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and Radiation Laboratory
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ABSTRACT

The metabolism of injected egg lipoprotein has been studied by ultracentrifugal methods in the normal and x-irradiated rabbit. On the basis of the removal of egg lipoprotein from the blood of normal and irradiated animals, it is concluded that there is no block produced in lipoprotein metabolism at the time of radiation or for at least four hours postirradiation.

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INTRODUCTION

It has been shown that an LD_{50} dose of total-body x-irradiation produces a hyperlipoproteinemia in the rabbit, commencing at about 12 hours postirradiation and reaching a maximum at 30 hours postirradiation.^{1,2} In view of the association between the lipoprotein pattern observed at 30 hours postirradiation and the subsequent time of death of animal,³ it was of interest to study further the mechanism of this postirradiation hyperlipoproteinemia.

The lipoproteinemia exhibited by the irradiated animal must obviously be due to an increased rate of entry into the blood or to a decreased rate of removal from the blood or to a combination of both factors. In order to determine which mechanism was operating, the removal from the blood of injected egg lipoprotein was studied in the normal and irradiated animal.

The rate of disappearance from the blood of injected egg lipoprotein is considerably slower than for some synthetic emulsions, and the egg lipoprotein exhibits the serial conversion of higher-Sf-rate molecules to those of lower Sf rates described previously in recovery from certain lipid metabolic disorders.⁴ Zilversmit⁵ states that relatively small amounts of phospholipid, remaining after the injection of labeled egg yolk, were found in the lung or spleen, thus indicating that egg-yolk lipids (egg lipoproteins) apparently do not block lung capillaries and are not rapidly phagocytosed.

These facts suggest that, in contrast to some synthetic emulsions, egg lipoprotein is handled by the animal in a manner similar to that for its own native lipoproteins.

METHODS

The egg lipoprotein was prepared by the procedure of Nichols⁶ and was injected into the rabbit's ear vein in a dose of about 0.5 g egg lipoprotein/kilo body weight. New Zealand white rabbits weighing about 7 lb were used in this experiment. The egg lipoprotein (as well as the other lipoproteins present in

the serum) was determined by the ultracentrifugal techniques as developed by Gofman and associates.⁷

