Influence of Body Fat on Duration of Thiopental Anesthesia. (19609)

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Brodie *et al.*(1) have shown that fat tissue has a high affinity for thiopental. Theoretically the amount of fat in the body should therefore influence the course of thiopental anesthesia. DeBoer(2) found that semi-starvation prolonged the sleeping time of dogs under thiopental anesthesia. This study was undertaken to see whether an effect of body fat on thiopental anesthesia is demonstrable and of sufficient magnitude to be of practical importance.

Experimental procedure. A fat group (F) and a lean group (L) of albino rats were prepared over a period of 30 days from an originally homogeneous group of rats. The fat group received *ad lib.* a mixture of Purina Dog Chow, and lard (30%) supplemented with choline chloride (0.1%) and thiamine (.017%). The lean group was individually caged and fed daily, on an individual basis, the amount of Purina Dog Chow which would induce a progressive small weight loss. The average starting and final weights of Group F were, respectively, 175 g and 199.3 g. Average starting and final weights for Group L were, respectively, 188.6 g and 169.0 g. Both groups appeared active and healthy at all times. Thiopental (1.4% solution in isotonic saline) was injected into the tail vein; pentobarbital (2% solution in isotonic saline) was administered intraperitoneally. No rat received more than one dose of an anesthetic in a 48-hour period. The time from loss of righting reflex until regaining of righting reflex was taken as the duration of anesthesia. The amount of body fat was estimated on the shaved, eviscerated animal by the specific gravity method developed by Rathbun and Pace(3).

Results and conclusions. The "fat" group of animals were found to contain 5 g % more fat than the "lean" group (Table I). This presumably represents at least a doubling of the adipose fat, since much of the fat of the lean group must be represented by phospholipids, cholesterol, etc.

The duration of thiopental anesthesia was more than doubled in the lean rats compared to the fat rats. It seems fair to ascribe this to the observed difference in body fat since the duration of pentobarbital anesthesia was identical in both groups. The difference in thiopental anesthesia can scarcely be attributed to possible difference in liver function in the 2 groups since Shideman and Gould(4) found that the rat destroys thiopental at a rate of only 10% per hour.

The relative dosage of thiopental required by the fat and lean rats for a given period of anesthesia was estimated by dosage response curves (Fig. 1). It is seen that the dose for a given period of anesthesia was about 40% greater for the fat animals. This would be explained if the 5 g % extra fat of these animals took up 8 times as much thiopental as the rest of the body. Brodie *et al.*(1) found that the adipose fat of the dog will take up 6 to 10 times as much thiopental as other parts of the body.

On the basis of the present data it would seem worth exploring the possibility that thiopental anesthesia in man would be more predictable if the dosage were adjusted with ref-

TABLE I. Effect of Body Fat on Anesthesia with Thiopental and Pentobarbital.

	F Fat group	L Lean group	L–F	Probability
No. of animals	17	18		
Body fat, %	13.5 ± .8*	8.5 ± .5*	— 5 ± 1 *	<.001
Duration of anesthesia (min)				
Thiopental, 30 mg/kg	23.5 ± 1.8	52.6 ± 6.3	+29.1 ± 6.5	<.001
Pentobarbital, 25 mg/kg	26.7 ± 4.2	26.7 ± 4.3	0 ± 6	1

* ± stand. error.

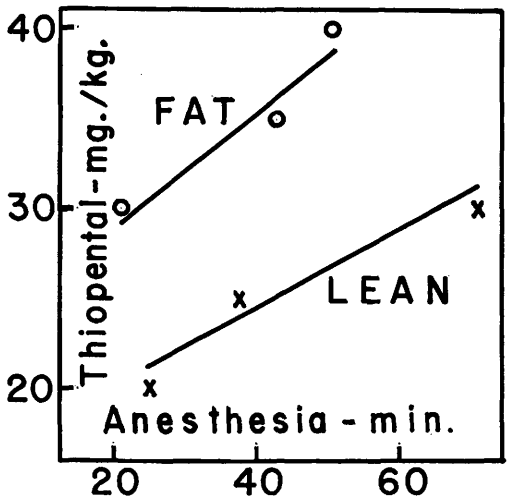

FIG. 1. Relationships between duration of anesthesia and thiopental dosage.

erence to the body fat.

Summary. A 5 g % decrease in body fat of the rat resulted in a 100% increase in length of thiopental anesthesia at a fixed thiopental dosage, or a 40% decrease in the amount of thiopental required for a given duration of anesthesia. In contrast the duration of pentobarbital anesthesia was unaffected by the amount of body fat.

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Casein and Factor 3 in Dietary Necrotic Liver Degeneration; Concentration of Factor 3 from Casein. (19610)

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It is a general experience that standard vit. E-free test diets which contain 10% or more of so-called "vit. free," *i.e.*, alcohol-extracted casein cannot be used for the production of dietary necrotic liver degeneration in rats. The deficiency does develop, however, when the animals are raised on rations containing only 4 to 6% of the "vit. free" casein(1,2). A purified, alkali-treated Hammarsten* casein ("casein VI"), on the other hand, had been used over a period of years at levels of 15 and even 30% for the production of dietary necrotic liver degeneration in experiments which led in 1944 to the detection of the protective activity of vit. E(3,4). It was stated at that time that "the most important condition for the development of the liver damage is to be seen in the nature of the casein used," and that "the occurrence of protective activity in completely dissimilar materials demonstrates that several different substances must exist which have an effect. . . ." (3). Evidence accumulated thereafter for a protective substance which was removed during the preparation of casein VI and which was different from cystine or from vit. E remained unpublished.† Recently, however, we reported the presence of such a factor in certain yeasts(6). The active principle, designated factor 3, prevents the development of dietary necrotic liver degeneration and is found in a wide variety of natural sources.‡

* "Hammarsten" casein (O. Hammarsten 1877, l. c. 7.) is prepared from freshly obtained casein by repeated acid precipitation from dilute alkaline solution and final drying by ethanol and ether.

† See discussion in: Liver Injury, Transactions of the Eighth Conference, Josiah Macy, Jr., Foundation, New York, 1949, p49.

‡ To be published separately.