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Stability of Serum Ac-Globulin.*

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Serum Ac-globulin is a clotting factor found in the globulin fraction of blood serum[1,2] which accelerates the change of prothrombin to thrombin. This factor is present in plasma in a much less active form, plasma Ac-globulin,[3-7] which serves as a precursor to serum Ac-globulin. The role of Ac-globulin in the total clotting reaction has been described as follows:[1,2] The clotting reaction is initiated by thromboplastin, which, in the presence of calcium ions, interacts with prothrombin to form thrombin. The thrombin in turn alters the plasma Ac-globulin so that it becomes serum Ac-globulin. The latter then intensifies the reaction between thromboplastin and prothrombin. Clotting is then accomplished by the action of thrombin on fibrinogen.

In the developmental work on Ac-globulin, oxalated bovine plasma was used as a potent stable source of plasma Ac-globulin[8] and bovine serum[1] a stable source of serum Ac-globulin. In working with the sera of other species involving man, dog, and guinea pig, we have found that while plasma Ac-globulin is relatively stable, serum Ac-globulin is inactivated and largely disappears within a few hours after the blood is drawn. Rabbit serum Ac-globulin is similar to bovine serum Ac-globulin in that it remains stable for longer periods of time.

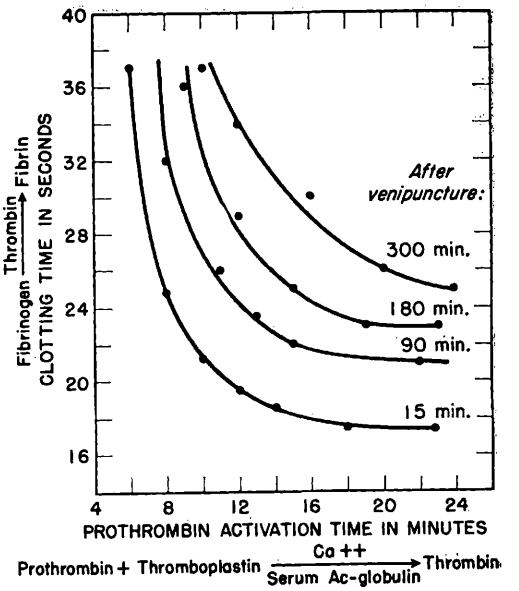

FIG. 1.
Change in Ac-globulin activity of human serum stored at 5°C.

In the study of the stability of serum Ac-globulin, blood was drawn and immediately centrifuged at 3,000 rpm for 10 minutes, and the serum was removed and stored at 5°C. Samples were analyzed for serum Ac-globulin by methods elsewhere described[1] after storage for periods of 15, 90, 180 and 300 minutes, as indicated in Fig. 1. In this procedure, human serum diluted 1,400 times was incubated for varying time intervals (as indicated on the horizontal axis, Fig. 1) with purified bovine prothrombin[9] and with optimal concentrations of thromboplastin and calcium.

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The amount of thrombin formed during this period was measured by the addition of fibrinogen and by observing the time required for a clot to form (vertical axis, Fig. 1). This observed time is an inverse measure of the amount of thrombin formed in the first reaction. The rate of thrombin production is proportional to the concentration of the Ac-globulin in the reacting medium. Thus, it may be seen that there is a definite decrease in serum Ac-globulin activity from the time that the blood was drawn. Within 300 minutes after blood was drawn less than one-third of the Ac-globulin activity remained. On standing at room temperature the loss of serum Ac-globulin activity was considerably more pronounced (not shown in Fig. 1).

One would naturally like to offer an explanation for these observed variations, but sufficient information is not available at this time. It has been shown that relatively large amounts of thrombin (30 units per cc or more) partially destroy the Ac-globulin activity of oxalated bovine plasma.[1] It is therefore possible that the instability of serum Ac-globulin in certain species may be due to the action of thrombin. Since the amount of thrombin present during and immediately following the clotting reaction is determined by the rate of thrombin formation and by the effective concentration of antithrombin, variations of these factors from one species to another may account for the differences in the stability of Ac-globulin activity. The stability of serum Ac-globulin may also be an inherent characteristic of the substance for each species.

The similarity in the stability of human serum Ac-globulin and that of Factor VI described by Owren[4] tends to confirm the suggestion that these two substances are identical.

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Effects of Diethylcholine and Ethionine on Growth Rate, Liver Fat, and Kidney Degeneration of Rats.

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It is now well established that a dietary deficiency of choline and methionine leads to an accumulation of fat in the liver, to the development of hemorrhagic degeneration of the kidney, and to a failure of young animals to grow on diets containing homocystine but lacking in labile methyl groups. The lipotropic action and kidney protection have been ascribed to the action of intact choline or choline-like molecules or their precursors, whereas growth on a low methionine diet containing homocystine is dependent upon the availability of labile methyl groups.

Diethylmethylhydroxyethyl ammonium chloride (diethyl choline)[1] and ethionine[2] have been reported to be toxic to rats on low methionine diets. These compounds are ethyl homologs of choline and methionine respectively, and their toxicity raised interesting questions as to the mechanisms by which they may interfere either with fat metabolism or with transmethylation. The present experiments were devised to investigate in the rat the influence of these two compounds on the three criteria of inadequate choline or methyl group intake-growth on a diet containing

* The data are taken from a thesis presented by Virginia L. Hardwick to the Graduate School of the University of Southern California in partial fulfillment of the requirements for the degree of Master of Science.

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