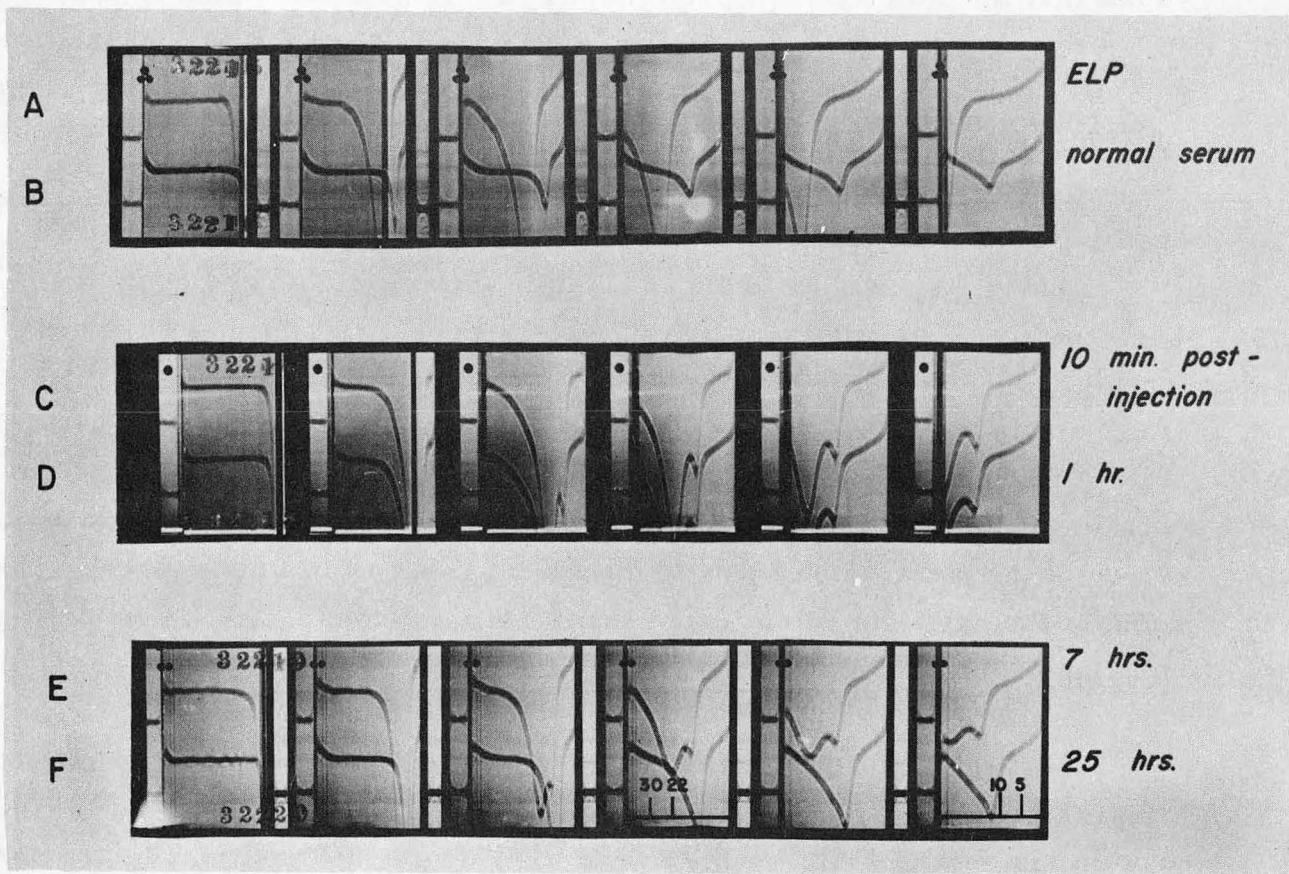
Results

Figure 1a shows the ultracentrifugal pattern of the egg lipoprotein diluted in saline to the concentration to be expected in the serum of the injected animal. It can be seen that the egg lipoprotein consists of a spectrum of molecules of Sf rates between 15 and 50. Figure 1b shows the serum lipoproteins of the rabbit prior to injection. Figures 1c, d, e, and f show the serum lipoproteins of the animal at 10 minutes, 1 hour, 7 hours, and 25 hours after the injection of the egg lipoprotein. The series of events following injection of egg lipoprotein in the normal rabbit may be described as follows.

1. Immediately after injection, the egg lipoprotein reacts with the serum lipoproteins normally present in the rabbit. This interaction alters the serum lipoproteins normally occurring in the animal, producing molecules of a higher Sf rate. This can be seen by the shift of the maximum ordinate of the normally occurring molecules from an Sf 8 to an Sf 14.

2. The total spectrum of egg lipoprotein disappears from the blood with a half time of about 7 hours. The components of higher Sf rate disappear first and, as this occurs, there is a slight increase in components of lower Sf rate. Concurrently, the native lipoproteins return to their normal Sf rates.

In order to determine the effect of irradiation on the removal of egg lipoprotein from the blood, eight rabbits were each injected with 0.5 g/kilo of egg lipoprotein. Four of the animals were irradiated with 800 r total-body x-irradiation 6 hours after the injection. Irradiation was done with a 220-kv, 15-ma beam filtered through 0.5 mm Cu and 1.2 mm Al. Four animals were used as nonirradiated controls. Blood samples were drawn by ear vein at 20 minutes, 10 hours, 20 hours, 38 hours, 3 days, and 6 days after the injection of the egg lipoprotein and the serum lipoproteins were determined. Two Sf classes are reported here: The Sf 22-30 class that represents the majority of the injected egg lipoprotein, and the Sf 5-10 class that represents the majority of the β -lipoproteins of the rabbit. The intermediate Sf 10-22 class represents a mixture of the two types of lipoprotein that are centrifugally identical. Figure 2 shows the Sf 22-30 class in the irradiated and nonirradiated animals. Following the injection of egg



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Fig. 1 Serum lipoprotein patterns following the injection of egg lipoprotein. From left to right, successive frames are at 0, 6, 12, 22, 30, and 38 min after the rotor has reached 52,640 rpm. A flotation rate scale at the bottom of the figure shows the location of the Sf 5-10 and Sf 22-30 classes.

