the initial examination. The children in the sodium fluoride group in this study had an average increase of 0.708 newly decayed, missing, or filled surfaces; and if this represents a reduction of approximately 40 percent in new decay, as previously reported by many other workers (*8*), then it is reasonable to suppose that a nontreated control group would have had 1.180 newly decayed, missing, or filled surfaces. Therefore, using the average increase in newly decayed, missing, or filled surfaces in the stannous chlorofluoride group (0.117), a reduction of 90 percent in dental caries is found when compared with children who did not receive fluoride therapy. These data strongly suggest that this new fluoride is superior to sodium fluoride in preventing new dental caries when used as a topical agent. Through the use of this compound, a greater reduction in dental decay may be expected for the children who do not receive the benefits of water fluoridation.

In the study begun in 1951, stannous fluoride was used as a topical agent, and children receiving it experienced greater protection than controls given sodium fluoride furnishing twice as much fluorine (*9*). This fact, together with the data reported here, suggests that the cation, tin, may influence the effectiveness of the fluorine and that additional studies should be made to find still more effective compounds.

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Reduction of Serum Lipides and Lipoproteins by Ethionine Feeding in the Dog

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A previous report from this laboratory dealt with the induction of fatty livers in rats by the administration of ethionine and related compounds(*1*). The observation of Farber and his associates (*2, 3*) that fat accumulated rapidly in the livers of fasted female rats after injection of DL-ethionine was confirmed. It was shown, in addition, that the L-isomer is also active. In order to determine the structural specificity of this action of ethionine, the following compounds were tested for their fatty-liver-inducing action: ethionine sulfoxide, S-propylhomocysteine, S-isopropylhomocysteine and S-ethylcysteine. Only ethionine sulfoxide was found active.

The effects of ethionine administration on serum lipides of the dog are described here (*4*). It is shown that, in addition to inducing fatty livers (*5*), prolonged oral administration of ethionine results in an almost complete disappearance of circulating lipides, which are restored to normal levels upon removal of ethionine from the diet.

The dogs used in this experiment had been fed a daily diet containing 30 g of lean meat and 3 g of sucrose per kilogram of body weight, 2 g of bone ash, 3 ml of fish oil containing 1200 AOAC units of vitamin D and 3000 units of vitamin A, one tablet containing a vitamin mixture (*6*) and another tablet containing a salt mixture (*7*). Along with the diet, 125 mg of DL-ethionine was fed daily in the form of a tablet. With few exceptions, the dogs ate well during the period of observation. When a dog lost appetite as a result of ethionine feeding, force-feeding was resorted to.

Low-density, serum lipoproteins were determined by ultracentrifuging according to the method of de Lalla and Gofman (*8*). High-density lipoproteins were divided into two fractions in which the concentrations of lipoproteins less dense than 1.125 (L) and 1.20

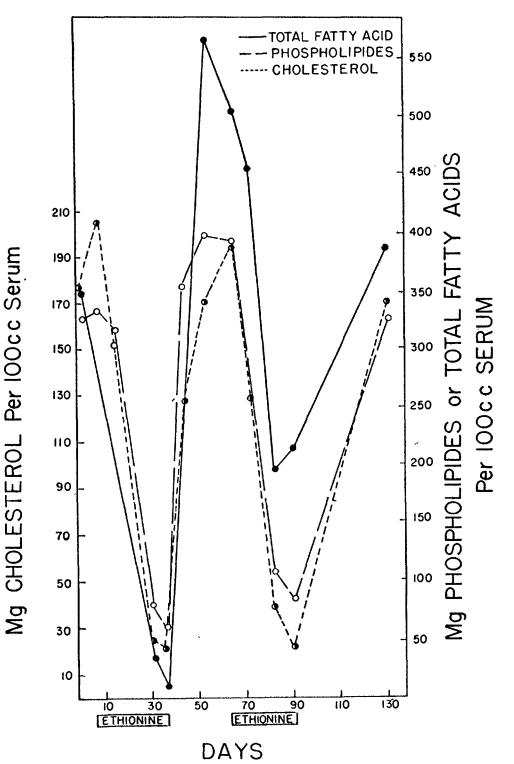

Fig. 1. Effect of ethionine feeding on concentrations of total fatty acids, phospholipides, and cholesterol of dog serum.

(L + T) were determined. The low-density lipoproteins were divided into four groups, Standard Sf 0–12, Standard Sf 12–20, Standard Sf 20–100, and Standard Sf 100–400, according to the system recently adopted by Gofman (*8*). The term *Standard Sf* signifies that the flotation rate has been determined under specified conditions in a solution of density 1.063 and that the concentrations in milligram percent have been corrected for the effects of concentration on flotation rate.

