

INCORPORATION OF C¹⁴-ACETATE IN CHOLESTEROL AND FATTY ACIDS OF THE LIVER OF ADRENALECTOMIZED RATS DURING IRRADIATION

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The influence of adrenalectomy on the process of cholesterol formation in the liver has been studied incompletely, and the results obtained are conflicting. Some authors [10,11] point out that adrenalectomy inhibits the synthesis of cholesterol and fatty acids, while others [13] report the stimulation of cholesterol synthesis after adrenalectomy. So far as the influence of irradiation on the rate of cholesterol synthesis in adrenalectomized animals is concerned, the only data given in the literature indicate that this operation does not prevent the increased rate of synthesis of cholesterol brought about by irradiation [6].

In previous investigations [3,4] we studied the role of hormonal factors in the reaction of acceleration of cholesterol synthesis in response to irradiation. The present study is a continuation of those undertaken previously and its purpose was to investigate the influence of adrenalectomy and irradiation on the incorporation of C¹⁴-acetate into cholesterol and fatty acids.

METHOD

The work was carried out on mongrel albino male rats weighing 130-160 g. The animals were used in the experiments on the 7th-8th day after bilateral adrenalectomy. During the postoperative period they received 0.85% sodium chloride solution by way of diet. Whole-body irradiation of the rats was provided by a type RUM-11 apparatus in standard conditions (180 kV, 15 mA, filters 0.5 mm Cu + 1.0 mm Al). The dose of irradiation was 800 R.

The animals were subdivided into 4 groups: group 1) control rats, group 2) adrenalectomized rats, group 3) adrenalectomized and then irradiated rats, group 4) irradiated intact rats. The animals of group 3 were divided into two subgroups: the rats of subgroup 3A continued to receive physiological saline after irradiation, while the rats of subgroup 3B received water by way of diet after irradiation.

Twenty hours after irradiation, the animals of all groups received a subcutaneous injection of neutralized acetic acid, labeled in its carboxyl group, in a dose of 30,000 pulses/min/mg. Four hours later the animals were sacrificed. The method of extraction of cholesterol and fatty acids from the liver, and the determination of their specific activity were described fully in a previous paper [2].

RESULTS

The data in Table 1 show that the cholesterol concentration in all the groups of adrenalectomized animals was higher than its normal level. The difference was statistically significant. In the rats of group 2 the incorporation of C¹⁴-acetate into cholesterol fell by 44% below the control level. This change was statistically significant ($P < 0.02$). Irradiation increased the incorporation of label into cholesterol in the rats of subgroup 3A. In the rats of subgroup 3B, no acceleration of cholesterol synthesis over the control level was observed. Comparison of the animals of this group with those of group 2 revealed a very slight acceleration of synthesis ($P < 0.05$). Irradiation of the intact rats was accompanied, as a rule, by a marked acceleration of cholesterol synthesis.

TABLE 1. Effect of Irradiation on Incorporation of C¹⁴-Acetate into Cholesterol in Liver of Adrenalectomized Rats

Group	No. of animals	Cholesterol			
		Concentration (in mg%)		Specific activity (pulses/min/mg)	
		<i>M</i> ± <i>m</i>	<i>P</i>	<i>M</i> ± <i>m</i>	<i>P</i>
1st	24	300 ± 13,4	—	75 ± 7,4	—
2nd	11	381 ± 9,8	<0,001	42 ± 8,5	<0,02
3rd (subgroup A)	11	340 ± 10,6	<0,05	255 ± 57,8	<0,02
3rd (subgroup B)	15	348 ± 10,1	<0,02	88 ± 17,8	<0,5
4th	17	293 ± 10,2	<0,5	246 ± 33,5	<0,001

TABLE 2. Specific Activity of Fatty Acids from Liver of Adrenalectomized Irradiated Rats.

Group	Fatty acids			
	Concentration (in g%)		Specific activity (pulses/min/mg)	
	<i>M</i> ± <i>m</i>	<i>P</i>	<i>M</i> ± <i>m</i>	<i>P</i>
1st . . .	2,5 ± 0,23	—	10 ± 0,55	—
2nd . .	2,4 ± 0,13	0,5	8 ± 0,68	<0,05
3rd (subgroup A)	2,4 ± 0,05	0,5	15 ± 1,93	<0,05
3rd (subgroup B)	2,2 ± 0,10	0,5	9 ± 1,11	0,5
4th . .	2,5 ± 0,15	—	20 ± 2,64	<0,01

The results in Table 2 show that in the adrenalectomized animals the specific activity of the fatty acids was lower than in the controls. Irradiation accelerated the synthesis of fatty acids in the animals of subgroup 3A and group 4. These changes were statistically significant. The concentration of fatty acids remained at the control level after adrenalectomy and irradiation.

The fall in the rate of cholesterol synthesis after adrenalectomy could be due to several factors. One of these is a decrease in the oxygen consumption [7,8] and depression of the activity of the cytochrome system in the liver [12]. An inadequate supply of oxygen to the tissues has an inhibitory action on cholesterol synthesis, which requires molecular oxygen in the final stages. Another factor may be the absence of adrenal cortical hormones. It has been found that cortisone [5,9] and desoxycorticosterone [13] stimulate cholesterol synthesis.

A marked acceleration of the synthesis of cholesterol and fatty acids was observed in the rats of group 4, 24 h after irradiation. At this time, according to results obtained in our laboratory [1], the concentration of corticosterone in the blood flowing from the adrenals of irradiated rats is increased. In experiments on hypophysectomized animals we showed [4] that cholesterol synthesis in these animals is not accelerated in response to irradiation. In contrast to this, adrenalectomy has no appreciable effect on the acceleration of the synthesis of cholesterol and fatty acids in the liver after irradiation.

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