

from analysis of all the salts in the system and the calculated degree of ionization. In systems in which this is not possible, due to the presence of unknown compounds as in blood serum, the  $\text{CO}_2$  from bicarbonates and  $\text{H}_2\text{CO}_3$ , the P from inorganic phosphates and the  $\text{H}^+$  must be determined. The only unknown is the  $\text{Ca}^{++}$  which may then be calculated from the equation

$$\text{Ca}^{++} = \sqrt{\frac{\text{K} \cdot [\text{H}^+]}{[\text{HCO}_3^-] [\text{HPO}_4^{=}]}}$$

#### 4 (2236)

#### Cystine metabolism. II.

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In our last communication<sup>1</sup> we stressed the data bearing on the equilibrium  $\text{Cystine} \rightleftharpoons \text{Cystein}$  and gave a general outline of the program of the investigation of cystine metabolism. The twelve preparations of cystine and cystein therein described have been fed to rabbits and the urines corresponding to them have been analyzed. The analysis of the large mass of data is not yet complete. In this communication we will discuss the fate of cystine and cystein as such and one of the derivatives and compare our results with data of other workers, *e. g.*, Wohlgemuth<sup>2</sup>, Lewis and Root<sup>3</sup> and Schmidt and Clark<sup>4</sup>. All the figures have been recast so as to give the increase in sulfur in mg. following the administration of cystine sulfur, as cystine or its derivative.

<sup>1</sup> Shiple, G. J., Rose, A. R., and Sherwin, C. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1923, **xx**, 360.

<sup>2</sup> Wohlgemuth, J. Z., *physiol. Chem.*, 1903, **xi**, 81.

<sup>3</sup> Lewis, H. B., and Root, L. E., *J. Biol. Chem.*, 1922, **i**, 303.

<sup>4</sup> Schmidt, C. L. A., and Clark, G. W., *J. Biol. Chem.*, 1922, **liii**, 193.

TABLE I.  
CYSTINE ELIMINATION.

	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.
<b>Wohlgemuth</b>	I			II					
Rabbits									
Av. control days...	155	126	30	158	121	37			
Cystine days .....	1242	726	516	692	420	272			
Do. less control .....	622	224	398	376	178	199			
Lag days less cont.	54	40	13	95	42	52			
Cystine S elimin....	675	264	411	471	220	250			
<b>Lewis and Root</b>	II			IV					
Rabbits									
Av. control days...	24	14	10	74	54	14			
Cystine days .....	110	91	19	109	96	15			
Do. less control .....	86	77	9	35	42	1			
Lag days less cont.	18	20	-2	7	10	1			
Cystine S elimin...	104	97	7	42	52	2			
<b>Schmidt and Clark</b>	I			II			IV		
Dogs									
Av. control days...	244	137	107	111	34	77	111	73	40
Cystine days .....	1371	714	656	888	714	174	1084	799	285
Do. less control .....	1027	577	549	777	680	97	973	726	245
Lag days less cont.	431	96	336	432	230	200	130	114	15
Cystine S elimin...	1458	673	885	1209	910	297	1138	863	261
<b>Rose and Sherwin</b>	I			II			III		
Rabbits									
Av. control days...	106	40	66	66	41	25	66	41	25
Cystine days .....	401	187	213	512	403	110	291	205	86
Do. less control .....	159	123	81	314	281	34	159	123	35
Lag days less cont.	29	24	0	0	0	0	65	58	6
Cystine S elimin...	188	107	81	314	281	34	223	182	41

	Wohlgemuth	Lewis and	Schmidt and	Sherwin and
Animals used .....	Rabbits	Root	Clark	Rose
Basal ration .....	Carrots	Rabbits	Dogs	Rabbits
		Milk and	Milk, fat	Carrots
		sugar	and crackers	

Grams of cystine  
in each dose ..... 3, 5, 0.5, 0.5 7.5, 7.5, 7.0 0.4, 0.4, 0.4  
Cystine days ..... 2, 1, 1, 1, 1, 1, 1, 3, 3, 3.

Lewis and Root, exp. LV, cystine given subcutaneously. Schmidt and Clark, exp. IV, a pup, the other two adults. Sherwin and Rose exp. III, cystein-hydrochloride used in place of cystine.

