

The living and heat-killed streptococcus and its toxins have specific affinity for muscles. The progressive weakness, fatigability, and the pathologic lesions of myasthenia gravis have been reproduced in monkeys and rabbits.

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Sulfur Partitions in Cat Urines Following Injections of Monobromobenzene, Cystine or Methionine.*

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Monohalobenzenes have been found to be conjugated with cysteine and excreted as mercapturic acids in the urine of the dog, rabbit, rat¹ and mouse.² The work herein reported was undertaken to see whether the cat could also effect such a synthesis. It also became of interest to carry out distributions of urinary sulfur after administration of cystine or methionine.

Cats were kept in metabolism cages, and urines collected at 24-hour intervals by gentle abdominal pressure. In the analysis, sulfur determinations were run by Folin's method, nitrogen by Kjeldahl, and disulfide compounds according to Virtue and Lewis.³ The cats were put on their dietary regime for 7 days before collection of urine was begun, and urines were analyzed 4 days before injections were made. To insure that a constant supply of the material whose metabolism was to be studied would be present in the body, all injections were subcutaneous, and were given as follows: half the amount 24 hours before the end of the metabolism period, one-fourth 6 hours before the end, and the remaining fourth 3 hours later. The metabolism period was limited to 24 hours because the animals were sacrificed at the end of that time to obtain information for other work. Thirty-three animals were used in the series. Typical results are shown in Table I.

As will be seen in the figures for cats 29 and 37, the organic

*Part of these data were presented before the American Society of Biological Chemistry at Washington, D. C., March 25-28, 1936.

¹ Lawrie, N. R., *Biochem. J.*, 1931, **25**, 1037.

² Stekol, J. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 115.

³ Virtue, R. W., and Lewis, H. B., *J. Biol. Chem.*, 1934, **104**, 415.

TABLE I.
Distribution of Urinary Sulfur of Cats Following Subcutaneous Injection of Monobromobenzene, Methionine and Cystine.

Cat.	Dietary Regime	Total N mg.	Total S mg.	Sulfate S mg.	Inorganic Sulfate-S mg.	Organic S mg.	Ethereal Sulfate-S mg.	Org. S
								Total S %
29	Fasting	1058	56	39	32	17	7	30
		1039	56	39	36	17	3	
		1004	56	39	34	17	5	
		953	57	40	34	17	6	
		*1655	85	48	20	37	28	
37	Meat Scraps	2339	123	59	40	64	23 } §	51
		2339	123	59	40	64	23 }	
		2594	141	70	49	71	21	
		2202	111	55	39	56	16	
		*2486	140	60	21	80	39	
9	Fasting	958	64	48	39	16	9	26
		985	64	48	39	16	9	
		963	55	41	35	14	6	
		864	49	35	30	14	5	
		†1005	120	92	88	28	4	
	“Extra S”		62	49	52	13	—3	
21	Fasting	1192	80	38		42		49
		1118	71	35		36		
		1273	78	42		36		
		1329	91	52		39		
		†1561	242	159		83		
	“Extra S”		162	117		45		

*1.5 gm. bromobenzene (in olive oil) per kilo; half at 24 hours, a quarter each at 6 and 3 hours before end of 24-hour period.

†Methionine, equivalent to 250 mg. S, given as sodium salt; half 24 hours, a quarter each at 6 and 3 hours before end of 24-hour period.

‡Cystine, equivalent to 250 mg. S, given as sodium salt; half 24 hours, a quarter each at 6 and 3 hours before end of 24-hour period.

§Analyzed together.

sulfur rose when either fasted or well-fed cats were given monobromobenzene. It seems justifiable to assume that this rise, at least in part, was due to the formation of mercapturic acids, for on treatment of these urines according to the method of McGuinn and Sherwin,⁴ white crystalline substances melting at 153° (Corr.) were obtained. When mixed with p-bromophenylmercapturic acid which had been isolated from rat urine† no depression of the melting points resulted.

⁴ McGuinn, A., and Sherwin, C. P., *Proc. Soc. Exp. Biol. and Med.*, 1933, **80**, 1115.

†The author wishes to express his thanks to Dr. Abraham White for a gift of the p-Bromophenylmercapturic acid from rat urine.

Since the nitrogen output was greatly increased after administration of monobromobenzene to fasting animals (Cat 29), it appears likely that the cats broke down their own tissues to obtain the cysteine necessary for the synthesis of mercapturic acids. High nitrogen values following injections were not obtained consistently with well-fed cats. (Cat 37).

The values reported for urines from cats 9 and 21 indicate that the "extra" sulfur from both cystine and methionine was for the most part excreted in the form of sulfate sulfur by this species. However, part of the "extra" organic sulfur from cystine (Cat 21) must have been excreted unchanged, for the urine of this animal gave a positive Sullivan reaction.

It has been suggested⁵ that demethylation may be a step in the metabolism of methionine, with the subsequent formation of homocysteine, and by oxidation, homocystine. A test for disulfide groups other than cystine has been reported in the urine of animals which had been given methionine.⁵ Analyses of urine for disulfide compounds were made, therefore, before and after injections of methionine. Calculated as homocystine, daily pre-experimental averages on 2 of these animals were 5 and 8 mg. respectively, while after injection of methionine these values rose to 16 and 22 mg. These urines gave negative Sullivan reactions for cystine.

The high proportion of organic sulfur excreted by the cat is noteworthy. The values for the pre-injection periods of the 4 animals included in Table I were 30, 51, 26 and 49%, respectively, and the average values for the entire series was 33% or higher. This is a much larger proportion of organic sulfur than has been found in normal urines from the dog or rabbit.

No other sulfur partitions on cat urines have come to the attention of the author.

Conclusions: 1. Fasting and well-fed cats excreted p-bromophenylmercapturic acid in their urines following the injection of monobromobenzene. 2. Cysteine necessary for the synthesis of mercapturic acids by fasting cats may arise their own tissues. 3. Sulfur partitions have been made on urines from cats.

⁵ Virtue, R. W., and Lewis, H. B., *J. Biol. Chem.*, 1934, **104**, 59.