter the original method was carried out exactly as described [Wiechowski 1907], and the figures for allantoin nitrogen, calculated from the weight obtained, as well as those given by the Kjeldahl analysis of the mercury acetate precipitate, are given. Most writers seem to consider the latter more accurate and I am inclined to agree with this view from subsequent observations when the diet was less simple in character than bread and water. The allantoin obtained melted in every case at 232° – 234° ; its solution was not precipitated by silver nitrate but gave a copious precipitate on further addition of ammonium hydrate, soluble in excess of the latter. Boiled with caustic soda it gave the glyoxylic reaction. A collection of the allantoin obtained once recrystallised from water gave the following analysis:

Found N = 35.0 %	Calculated N = 35.44 %
C = 29.73 %	C = 30.3 %
H = 3.82 %	H = 3.8 %

The rats were fed on white bread and water for two weeks before and throughout the experiments. The amount of bread eaten was not limited, for although white bread contains traces of allantoin [Ackroyd 1911] the quantity in the bread eaten by a rat is negligible in comparison with the amount excreted.

All the figures given are calculated as excretion of one rat for one day and represent an average of seven days' excretion for two rats.

During the second week 0.45 g. of hypoxanthine was given to each pair of rats; this was given in equal portions with the first food in the morning of the first five days of the period, the last two days were intended to cover any delayed excretion. This would be equivalent to 0.013 g. purine nitrogen per rat per day calculated for the whole seven day period.

Rats A. Two males weighing 158 g. and 174 g.

Date	Total N mg.	Purine N mg.	Allantoin N		Diet
			mg. by weight	mg. by Kjeldahl	
Jan. 19-26	191	0.62	10	9.5	Bread, water
Jan. 26-	182	0.95	18.3	17.4	Bread, water. 13 mg.
Feb. 2					hypoxanthine N
Feb. 2-9	137	0.51	9.4	8.7	Bread, water
Feb. 9-16	156	0.5	8.7	8.5	Bread, water

The average excretions of the first, third and fourth periods are: purine nitrogen 0.54 mg.; allantoin nitrogen 8.9 mg. The increased excretions over these averages in the second period are 0.41 mg. purine N and 8.5 mg. allantoin N equivalent to a recovery of 3.1 % as purine N and 65 % as allantoin N of the extra hypoxanthine N given.

Rats B. Two males weighing 133 g. and 165 g.

Date	Total N mg.	Purine N mg.	Allantoin N.		Diet
			mg. by weight	mg. by Kjeldahl	
Jan. 20-27	172	0.66	8.7	8.5	Bread, water
Jan. 7-	191	1.06	17.4	16.3	Bread, water 13 mg.
Feb. 3					hypoxanthine N
Feb. 3-10	180	0.6	9.8	10	Bread, water
Feb. 10-17	145	0.63	7.5	7.7	Bread, water

The average excretions of the first, third and fourth periods are purine N 0.63 mg., allantoin N 8.4 mg. The increased excretions over these averages in the second period are: purine N 0.43 mg., allantoin N 7.9 mg. equivalent to a recovery of 3.3 % as purine N and 60.7 % as allantoin N of the extra hypoxanthine N given.

CONCLUSION.

The purine metabolism of rats is like that of other lower mammals and unlike that of man¹.

REFERENCES.

Ackroyd (1911), *Biochem. J.* **5**, 400.

Folin and Morris (1913), *J. Biol. Chem.* **14**, 509.

Jones and Rhodé (1909), *J. Biol. Chem.* **7**, 237.

Völtz (1912), Abderhalden, *Handbuch der biochemischen Arbeitsmethoden*, **5**, 1044.

Wiechowski (1907), *Beiträge*, **11**, 109.

¹ Since this work was finished (February 1914), Hunter and Givens (Proceedings of the American Society of Biological Chemists, *J. Biol. Chem.* **17**, xxiii) published an analysis of rats' urine; they find that of the purine + allantoin nitrogen 93 per cent. is present as allantoin, 4 per cent. as uric acid and 3 per cent. as purine bases.