The total sulfur varies with the food and is reasonably constant. It is highest on the carrot diet, about 50 mg. per kilo, and lowest on the milk diet, 8 to 16 mg. per kilo. The sulfur partition of the control periods bears no relation to anything which is at present known. The per cent of total sulfate sulfur in the average control day urines is given as line A, the order of sequence being the same as that in the general table (I).

	W		S and R		S and C			Authors		
A	81.0,	76.5	58.5,	73.0	55.0,	30.3,	66.0	55.0,	62.3,	62.0
B	41.0,	35.5	92.0,	48.8	72.3,	60.2,	61.0	88.1,	98.0,	93.0
C	61.0,	47.0	93.2,	100.0	46.2,	75.3,	75.5	57.0,	89.1,	82.0

Arranged in the same way (line B) are the increments in per cent of total sulfur following the administration of cystine, that is the cystine sulfur eliminated. The two sets have about the same range, but are by no means parallel. The 81 per cent of the controls does not come opposite the 93 per cent of the eliminations nor does the 36 per cent from the line of eliminations come opposite the 30 per cent in control. We have no explanation whatever for the first set of figures. They can not be correlated as to diet, species, sex, nor age. The second set bears some relation to the dosage of cystine. Wohlgemuth gave his rabbits 2000 mg. per kilo and got the lowest elimination; the authors gave 133 mg. in three parts and got the largest elimination. The other two are properly intermediate. An increase in sulfate sulfur at the expense of the sulphydrate sulfur indicates an oxidation of cystine sulfur. The sulfate sulfur in per cent of the cystine sulfur eliminated is arranged in line C. If there is any parallelism between the cystine sulfur eliminated and the oxidation, it is certainly not striking. Apparently a slow absorption facilitates oxidation. Attention should be called to the large differences in retention of the cystine and to the lag of elimination.

The authors assume that the cystine may be attacked in the body at three points of the cystine molecule; the amino, the carboxyl and the sulphydrate. We have demonstrated<sup>1</sup> that in the organism cystine can change into cystein, and cystein into cystine. This is not only true of cystine but also of its derivatives. We may therefore speak of the sulphydrate group in cystine in this special connection. If organic radicles are attached at these vulnerable points the attack on cystine may be inhibited and perhaps prevented. Lewis and Root have presented data on phenyluraminocystine which indicate that this hypothesis is tenable. This is supported also by a number of our own experiments. The degree of inhibition is not the same for the different agencies of blocking and by blocking all around the oxidation might almost be considered as totally prevented. To illustrate this matter we will give the data from experiments

with phenyluraminocystine and phenyluramino cystein and for comparison some figures from Lewis and Root. It is to be noted in both these tables that in these experiments cystine and cystein act in identical manner.

TABLE II  
CYSTINE AND CYSTEIN PHENYLURAMINO SULFUR ELIMINATION.

	I			II		
	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.
Lewis and Root						
Av. control days.....	45	35	10	24	14	10
Cystine days .....	121	55	66	115	38	77
Do. less control.....	76	20	56	91	24	67
Lag days less control.....	12	0	12	23	7	16
Cystine S eliminated .....	88	20	68	114	31	83

Per cent cystine S eliminated: I 65.6, II 87.0.

Per cent of this S as total "SO<sub>4</sub>: I 21.3, II 27.0.

	I			II		
	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.	Tot. S mg.	"SO <sub>4</sub> S mg.	RSH S mg.
Sherwin and Rose						
Av. control days.....	88	53	35	64	36	29
Cystine days .....	424	257	168	399	184	215
Do. less control.....	160	97	63	207	76	128
Lag days less control.....	9	9	0	40	23	17
Second lag day less control	50	15	35	16	4	12
Cystine S eliminated .....	219	121	99	263	103	157

Per cent cystine S eliminated: I 69.5, II 79.0.

Per cent of this as total "SO<sub>4</sub>: I 55.0, II 39.0.

Phenyluraminocystine given by Lewis and Root, 1 gram in one day; by Sherwin and Rose, 0.8 gram on each of three days. The second experiment by Sherwin and Rose is with the cystein derivative.

## 5 (2237)

A quantitative study of the destruction of vitamin B by heat.

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Using the rat growth method with the system of controls and precautions developed by Dr. Edgeworth, Dr. Spohn and the authors, studies were made of the percentage destruction of vitamin B at the temperatures 100°, 110°, 120°, 130° C when