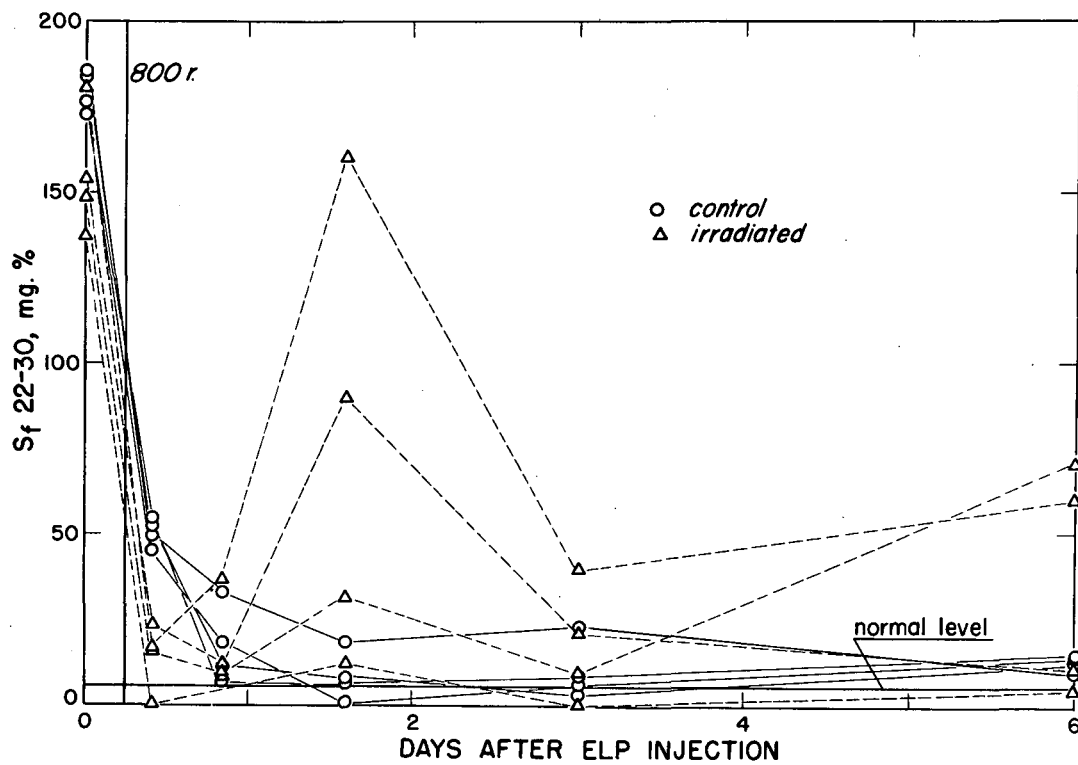
lipoprotein the level of this class of lipoprotein increased some tenfold over the value seen in the normal rabbit. As the lipoprotein is metabolized, the serum level of Sf 22-30 falls toward normal. The serum level of this class of lipoprotein continued to drop for at least four hours postirradiation in the animals receiving 800 r total-body irradiation. This rate of removal was equal to or greater than that in the nonirradiated animals. Previous work has shown that the radiation lipoproteinemia in this Sf class begins to appear at 12 hours postirradiation, reaches a maximum at 30 hours postirradiation and then decreases toward normal.² Figure 2 also shows the radiation-induced hyperlipoproteinemia in the Sf 22-30 class. This can be seen in the figure as the large increase in the Sf 22-30 serum lipoprotein between 1 and 2 days after egg lipoprotein injection in the irradiated animals.

Figure 3 shows the Sf 5-10 class in the irradiated and control animals. The radiation lipoproteinemia in this class appears at about 2 days postirradiation and reaches a maximum at 3 days. Immediately after injection of egg lipoprotein, the Sf 5-10 class is lowered below normal, owing to the shift of the native molecules to higher -Sf- rate classes. As the egg lipoprotein is removed from the blood, the Sf 5-10 class increases owing to the return of the native molecules to normal Sf rates and to the conversion of some of the egg lipoprotein to molecules of this class. Again there is no blocking of this process at the time of radiation in those animals receiving 800 r total body irradiation.

On the basis of the removal of egg lipoprotein from the blood of normal and irradiated animals, it is concluded there is no block produced in lipoprotein metabolism at the time of radiation or for at least four hours postirradiation.