Aliquots of serum were analyzed for total fatty acids, total cholesterol, and lipide phosphorus, according to methods previously published (*9–11*).

Twelve dogs were used in this study, and typical results obtained with dog 110 are shown in Figs. 1 and 2. The total period of observation was 130 days, and during that time ethionine was fed from the 9th to the 36th day and from the 65th to the 90th day. The daily feeding of 125 mg of ethionine resulted in a pronounced fall in the concentration of all lipide constituents of the serum. When the feedings of ethionine were discontinued, the levels of all lipide constituents in serum promptly returned to normal.

The four groups of low-density lipoproteins decreased during the ethionine administration. The distinction between the high-density L-lipoproteins and the high-density T-lipoproteins is not so clearly defined in dogs as it is in human beings. Both, however, shared in the decrease, and both returned to normal upon withdrawal of ethionine from the diet.

The tissues of two dogs were examined histologically 65 days after the last administration of the ethionine (*12*). No damage attributable to the ethionine was detected.

The results of the present investigation show that the accumulation of fat in the liver resulting from ethionine administration is accompanied by a pronounced fall in circulating lipides, involving phospholipides, cholesterol, and fatty acids. In view of the reduction of the serum lipides, a simultaneous decrease in the levels of serum lipoproteins was to be expected, but it is of particular interest, in this connection, that ethionine administration reduced all fractions of the high- and low-density lipoproteins to about the same extent.

The question arises whether the effects observed here on lipoproteins resulted from a primary action upon lipide metabolism or upon protein metabolism. It has been suggested that ethionine interferes with protein formation (*13*), and it is reasonable to infer that the lipide changes in liver and serum reflect the action of ethionine on protein formation. Since practically all serum lipides exist as lipoproteins, it is conceivable that an interference with the formation of lipide-carrying proteins in the liver is responsible for both the development of the fatty liver and a concomitant decrease in the concentration of all lipides in serum.

Summary. (i) The effects of daily oral administration of 125 mg of DL-ethionine upon the serum lipides and lipoproteins of dogs were studied. (ii) The feeding of the ethionine resulted in a prompt reduction in the levels of serum fatty acids, phospholipides, and cholesterol. At the end of 25 days, negligible amounts of these lipides remained in serum. (iii) A reduction in the levels of low- and high-density lipoproteins also resulted from the feeding of ethionine. In general, the extent of reduction in all lipoprotein fractions paralleled that observed in lipides. (iv) The removal of ethionine from the diet led to a prompt restoration of the concentrations of all lipide and lipoprotein constituents to normal.

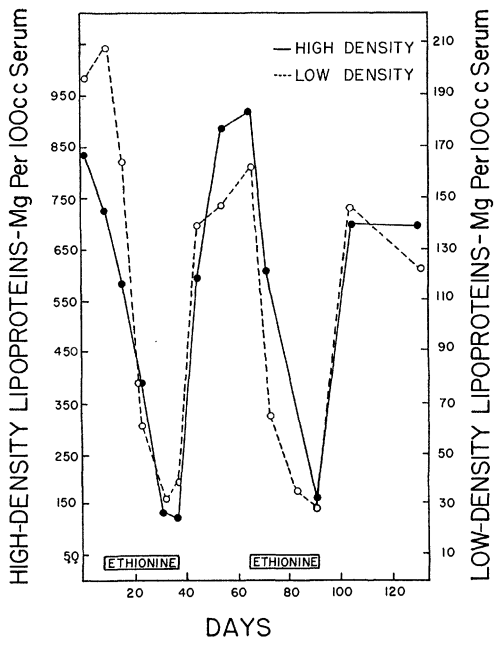

Fig. 2. Effect of ethionine feeding on concentrations of high-density and low-density lipoproteins of dog serum.

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6. Each vitamin tablet contained 0.2 mg thiamin hydrochloride, 0.2 mg riboflavin, 0.2 mg pyridoxine, 6.0 mg calcium pantothenate, 4.0 mg niacinamide, 50 mg inositol, 0.2 mg folic acid, 6 mg para-aminobenzoic acid, and 0.01 mg biotin.
7. Each salt tablet contained 600 mg NaCl, 450 mg magnesium citrate, 200 mg KH_2PO_4, 130 mg $CaHPO_4 \cdot 2H_2O$, 30 mg ferric citrate, 115 mg KCl, and 0.1 mg KI.
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