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SHORT COMMUNICATIONS

The incorporation of ^{14}C-acetate into cholesterol in rats exposed to carbon disulphide

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PROLONGED exposure to carbon disulphide results in elevated levels of lipids (cholesterol, phospholipids, triglycerides, B-lipoproteides) in the serum.[1–10] The mechanism by which these changes occur is not known.

The aim of this investigation was to investigate whether chronic exposure to carbon disulphide results in increased rate of synthesis of lipids in the liver. Cholesterol has been chosen as a model compound because its metabolism is best known and disturbances in its levels under the influence of exposure to carbon disulphide were most pronounced and frequently described.

This investigation is concerned with the measurement of the rate of incorporation of ^{14}C-acetate into cholesterol of the liver, *in vivo*.

The experiment was performed on white female rats of the Wistar strain, mean body weight 185 g, fed standard LSM* diet. The animals were exposed to vapours of carbon disulphide in a chamber at concentration of 1·5 mg/l. for 5 hr daily. Group I was exposed 6 days a week over the period of 6 months. Group II was exposed for only few subsequent days. Appropriate controls were used for both experiments separately.

After the preselected period of exposure rats were starved over 24 hr and thereafter were given a single intravenous dose of sodium acetate—1-^{14}C, 25μc per 100 g of body weight, specific activity 0·25 μc/mg, in saline. Three hours later the animals were sacrificed and the incorporation of ^{14}C-acetate into cholesterol was assessed in the liver.

The total ^{14}C cholesterol in liver was determined after Swell.[11] The total cholesterol fractions of each liver extract were precipitated as the digitonides and washed. The digitonide ^{14}C activity was measured in a gas flow counter with window at a constant thickness plating of the digitonide. The error of the methods including sample preparation and counting was $\pm$ 7 per cent.

The total cholesterol of liver was determined using the method of Sperry and Webb.[12]

Table 1 shows that rats exposed to carbon disulphide for 6 months differed from the controls in their ability to incorporate the ^{14}C-acetate into cholesterol. In order to obtain approximate data how quickly this change appears under the influence of CS_2 the second experimental group has been exposed for 3 days only. In this case too a tendency for increase of the rate of incorporation ^{14}C-acetate into cholesterol was observed. However, due to some difference in the total cholesterol level in the experimental group and in the control, significant change was found only with respect to the total ^{14}C-cholesterol content of the whole organ.

The reported results point to the increased rate of ^{14}C-acetate incorporation into cholesterol in animals after long-term exposure to carbon disulphide. An alternative explanation of the phenomena described, namely, that decreased rate of decomposition of cholesterol took place is less probable: the latter process is relatively slow (half-life in liver approximately 4 days[13–15]) and therefore could not have influenced the results obtained shortly after the injection of ^{14}C-acetate.

From the toxicological point of view it is essential to know whether the changes observed are dependent directly upon presence of carbon disulphide and of its metabolites in the body or result from permanently altered metabolic processes. Comparing the results obtained in experiments I and II (Table 1) the second alternative seems to be more likely. One may not exclude entirely a direct influence of carbon disulphide and its metabolites on the rate of cholesterol synthesis, it seems, however, obvious that the changes became deeper and more evident with prolonged duration of exposure to carbon disulphide. The existing data indicate that neither this compound nor its metabolites are

* Standard diet for rats and mice; manufacturer: Wytwórnia Pasz, Łowicz.

TABLE 1. THE LEVEL OF ^{14}C-CHOLESTEROL AND OF THE TOTAL CHOLESTEROL IN THE LIVER OF RATS EXPOSED TO CS_2

Group of animals	Total cholesterol	Labelled cholesterol	
	Wet tissue (mg/g)	cpm/1 mg of total cholesterol	cpm/whole organ
Experimental group I (6 months)	2·0 ± 0·15	443* ± 115	6·393* ± 1·71†
Control I	2·07 ± 0·055	197 ± 68	2·966 ± 1·243
Experimental group III (3 days)	2·2† ± 0·093	226 ± 37	3·685† ± 607
Control	2·06 ± 0·09	195 ± 12	2·889 ± 329

Mean values ± S.D. are given in groups of 5 rats each. Results significantly different from the control indicated:

* $P \leqslant 0{\cdot}01$.

† $P < 0{\cdot}05$.

subject to substantial accumulation in the body in course of chronic exposure.[16–18] Thus, the mechanism of increased incorporation of ^{14}C-acetate into cholesterol seems rather to involve a substantial permanent or semi-permanent deviation of cholesterol metabolism.

As liver occupies a central position in the metabolism of cholesterol in the body, the increased synthesis in this organ may contribute to explanation of the elevated level of cholesterol in serum, observed in chronic intoxication with carbon disulphide.

Department of Biochemistry,
Institute of Occupational Medicine,
Łódź, Teresy 8, Poland

T. WROŃSKA-NOFER

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