Studies on Adrenal Cortex of Pantothenic Acid-Deficient Rat. IV. Adrenal and Serum Cholesterol Levels.* (19489)

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Previous communications from this laboratory(1-4) have dealt with the functional and morphological aspects of the adrenal cortex of the pantothenic acid-deficient animal. The results of these studies have been interpreted as indicative of an adrenal insufficiency in these animals, a conclusion which in certain respects supports the findings of other workers(5,6). In a review of the problem, Cowgill *et al.*(3) discussed certain of the theoretical aspects of the role of this vitamin in adrenal metabolism. One of the possibilities entertained was that coenzyme A (the functional form of pantothenic acid in metabolism) participates in the utilization of acetate in the synthesis of cholesterol, which is recognized as the parent compound of the adrenal corticoids (7,8). It was thus decided to measure the level of cholesterol in the adrenals of such animals. Serum cholesterol and total extractable liver lipids were also determined.

Methods. The animals, diets and conditions were the same as described previously(1). The deficient animals as here referred to indicate those that are placed on the pantothenic acid deficient diet at weaning and allowed to subsist thereon for a period of 5-6 weeks. The theoretical advantages of using an animal of this age have been discussed previously(3). The food intake of control rats (with pantothenic acid) was restricted to approximately that of the deficient animals. Total cholesterol was determined on the adrenals and on serum (from tail blood) by the Sperry-Schoenheimer method(9). Total extractable lipids on the livers were determined by the A.O.A.C. method(10). Since the adrenal cholesterol is known to change in response to "alarming stimuli"(7), animals for adrenal cholesterol determinations were in the "resting state"—*i.e.* care was taken to avoid stressing either group prior to sacrificing them for adrenal cholesterol analysis.

TABLE I. Cholesterol Levels of Adrenal Glands and of Serum of Pantothenic Acid-Deficient and Control Rats.

Group	No. animals	Total cholesterol	
		Serum, mg %	Adrenal, g %
Control	7	92 ± 4	4.09 ± .11
Deficient	10	104 ± 9	1.36 ± .21

All data expressed as mean with S.E.

Differences between the 2 groups with respect to adrenal cholesterol are statistically significant ($p = < .01$). Differences between the levels of serum cholesterol are not statistically significant ($p = > .1$).

Results. Data for the total adrenal cholesterol of 10 deficient and 7 pair-fed controls are shown in Table I. These data show that the deficient animals exhibit a marked depression of adrenal cholesterol, while the control animals are within the accepted range of normal. These findings support our previous demonstration of a lowered adrenal cholesterol by histochemical technics(4). The serum cholesterols of the two groups (Table I), however, do not differ appreciably. Earlier, Scudi and Hamlin(11) had reported that the serum cholesterol of the pantothenic acid deficient dog was reduced. This finding, however, is in all probability related to the "fatty liver" which develops in this species on a pantothenate deficient regimen(11,12). Inanition is also of common occurrence in such animals and this factor undoubtedly exerted some effect on the blood cholesterol. In the rat, under the circumstances of the present experiment, inanition(1) was not a serious problem and no significant differences in total liver lipids was noted between the deficient and control rats. All total lipid liver values were in the normal range of 3-5%.

Discussion. The finding of lowered adrenal cholesterol levels in rats deficient in pantothenic acid may be the result of either: a)

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reduction in synthesis or b) increase in utilization of this steroid. In normal animals, such a finding is usually indicative of recent adrenal cortical stimulation(7). However, in the face of previous evidence pointing to the presence of an adrenal insufficiency of the C-11 oxysteroid hormone in the pantothenate deficient rat(1-4,5,6) it is reasonable to suggest that in these animals the reductions are due to decreased synthesis. In view of recent work indicating that coenzyme A plays a prominent role in acetate metabolism and the finding that acetate can be converted to cholesterol by the isolated adrenal gland(13,14) as well as to the complete hormone(15), this is an especially interesting theory.

Conn *et al.*(16) have adduced indirect evidence that the adrenal cholesterol may arise in part from the serum cholesterol. This finding is interesting in view of the results here presented in which the levels of serum cholesterol are not appreciably reduced. At present, we cannot interpret these conflicting results.

Summary. The 5-6-week pantothenic acid deficient rat shows a marked reduction in the total cholesterol content of the adrenal glands in the "resting state". The serum cholesterols, however, were normal. These animals do not develop fatty livers. It is suggested that in view of previous functional studies on the adrenal cortices of such animals, that the reduction in the cholesterol content of the adrenal glands may represent a decreased synthesis rather than an increased utilization of this steroid for further conversion to hormone. It may be that coenzyme A, the functional form of pantothenic acid in metabolism is a necessary part of the enzymatic complement of the adrenal cortex which synthesizes cholesterol.

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