the formation of a necrotic lesion of the skin, the second, on the other hand, did not produce macroscopically visible local lesions.

Nothing definitive can be said about the possible mechanism of the local resistance observed. It is quite possible that the inflammatory state provoked by the formalin diminished the absorption of the lethal dose.[7,8,9]

Although local resistance is not frequently encountered, it is not a new phenomenon. Rosenthal, Tabor, and Lillie observed that mice surviving tourniquet shock because of salt treatment would survive a repetition of the same shock without salt, if given in the same leg, but would die if it was given in a different leg.[10] Similarly, according to a review by J. Levy, animals in which resistance to arsenic has been built up *per os* do not tolerate a toxic dose administered subcutaneously.[11]

Summary. When mice were pretreated with adrenalin they showed general resistance to a lethal dose of this substance but not cross resistance to formalin, either local or general. On the contrary, animals pretreated with formalin revealed only a local resistance, whether they were subjected to a lethal dose of formalin or of adrenalin. These observations seem to question Selye's interpretation of some of his experiments on general adaptation to the same or different "alarming" stimuli.

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Renal Reabsorption of Methionine in Normal Dogs.*

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(Introduced by Richard Ashman.)

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It is known that at normal plasma concentrations, reabsorption of amino acids from the glomerular filtrate is practically complete. Experiments in which the plasma concentration has been raised above normal levels have shown, however, that there are differences in the efficiency with which individual amino acids are reabsorbed. These differences are manifested in the rates of reabsorption of the various acids prior to the attainment of the maximal rate (Tm), and also in the levels at which the Tm is reached.[1-5]

The experiments to be described were designed to study the renal reabsorption of methionine. Shortly after they were concluded, experiments utilizing the microbiological method of analysis were reported[5] which indicated that the reabsorption of methionine is practically complete at plasma levels up to 115 mg % (equivalent to about 10.8 mg

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TABLE I.

The Relationship Between the Amount of *dl*-Methionine Alpha-amino Nitrogen Filtered and the Amounts Excreted and Reabsorbed in a Normal Dog.

Dog No. III

Exp. No.		Period	Urine flow, cc/min.	Glomerular filtration rate, cc/min.	Alpha-amino nitrogen: Plasma conc. mg %	Urine conc. mg%	Filtered mg/min./ sq.m.	Excreted mg/min./ sq.m.	Reabsorbed mg/min./ sq.m.	Ratio Reabsorbed / Filtered
1		Control	0.37		3.9	3.6		0.03		
	1% methionine, 0.5% inulin	1	4.57	46.5	9.4	2.1	10.1	0.22	9.88	.98
	(Wt, 7.7 kg; S.A.,* 0.437 sq.m.)	2	4.77	46.2	11.4	7.0	12.1	0.77	11.3	.93
		3	6.23	52.2	13.4	11.6	16.0	1.65	14.4	.90
		4	6.37	48.3	15.0	18.1	16.6	2.64	14.0	.84
2		Control	—		3.9	—		—		
	1.3% methionine, 0.5% inulin	1	2.47	49.8	11.0	12.4	12.5	0.70	11.8	.94
	(Wt, 7.7 kg; S.A., 0.437 sq.m.)	2	4.63	51.6	12.9	16.9	15.2	1.79	13.4	.88
		3	5.67	44.8	15.1	22.8	15.5	2.96	12.5	.81
		4	5.60	53.1	16.8	35.3	20.4	4.52	15.9	.78
3		Control	0.17		3.5	6.8		0.03		
	1.5% methionine, 0.5% inulin	1	2.63	61.9	10.4	7.6	14.1	0.44	13.7	.97
	(Wt, 8.2 kg; S.A., 0.455 sq.m.)	2	7.26	65.7	15.5	23.6	22.4	3.77	18.6	.83
		3	7.47	58.9	17.2	30.2	22.3	4.96	17.3	.78
		4	6.67	52.4	18.7	21.0	21.5	3.08	18.4	.86
4		Control	—		—	—		—		
	2% methionine, 0.5% inulin	1	2.57	58.5	11.4	20.7	13.2	1.06	12.1	.92
	(Wt, 9.55 kg; S.A., 0.504 sq.m.)	2	4.63	58.2	14.7	27.7	17.0	2.54	14.5	.85
		3	7.80	57.5	19.6	34.1	22.4	5.28	17.1	.76
		4	8.77	52.2	27.0	42.9	28.0	7.46	20.5	.73

* Surface area in square meters $= 0.112\sqrt[3]{(\text{body wt in kg})^2}$ (Lusk, G., *The Science of Nutrition*, W. B. Saunders Co., pp. 122-123).

% methionine α-amino nitrogen). The results of the present study, based upon α-amino nitrogen determinations and extending the plasma concentrations beyond the levels previously reported, provide further evidence for the high efficiency of the renal reabsorptive process for methionine.

Methods. The experiments were carried out upon 2 healthy female dogs in the manner described in detail elsewhere.[4] Infusions of appropriate concentrations of inulin and dl-methionine in physiological saline were made into the femoral vein at a rate of about 5 cc per minute. Urine collections were made from the bladder with an indwelling catheter and blood samples were taken from the femoral artery by the use of an indwelling spinal needle cut to a length of 4 cm and equipped with a tightly fitting stylet. Periods were 30 minutes in duration. Blood samples of 10 cc were taken at the beginning, mid-point and end of each period and the average amino acid and inulin concentration of the 3 samples employed to indicate the level for the period.