DISCUSSION

The observation that egg lipoprotein disappears as rapidly from the serum of the irradiated animal as from the serum of the nonirradiated one would tend to support the hypothesis that the radiation-induced hyperlipoproteinemia represents an increased fat mobilization rather than a blocking of lipid metabolism. This hypothesis has already been mentioned in connection with the survival data.³ It was shown that animals with extremely high serum lipoprotein levels following LD₅₀ irradiation were more likely to survive than those showing only a moderate increase. Also, those animals showing essentially no increase tended to survive. Thus the lipoprotein



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Fig. 2 Concentrations of serum lipoprotein of the Sf22-30 class in irradiated and nonirradiated animals following the injection of egg lipoprotein.

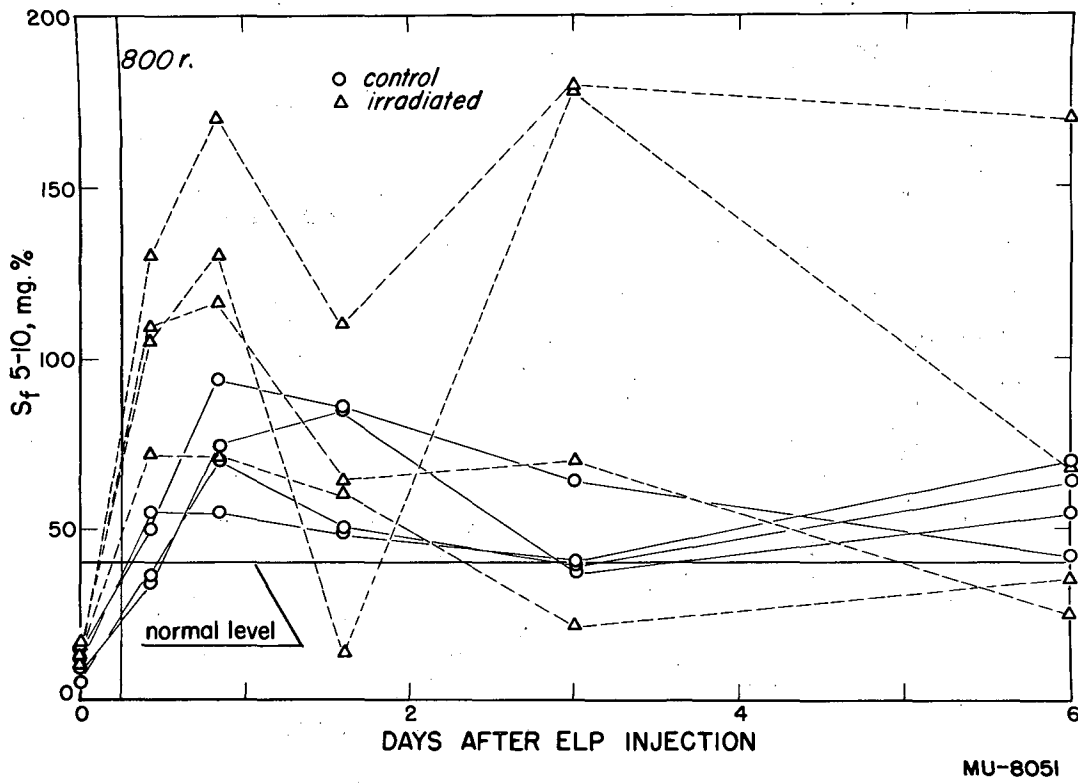


Fig. 3 Concentrations of serum lipoprotein of the Sf5-10 class in irradiated and nonirradiated animals following the injection of egg lipoprotein.

spectrum at 30 hours postirradiation may show if there is an increased need for fat metabolism and also whether this need has been adequately met.

The egg lipoprotein itself represents a readily available source of lipoprotein which, when injected intravenously, seems to be handled in a manner similar to that for the native lipoproteins present in the serum.

The removal of egg lipoprotein from the blood may give a reliable index of the efficiency of the lipoprotein metabolism taking place in the animal, and this technique may be of value in the study of various lipid metabolic disorders.

SUMMARY

1. The metabolism of injected egg lipoprotein was studied by ultracentrifugal methods in the normal and x-irradiated rabbit.
2. The x-irradiated animals metabolized the egg lipoprotein as rapidly as the nonirradiated in the first four hours following irradiation.
3. The results indicate that there is no block produced in lipoprotein metabolism at the time of irradiation.
4. The hypothesis that the radiation-induced hyperlipoproteinemia is due to an increased fat mobilization is discussed.
5. Egg lipoprotein has been shown to represent a readily available source of injectable lipid.

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