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Effect of Feeding Fat on Duration of Thiopental Anesthesia. (20280)

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Studies of the mechanism of thiopental detoxication have led to the conclusion that its short duration of action is due to its localization in the fat depots of the body, rather than to its rapid destruction(1). This conclusion implies that the amount of body fat greatly influences the duration of thiopental anesthesia. Hermann and Wood(2) successfully demonstrated this by showing that a 5 g % decrease in body fat resulted in a 100% increase in the duration of thiopental anesthesia. As a result of these findings it was deemed of interest to determine the effect of dietary fat on the duration of thiopental anesthesia.

Methods. A homogeneous group of non-starved albino white rats was divided into two groups with an equal number of both sexes in each group. Two hours before the injection of thiopental each member of one group was fed 2 cc of corn oil by stomach tube while the other group received nothing, other than their normal diet. Then 30 mg/kg of sodium thiopental* (10 mg/cc in isotonic saline) was injected into a tail vein. The anesthesia time was determined by the duration of the loss of the righting reflex, that is the time taken for the animals to roll over onto their feet from the supine position. The rats were not injected oftener than once every 14 days to avoid an acute thiopental tolerance (3).

Results. Throughout this experiment considerable difficulty was encountered because of a large day to day variation in anesthesia time, which cannot be satisfactorily explained. On some days a mean sleeping time of 76 minutes for the control group and 25 minutes for the oil group has been obtained; while on other days, using the same dose, a mean sleeping time of 22 minutes for the control group was obtained as opposed to 11 minutes for the oil group. The results tabulated in Table I Exp. A and B demonstrate this wide day-to-day variation, but also show that in spite of this daily variation there consistently remained a significant difference between the sleeping time of the control and the oil fed group. The data presented in Table I, Exp. C were obtained by processing the entire lot of 34 rats in one day to eliminate the day-to-day variation. It can be readily observed that a highly significant decrease in anesthesia time was induced by the oral administration of oil.

Discussion. A review of the work of Brodie *et al.*(4) suggests a possible explanation for this difference. Brodie has shown that following the administration of thiopental a shift in concentration occurs until an equilibrium is reached at which time the body fat contains about 15 times the concentration of thiopental of the plasma and other body tissues. Under the conditions of this experiment a chylomicronemia and hyperlipemia might be expected to occur following the ingestion of the oil. When the thiopental is injected it may be taken up by the chylomicrons, thus reducing its effective blood concentration and therefore decreasing its anesthetic action. This might be visualized as a partition of the thiopental between the lipid and aqueous phases of the body. The additional lipid supplied by the ingestion of the oil causing a reduction in the thiopental in the aqueous phase.

* Pentothal (Abbott).

TABLE I. Effect of Feeding Corn Oil on Duration of Pentothal Anesthesia in Rats on 3 Different Days.

Exp.		No. animals	Mean anesthesia time	Stand. dev.	Probability Student t test
A	Oil	9	25	6.2	
	Control	9	76	38.9	
	Mean diff.		51		<.01
B	Oil	7	11	3.5	
	Control	10	22	6.1	
	Mean diff.		11		<.001
C	Oil	17	13	2.85	
	Control	17	30	15.6	
	Mean diff.		17		<.001

Perhaps the fact that the standard deviation of the oil fed group was lower than that for the control group is also of some significance. It was noticed throughout the experiment that the control group was much more erratic than the oil group. The wide variations in the sleeping time of the control group could be attributed to small variations in the percentage of body fat, which Hermann and Wood(2) demonstrated to have a marked effect on sleeping time. The relative uniformity of the sleeping time of the oil fed group could be attributed to the hyperlipemia which may cause a much greater shift in the thiopental equilibrium to the lipid phase so that small variations in body fat do not result in as marked variations in sleeping time.

Summary. 1. It has been shown in rats that ingestion of oil preliminary to thiopental anesthesia will decrease the anesthesia time by about 50%. 2. A suggested explanation for this action is the production of a hyperlipemia by the oil, with the resultant uptake of the circulating thiopental by the chylomicrons.

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Inhibition of Lysozyme by Heparin.* (20281)

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The function of lysozyme in various mammalian fluids and cells has never been known. The presence of the enzyme has been demonstrated by its lytic effect on various microorganisms(1-3), but a natural substrate in the tissues has not been found(4). Meyer(4) has emphasized certain characteristics which are common to lysozyme and hyaluronidase. Hyaluronidase is inhibited by heparin(5,6), and the inhibition has been assumed but not demonstrated to be competitive because of the chemical similarity of the inhibitor and hyaluronic acid. Similarly, inhibition of lysozyme by heparin and related polysulfonates has been shown(7), again without investigation of the nature of the inhibition. The present study establishes the fact that the

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