

been suggested previously.³ The situation would be additionally complicated by the fact that body surface formulae are derived from rats on stock diet. It is known that, after starvation or over-feeding, the composition of the body changes with respect to the basic constituents such as protein.⁸ With such changes, the relation between body weight and surface area may change. Therefore, we have compared our results in each group with rats on stock diet at the same weight.

⁸ Addis, T., *Proc. 6th Pacific Science Congress*, 1939, **6**, 677.

Summary. 1. Drastic changes in protein, fluid, and salt consumption do not produce striking changes in blood and plasma volumes of the rat, over the periods studied. 2. Increased fluid consumption produced an increase of about 10% in total blood volume and plasma volume at the end of 17 hours, only when salt consumption was simultaneously increased. 3. A high protein diet increased blood and plasma volumes slightly at the end of 7 days, but did not appreciably alter the serum protein concentration. 4. All protein-deficient diets reduced the total circulating protein by 15-20% at the end of 7 days.

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Effect of Lipotropic Agents in a Diet Containing Pure Amino Acids in Place of Protein.

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In an experiment where an amino acid mixture replaced casein in a diet deficient in lipotropic factors, Rose, Machella, and György¹ found no appreciable effect of methionine fed to rats at a level of 50 mg per day or equivalent to about 0.8% of the diet. It was not immediately possible to extend this work but the need to determine whether more methionine would be effective or whether some other factor was involved was recognized. In the present study the effect of methionine in the original and in larger dosage was compared with that of choline.

Experimental. The experimental diet and the procedure followed were as previously described. Male albino rats, weighing 150 to 165 g were divided into 4 groups of which one received basal diet alone, the others receiving in addition respectively, 50 mg of methionine, 100 mg of methionine and 25 mg of choline chloride per day in aqueous solution. For about three-fourths of the animals we followed our usual procedure of giving the

supplement in a Caster Cup. Since some of the rats disliked the solution of methionine a stomach tube was used for supplementing those animals which started later in the experiment (equal numbers of all groups). The animals were sacrificed at the end of 3 weeks and the liver fat determined.

Results and Discussion. The experimental data are summarized in Table I. As previously observed¹ the basal diet was quite inadequate in maintaining the weight of the animals and addition of the sulfur containing amino acid neither improved the nutritive value of the ration in this regard to any great extent, nor encouraged appetite. Choline was equally without effect on these factors. Food intake was remarkably constant in all of the groups but much lower than in the previous experiment. The average consumption was 4.1 g per day as compared with 5.9 g in the earlier study.

In the control animals the low food intake and weight loss did not prevent the development of fatty livers, an average value of 20.4% being found. A greater effect of methionine was observed in this experiment than in that previously reported. There was

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¹ Rose, C. S., Machella, T. E., and György, P., *PROC. SOC. EXP. BIOL. AND MED.*, 1947, **64**, 352.

TABLE I.
Effect on Body Weight, Food Intake, and Liver Fat of Adding Methionine and Choline to a Diet Free of Sulfur-Containing Amino Acids.

Group	Special supplement (daily)	No. of rats	Weight of animals		Food intake, g/day	Liver	
			Initial, g	Change, %		Wt, g	Total lipid, %
I	None	12	156 (150-164)	-32 ± 1.4	4.2 ± 0.18	4.7 ± 0.12	20.4 ± 1.6
II	50 mg Methionine	12	155 (150-165)	-26 ± 1.2	4.1 ± 0.13	4.3 ± 0.15	13.3 ± 1.3
III	100 " "	12	155 (150-160)	-27 ± 1.9	4.1 ± 0.17	4.2 ± 0.15	9.7 ± 0.75
IV	25 " Choline	12	154 (150-162)	-29 ± 1.1	4.0 ± 0.11	3.8 ± 0.12	6.8 ± 0.36

significant reduction of liver fat at the 50 mg level (average fat, 13.3%), with still lower values when 100 mg were given (average fat, 9.7%). This result, with the lower food intake and greater weight loss in this experiment, suggests that the 50 mg level of methionine was at the borderline of effective dosage, and in the present case, the higher ratio of methionine in the diet (1.2%) was sufficient to produce a lipotropic effect.

When choline was given it showed its usual efficient lipotropic action. The average liver fat content of the choline-fed group was 6.8%, an almost normal value. Methionine in the 100 mg dosage gave a 40% higher fat content of

the liver. The total methyl in this amount of methionine is 25% greater than in the choline.

It may be noted that the weight of the livers paralleled the fat content consistently.

Summary. Rats fed an alipotropic diet in which a mixture of amino acids replaced protein developed fatty livers in spite of low food intake and emaciation. Methionine in adequate dosage exerted a lipotropic effect although there was still 10% of fat in the liver when the methionine constituted 2.4% of the diet. When 25 mg of choline chloride per day were fed the livers were essentially normal.

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Therapeutic Effectiveness of Single and Divided Doses of Penicillin in a Streptococcal Infection in Mice.

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In a preliminary study on penicillin dosage and its therapeutic effectiveness it was found that a single oral dose containing 10 mg of penicillin G per kg of body weight protected a large proportion of mice in an otherwise fatal experimental streptococcal infection.¹ The results of further studies on the effect of single doses of drug, administered orally or

subcutaneously, are given in the present communication.

In addition, a comparison between the effect of a given amount of penicillin when administered as a single dose and as a series of equally spaced smaller doses has been included in this report. Such a comparison is of interest, since it is commonly assumed that the therapeutic effectiveness of penicillin in aqueous solution depends upon repeated

¹ White, H. J., Lee, M. E., and Alverson, C., *Proc. Soc. Exp. Biol. and Med.*, 1946, **62**, 35.