liferation in bone marrow cultures because of an excess of inhibiting substances over accelerating substances present.

4. Individual urine and blood serum specimens have been shown by adsorption on Norit and elution with NaOH and ammoniacal acetone to have both inhibiting and accelerating substances present.

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The Effect of Methionine on Blood Coagulation.*

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In 1936 Sterner and Medes[1] reported that cysteine and methionine prolonged both the bleeding and coagulation times for several hours when administered orally or intravenously to human subjects. They further concluded that the effect was mainly on one factor of the coagulation system, namely, prothrombin. From the data reported by these investigators one could conclude that methionine might possibly be an effective and much safer anticoagulant for clinical use than either dicoumarol or heparin. Because of these possibilities the effects of methionine on blood coagulation and quantitative prothrombin levels were studied more fully in human subjects.

In these studies dl-methionine was used. The solutions (2.5 g of methionine per 100 cc) for intravenous administration were made isotonic by the addition of sodium chloride and the pH adjusted to near neutrality by the use of sodium dibasic phosphate. The prothrombin determinations were done by the method of Quick[2] and the coagulation time by the intravenous test tube method of Lee and White.[3] Control studies were also done. All studies were done over a 6 hour period with observations at the initial 30 minute period and then each hour for the 6 hour period.

Control Studies. The coagulation times and prothrombin levels were determined in 3 persons in a fasting state over a 6 hour period. Changes were minimal. These studies were repeated in 3 persons after a routine hospital breakfast. Slight changes were noted in that the coagulation time was decreased after a period of from 4 to 5 hours, the maximum being 4½ minutes, this being within the range of experimental error.

Oral Methionine. Methionine was given to 2 individuals in 3.0 g amounts. No effect on the coagulation time was noted. No prothrombin determinations were made.

Intravenous Methionine. The individuals with normal prothrombin levels. Amounts of 1.3 g were administered to 2 subjects and no significant changes were noted in either the coagulation times or the prothrombin levels. Methionine in 2.5 g doses was given to 8 subjects, one fasting and 7 on routine hospital diet. In no instance was the coagulation time increased or the prothrombin level altered. In 4 individuals, including the fasting subject, the coagulation time was decreased, the maximum being a 10 minute decrease in one individual. The curve was a moderate exaggeration of the one obtained in the control subjects who had breakfast. Methionine in 5.0 g doses was administered to 3 subjects. No significant changes were noted in either the coagulation times or the prothrombin levels.

Intravenous Methionine. Individuals with decreased prothrombin. 2.5 g were administered to an individual with cirrhosis of the liver and observations made over a 6 hour period. The initial prothrombin level was

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2 Quick, A. J., *J.A.M.A.*, 1938, **110**, 1658.

3 Lee, R. I., and White, P. D., 1913, **145**, 495.

35% of normal. No changes of any significance were noted in the coagulation times.

Conclusion. It has been previously reported that methionine prolonged the bleeding and coagulation times. In this study the effects of dl-methionine on the intravenous coagulation time and prothrombin were observed in human subjects. The changes were insignificant and dl-methionine has no clinical value as an anticoagulant.

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Vitamin B_6 Group. XV. Urinary Excretion of Pyridoxal, Pyridoxamine, Pyridoxine, and 4-Pyridoxic Acid in Human Subjects.*

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The earliest investigations of the excretion of vitamin B_6 by animals were made using the chlorimide reaction for analysis.[1,2] The method as then used was not specific for the determination of pyridoxine, but since the complex nature of vitamin B_6 was then unknown, all material found by this method was called *pyridoxine*. These early investigations did establish the fact that pyridoxine was rapidly absorbed from the digestive tract and rapidly cleared in the renal pathway. Although the recovery of the ingested vitamin in the rat was 50 to 70%,[1] only 10 to 20% of the dose was recovered when pyridoxine was fed to dogs or to human subjects.[2]

Subsequent refinement of the chlorimide method showed that small amounts of some substance other than pyridoxine were excreted in the urine of the dog and man after feeding a large dose of pyridoxine.[3] It was also shown that both pyridoxine and the unknown metabolite occurred in part as conjugated forms which did not react with 2, 6-dichloroquinone chlorimide, but which could be hydrolyzed with acid to give pyridoxine and the unknown metabolite.

The demonstration of the occurrence of *pseudopyridoxine* in human urine both before and after administration of pyridoxine[4] and the subsequent characterization of *pseudopyridoxine* as pyridoxal and pyridoxamine,[5] suggested the identity of the unknown metabolite of Scudi *et al.*[3] with pyridoxal or pyridoxamine.

The main metabolic product excreted after ingestion of pyridoxine was discovered by Huff and Perlzweig and identified as 4-pyridoxic acid.[6] This compound does not produce a color with the chlorimide reagent, and is inactive in promoting growth of microorganisms in vitamin B_6-free media.

Although pyridoxal and pyridoxamine are now known to be the forms of vitamin B_6 present in largest amounts in many foodstuffs and tissues,[7,8] no information is available concerning their metabolic fate. Development of a differential assay procedure for pyridoxal, pyridoxamine, and pyridoxine[8] makes such a study feasible. Results of such an investiga-

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