The plasma amino acid concentration was determined manometrically by the ninhydrin-carbon dioxide method of Hamilton and Van Slyke[6] and urinary amino acid was similarly determined by the method of Van Slyke, MacFadyen and Hamilton.[7] Inulin was determined by the method of Hubbard and Loomis[8§] using a Coleman spectrophotometer to measure the intensity of color developed.

Results. Eight different experiments, involving 31 periods, were performed upon one dog and 3 experiments involving 8 periods on another. Plasma levels up to 27 mg % of α-amino nitrogen and filtration rates up to 34.8 mg per minute per square meter of body surface were obtained. In all of the experiments, the efficiency of the renal tubules in reabsorbing methionine from the glomerular filtrate proved to be very high. There was no indication that the maximal rate of reabsorption was reached at any of the levels of glomerular filtration which were attained.

Table I shows the essential data obtained in four of the experiments performed upon Dog III. Each of these experiments was repeated upon the dog with similar results. Inulin clearance has been used as a measure of glomerular filtration rate[9] and the rates of filtration, excretion and reabsorption of α-amino nitrogen have been calculated as previously described.[4] It is seen that as the filtration of amino nitrogen increases through 14 mg/min/square meter reabsorption is well over 90% complete. Beyond this level, the proportion reabsorbed decreased slightly for this dog, but remained remarkably high throughout the experiments. In the experiments upon the second dog (No. IV), plasma α-amino nitrogen concentrations up to 19.8 mg % and filtration rates up to 32.5 mg/min/square meter were attained. Except for the fact that the ratio of reabsorbed : filtered amino nitrogen remained above 0.82, even at the highest filtration levels, the results were in all respects similar to those described for Dog III.

Fig. 1 shows graphically the relationship between the amount of methionine α-amino nitrogen filtered and that reabsorbed in all eight of the experiments performed upon Dog III. It will be noted that although the slope of the curve decreases somewhat beyond filtration rates of around 14 mg/min/square meter, there is no tendency to plateau even at the highest levels attained.

From these experiments it is evident that the tubular capacity for the reabsorption of methionine is relatively high. In terms of α-amino nitrogen it exceeds 25 mg/min/square meter. In this respect, methionine resembles glycine[1] and alanine.[2] These substances manifest reabsorption capacities

[6] Hamilton, P. B., and Van Slyke, D. D., *J. Biol. Chem.*, 1943, **150**, 231.

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[8] Hubbard, R. S., and Loomis, T. A., *J. Biol. Chem.*, 1942, **145**, 641.

§ This method was modified to the slight extent of heating the color-forming solution at 80°C for 14 minutes instead of 8 as prescribed by the authors. This modification assured the maximal development and stability of color.

[9] Smith, H. W., *The Physiology of the Kidney*, Oxford University Press, 1937.

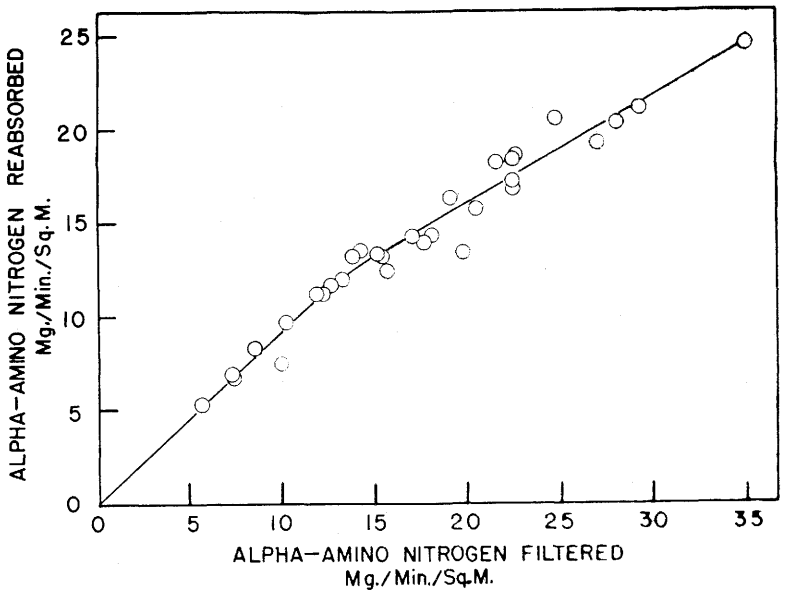

FIG. 1.
The relation between renal filtration and reabsorption of alpha-amino nitrogen of *dl*-methionine in Dog III.

which are considerably higher than the maximal rates reported for leucine, isoleucine and valine[4] and which stand in strong contrast to such low threshold amino acids as arginine and lysine.[3,5]

Summary. The relation between the rate of renal filtration and reabsorption of dl-methionine α-amino nitrogen has been studied in normal dogs. As the amount filtered was increased to 34.8 mg α-amino nitrogen/min/square meter, the highest level attained in these experiments, the rate of reabsorption increased to 24.8 mg/min/square meter and there was no evidence that a Tm value was obtained. The data demonstrate the high efficiency of the renal mechanism for the reabsorption of methionine.

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Cataracts Resulting from a Deficiency of Phenylalanine in the Rat.*

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Experimental cataracts in the rat have been shown to result from deficiencies of either of 2 of the essential amino acids. What apparently were cataracts due to tryptophane deficiency in the rat were first described by Curtis, Hauge and Kraybill.[1] Totter and Day[2] later made a careful study of the cataracts resulting from this deficiency. Recently,

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2 Totter, J. R., and Day, P. L., *J. Nutrition*, 1942, **24**, 159.