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Reabsorption of Certain Amino Acids and Derivatives by the Kidney Tubules.

J. R. Doty. (Introduced by Richard Ashman.)

From the Department of Physiology, Louisiana State University School of Medicine.

Evidence has been presented previously showing a marked variation in the extent of the excretion of different amino acids after their intravenous administration.[1] This study was designed to measure the rates of tubular reabsorption of l-tyrosine, N-acetyl-l-tyrosine, N-methyl-l-tyrosine and l-histidine. The results were obtained by using sodium ferrocyanide to measure the rate of glomerular filtration during the period of study of each substance. The procedure is an adaptation of one elaborated by Van Slyke, Hiller and Miller.[2]

Dogs received an intraperitoneal injection of 200 cc of a solution containing a suitable amount of sodium ferrocyanide together with the compound being studied. After a lapse of 15 minutes the bladder was emptied by catheterization and washed with distilled water. The urine was collected for a period of approximately one hour. Tyrosine and its derivatives were determined by the Folin-Ciocalteu phenol reagent; histidine by the Jorpes modification[3] of the Koessler-Hanke method.[4] A sample of blood was obtained about 15 minutes after the beginning and again 15 minutes before the end of the experimental period. The average of the values for the 2 samples of blood was used in each calculation. Volume of glomerular filtrate was obtained by dividing 100 x mg of ferrocyanide excreted by the average mg % of ferrocyanide in the plasma. By using this volume of glomerular filtrate and the plasma concentration of amino acid it was possible to calculate the amount of amino acid in the glomerular filtrate. Knowing the amount of amino acid excreted one obtained by difference the amount of the amino acid reabsorbed by the tubules.

From Table I it appears that only a small fraction of the acetyl derivative is reabsorbed whereas approximately two-thirds of the methyl derivative is taken up under similar conditions. It is difficult to raise the plasma concentration of tyrosine to a level com-

1 Eaton, A. G., and Doty, J. R., *J. Nutrition*, 1941, **21**, 25.

2 Van Slyke, D. D., Hiller, A., and Miller, B. F., *Am. J. Physiol.*, 1935, **113**, 611.

3 Jorpes, E., *Biochem. J.*, 1932, **26**, 1507.

4 Koessler, K. K., and Hanke, M. T., *J. Biol. Chem.*, 1919, **39**, 497.

TABLE I.
Tubular Reabsorption of Amino Acids and Derivatives.

Dog No.	Compound administered	Vol. of glomerular filtrate, × 100 cc/hr	Amt amino acid				
			In plasma, mg%	In glomerular filtrate, mg/hr	In urine, mg/hr	Reabsorbed by kidney tubules	
						mg/hr	%
1	N-acetyl-l-tyrosine	20.1	72.0	1447	1145	302	21
1	" "	22.5	51.0	1147	1010	137	12
1	" "	15.3	108.0	1652	1646	6	0.4
2	l-tyrosine	29.0	15.5	450	15	435	97
1	"	17.8	12.0	214	8	206	96
1	N-methyl-l-tyrosine	22.7	44.0	999	355	644	64
1	l-histidine	14.8	41.0	607	6	601	99

parable with that obtained with the other compounds but under the conditions of the experiments the reabsorption of this amino acid is practically complete. All but a trace of histidine is reabsorbed even when the plasma level of this substance is rather high. It is obvious that these rates of reabsorption must be higher than indicated if there is a pronounced "tubular excretion" of these compounds. It seems unlikely, however, that "tubular excretion" could have a significant effect at the higher plasma levels.

It is interesting to note that N-acetyl-l-tyrosine is almost quantitatively excreted[5] whereas tyrosine[6] and histidine[1] are quite rapidly metabolized by the dog. Separate analyses of the filtrates of whole blood and of plasma show that very little of the compounds enters the blood cells during the course of the experiments.

The results presented here seem to offer a promising mode of attack upon the fundamental problem of the mechanism of selective absorption of amino acids by the kidney tubules. Furthermore, such data extended to other amino acids would seem to be essential for a knowledge of the limit to which the plasma concentrations of amino acids could economically be raised during parenteral administration of these substances.

[5] Doty, J. R., unpublished data.

[6] King, F. B., and Rapport, D., *Am. J. Physiol.*, 1933, **103**, 288.