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Effect of Diphenylhydantoin Administration upon Concentration of Liver and Aortic Lipids.* (27650)

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Intraperitoneal administration of large amounts of sodium bi-phenyl hydantoinate (Dilantin) to rats has been shown to alter profoundly the chemical composition of the connective tissue (dermis) of these animals (1). Recently(2) it was shown that Dilantin administration resulted in a significant decrease in dermal concentrations of both neutral glycerides and phospholipid. The present study was to explore whether similar effects upon lipid concentration would be observed in other tissues such as liver and particularly the aorta.

Methods. A group of 22 male Wistar rats weighing 300-360 g each were divided into 3 groups: one group of 8 animals was kept as normal controls; another group of 6 animals was subjected to 12 daily intraperitoneal injections of 1 ml of isotonic saline to serve as injected controls; and the remaining 8 animals received 12 daily intraperitoneal injections of 1 ml of saline suspension of 25 mg of Dilantin. Following an overnight fast, all animals were sacrificed by chloroform. These animals had been fed and watered *ad lib.* on Purina laboratory chow. Approximately 2.5 g of liver tissue was removed from each animal and lipids extracted with chloroform-methanol. The thoracic aortas of each rat were removed and cleaned of adherent tissues with the aid of a magnifying glass. These aortas were randomly pooled into 2 equal collections each representing half of the animals in each of the 3 experimental groups. These pools of aortic tissue were similarly extracted with chloroform-methanol and cholesterol, phospholipids and neutral glycerides determined. Methods for lipid extraction and chemical analyses have been described(2). The results were expressed in mg of lipid per g of fresh wet tissue.

Results and discussion. The effect of Dilantin administration and control injection upon mean and standard deviations of the lipid content of liver tissue are compared in Table I with the results obtained from normal intact animals. Although intraperitoneal injections of isotonic saline resulted in a significant increase in the neutral glyceride concentration of the liver tisue, Dilantin administration resulted in a significant decrease of this lipid in the liver in both normal and control animals.

Similar data for lipid concentration of the aorta from normal, control and Dilantin treated animals, presented in Table II, indicates that the amount of neutral glycerides in both pools of aortic tissue from the Dilantin treated animals differed by more than 3 standard deviations (3×2.5) from the mean concentrations of both pools of aorta obtained from normal and control groups of animals.

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TABLE I. Lipid Analyses (mg/g) of Liver Samples from Groups of Normal, Injected Control and Dilantin Treated Rats.

	No. animals	Total cholesterol	Phospholipids	Neutral glycerides
Normal	6	1.91 ± .15	27.3 ± 1.31	3.47 ± .73
Control	6	2.01 ± .14	26.4 ± 3.09	7.08 ± .58*
Dilantin	6	1.85 ± .14	24.4 ± .92*	1.23 ± .24†

* Significantly different from normal value.
† Significantly different from both control and normal values ($p < .01$).

These results suggest that the effect of Dilantin upon tissue lipids was primarily confined to the glycerol containing lipids. A similar effect of this drug has also been previously described(2) for rat skin. The mechanism through which Dilantin affects the lipid content of such different tissues as skin, liver and aorta remains obscure. However, it would appear to be of great interest to explore the possible effects of Dilantin upon atherosclerosis.

TABLE II. Lipid Analyses of 2 Pools of Rat Aorta (mg/g) in Normal, Injected Control and Dilantin Treated Animals.

		Total cholesterol	Phospho-lipids	Neutral glycerides
Normal	a)	.95	7.2	13.2
	b)	.78	6.2	9.5
Control	a)	1.41	8.0	16.5
	b)	1.33	8.4	12.2
Dilantin	a)	1.07	6.3	2.69*
	b)	1.21	5.9	2.85*

* Differ by more than 3 standard deviations from the mean of normal plus control values (12.8 ± 2.5).

Summary. Twelve daily intraperitoneal injections of one ml suspensions of 25 mg of sodium bi-phenyl hydantoinate (Dilantin) in isotonic saline to rats resulted in a significant decrease in tissue concentration of neutral glycerides of both the aorta and liver when compared with the tissue from both normal and saline injected control animals.

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Effect of Dimethyl Sulfoxide and Glycerol on Cation Content of Freeze-Thawed Cardiac Muscle.* (27651)

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Dimethyl sulfoxide (DMS) has been reported to be effective in protecting against cellular damage and death in freeze-thawed tissues, including isolated hearts(1-7). Since the preservation of mammalian tissue by low temperatures and freezing is in part limited by the deleterious effects of intracellular dehydration and subsequent concentration of intracellular ions(8), the protective effect of DMS on heart might be related to its ability to prevent or modify this critical change of water and salt concentration. Experiments were therefore performed on isolated cardiac tissue preparations, frozen and thawed with and without DMS. Analysis of total tissue potassium (K) and sodium (Na) was made and results compared to freshly dissected tissue. For comparison, glycerol treated tissue was also studied since this substance is known to be an effective protective agent in the freeze-preservation of a variety of cells and tissues(8).

Methods. Hearts from white New Zealand rabbits were used. The animals were sacrificed by a blow on the head and the heart

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