vivo is unknown, the effect observed cannot be regarded as incontrovertible evidence of a role of $^1O_2$ in the mechanism of oxygen toxicty.

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EFFECT OF AN ATHEROGENIC DIET ON AGE DIFFERENCES IN CHOLESTEROL BIOSYNTHESIS IN THE RAT LIVER

P. P. Chayalo

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After intraperitoneal injection of radioactive sodium acetate into rats of two age groups (6-8 and 28-32 months) the dynamics of cholesterol biosynthesis in the liver was observed to be slower in the older animals. The specific liver cholesterol activity of the older rats was lower at the maximum of uptake of the label than in the younger rats. An atherogenic diet for 20 days (0.25 g cholesterol/100 g body weight) led to an increase in the total cholesterol content but to inhibition of its biosynthesis in the liver, and this effect was most marked in the younger rats. Continued administration of cholesterol depressed its biosynthesis still more, especially in the older animals.

KEY WORDS: *liver*; *cholesterol biosynthesis*; *age*.

The metabolism of cholesterol and its esters is intimately connected with the metabolism of certain hormones and vitamins [5]. The role of cholesterol in pathology is determined by

Laboratory of Pathophysiology, Institute of Gerontology, Academy of Medical Sciences of the USSR, Kiev.

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TABLE 1. SA of Cholesterol (counts/min/mg) from Liver of Normal Rats of Different Ages (M ± m)

Group of rats	Duration of exposure, min					
	15	30	45	60	90	120
6—8 months	326±56 (7)	457±42 (8)	762±56 (10)	957±58 (11)	657±85 (7)	372±32 (7)
28—32 months	259±40	447±48 (7)	541±45 (9)	787±46 (9)	691±65	459±74 (7)
P			<0,01	<0,05		

Note. Here and in Table 2, number of animals shown in parentheses.

TABLE 2. Total Cholesterol Content in Blood and Liver and Its SA in Liver of Rats of Different Ages on Normal and High-Cholesterol Diets (M ± m)

Group of rats	Cholesterol content		
	in blood, mg %	in liver, mg/g wet weight of tissue	SA of liver cholesterol, counts/min/mg
6—8 months			
Control	105,4±8,6 (11)	3,68±0,25 (11)	957±58 (11)
Receiving cholesterol			
20 days	112,6±9,7 (9)	7,10±0,55 (9)	538±87 (9)
40 days	116,6±9,8 (9)	7,36±0,62 (9)	496±73 (9)
28—32 months			
Control	89,7±6,5 (10)	4,12±0,44 (10)	787±46 (9)
Receiving cholesterol			
20 days	104,3±11,5 (9)	7,86±0,82 (8)	568±75 (9)
40 days	112,5±9,8 (7)	8,78±1,03 (7)	312±38 (7)

the part which it plays in the development of such widespread diseases as atherosclerosis and cholelithiasis. The cholesterol level in the body is regulated mainly by the liver, where most of it is synthesized. Esterification of cholesterol also takes place in the liver [7]. Data on age differences in cholesterol metabolism [4, 9, 10] have been obtained by different methods and the results are not strictly comparable. Some workers have simply stated the weight of the experimental animals without indicating their precise age. At the same time, there is convincing evidence that age leaves a definite imprint on the character and degree of disturbances of lipid metabolism and the severity of experimental atherosclerotic changes [1].

Cholesterol synthesis was investigated in animals of different ages kept on a normal or a high-cholesterol diet.

EXPERIMENTAL METHOD

Experiments were carried out on 129 male albino rats of two age groups: 6-8 months (young) and 28-32 months (old). The cholesterol precursor radioactive sodium acetate was injected intraperitoneally in a dose of 10 μCi/100 g body weight. Lipids were extracted from the liver [6]; cholesterol was precipitated by digitonin. Radioactivity was measured in a "Protoka" gas-flow counter. The specific activity (SA) of cholesterol was expressed in counts/min/mg. A correction was introduced for background activity and self-absorption [2]. The atherogenic loading consisted of a solution of cholesterol in sunflower oil, which was given in a dose of 0.25 g cholesterol/100 g body weight for 20 and 40 days. Cholesterol was determined quantitatively in the tissues and blood serum [8] and the SA of cholesterol from the liver was recorded 60 min after injection of the precursor [8]. The results were analyzed by the method of indirect differences [3].

EXPERIMENTAL RESULTS

Data on cholesterol biosynthesis in the liver of control rats of different ages are given in Table 1. SA of cholesterol extracted from the liver was determined 15-120 min after injection of the isotope. The dynamics of incorporation of the label into cholesterol differed depending on the animals' age. In the old animals the maximum of label incorporation was spread over a somewhat longer period of time, and the values after 60 and 90 min did not differ significantly. In the young rats, however, the uptake of label into cholesterol at the 90th minute of the experiment was significantly smaller ($P < 0.02$) than at the 60th minute. The maximal value of SA for the liver cholesterol of the old rats was significantly lower than

for the young animals. In the young rats elimination of the label from cholesterol also took place faster, indicating a more rapid turnover of this compound in the liver of the young rats than of the old.

As Table 2 shows, administration of cholesterol for 20 days to the rats considerably increased the total liver cholesterol (about equally in the animals of the two age groups). The serum cholesterol concentration was almost unchanged in the animals of the two groups. Cholesterol biosynthesis in the liver was sharply inhibited. After 20 days of a high-cholesterol diet this inhibition was greatest in the young rats, but after 40 days it was greatest in the old rats. The degree of this inhibition in the animals of both age groups depended on the duration of cholesterol feeding.

Depression of biosynthesis of endogenous cholesterol during administration of exogenous cholesterol has been discussed in the literature [7]. The accumulation of cholesterol in the tissues inhibits, in particular, the conversion of β-hydroxy-β-methylglutaryl-CoA into mevalonic acid. In the light of these findings, the age differences in the character of cholesterol biosynthesis in rats receiving a high-cholesterol diet can be attributed to differences in the total cholesterol content in the liver of rats of different ages.

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