CHOLESTEROL METABOLISM IN EXPERIMENTAL LEAD POISONING

G. S. Konikova

Clinico-Biochemical Laboratory (Director, Candidate Med. Sci. A. V. Shcheglova), Clinical Department (Director, Professor M. A. Kovnatskii), Leningrad Research Institute of Work Hygiene and Occupational Diseases (Director, Professor Z. E. Grigor'ev)
(Presented by Active Member AMN SSSR V. M. Karasik)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 54, No. 11, pp. 65-67, November, 1962
Original article submitted December 18, 1961

According to clinical observations and experimental findings, lead poisoning may give rise to the development of atherosclerosis [2] and may affect the cholesterol metabolism [5, 6]. It has been shown, in particular, that lead poisoning in experimental atherosclerosis increases hypercholesteremia [6].

In a previous investigation [3] we found an increased total cholesterol, uncombined cholesterol and cholesterol loosely combined with protein in the blood serum of persons exposed to the action of lead, i.e., an increase in the concentration of the least stable fractions readily undergoing deposition in the walls of the blood vessels. Several writers [1, 4] consider that an increased concentration of uncombined cholesterol or of cholesterol loosely combined with protein in the blood is one of the causes of lipoidosis of the blood vessels.

The present research was devoted to the study of the effect of lead poisoning on the concentration of protein-bound cholesterol and on the strength of the bond between the cholesterol and protein.

EXPERIMENTAL METHOD

Blood for the investigation was taken from rabbits in which the effect of lead poisoning on the development of atherosclerosis had been studied (L. K. Cherednichenko, G. N. Kuz'minskaya). In their experiments, these workers had fed the rabbits on pure cholesterol in a dose of 0.6 g daily for $3^1/_2$ months; lead poisoning was produced by enteral administration of a 10% solution of lead acetate in a dose of 0.026 g/kg body weight daily for 1 month, and after an interval of 3 days, for a further 15 days [6].

We investigated the blood of 10 control (group 1) and 16 experimental rabbits. Of the latter, 5 animals received cholesterol, 6 received cholesterol and lead acetate, and 5 received lead acetate alone. The total cholesterol and the cholesterol combined with protein were determined in the blood serum of all the rabbits, and the stability of the bond between the protein and cholesterol was assessed.

The total cholesterol was determined by Bloor's method; the protein-bound cholesterol and the strength of the bond between them by the method of Okunev and Kruglova [3], as modified by ourselves. All the experimental rabbits were investigated three times, and 6 of them four times. The rabbits receiving cholesterol alone were investigated after 23 (group 2), 48 (group 3), and 90 (group 4) doses of cholesterol; in addition, two rabbits were investigated after 150 doses of cholesterol. The rabbits receiving cholesterol and lead were studied after 23 doses of cholesterol alone, after 48 doses of cholesterol of which 25 were combined with lead (group 5) and, finally, after 90 doses of cholesterol of which 37 were combined with lead (group 6); two rabbits were also investigated after 150 doses of cholesterol, 70 of which were combined with lead. The rabbits receiving lead without cholesterol were studied before administration, and also after 25 and 37 doses of lead; 2 rabbits were also investigated after 70 doses of lead.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the total cholesterol concentration in the rabbits receiving cholesterol without lead increased several-fold after 23 doses, and rose thereafter with the number of doses. After 23, and actually after 48 doses, in 3 of 5 rabbits the whole of the cholesterol was protein-bound, and only after 90 doses was the mean concentration of cholesterol not combined with protein greater than in the control group by a statistically significant degree. The combination of nearly all the cholesterol with protein in the first stages of administration of cholesterol was possibly a compensatory reaction, the mechanism of which cannot yet be explained.

In the rabbits receiving cholesterol in conjunction with lead, after 48 doses of cholesterol of which 25 were combined with lead, the mean concentration of cholesterol not combined with protein rose several-fold by comparison with the control group, and increased with the number of doses. Nearly all the cholesterol was loosely combined with protein.

After 48 doses of cholesterol of which 25 were combined with lead, the concentration of total and loosely combined cholesterol and of cholesterol not combined with protein was higher than in the rabbits receiving the same amount of cholesterol without lead. However, the difference between the concentrations of total and loosely combined cholesterol in these two groups was not significant. After 90 doses of cholesterol of which 37 were combined

TABLE 1. Concentration of Total Cholesterol and Its Fractions in the Blood Serum of Rabbits Receiving Cholesterol with or without Lead

Group of rabbits	Experimental conditions	No. of rabbits	Cholesterol (in mg%)				
			total composition	protein-bound			not combined with protein
				total	loosely combined	firmly combined	
1	Control	10	32.4 ± 2.6	24.7	22.0 ± 2.6	3.2	7.7 ± 1.3
2	After 23 doses of cholesterol	5	231 ± 43	223	218 ± 44		
3	After 48 doses of cholesterol	5	380 ± 87	362	359 ± 88		
4	After 90 doses of cholesterol	5	470 ± 92	436	428 ± 86		34.6 ± 11
5	After 48 doses of cholesterol, 25 of which were combined with lead	6	428 ± 63	390	381 ± 58		38 ± 11
6	After 90 doses of cholesterol 37 of which were combined with lead	6	798 ± 75	729	720 ± 76		69 ± 4.6
	P between groups 5 and 3	In %	< 50		< 50		< 5
	P between groups 6 and 4		< 5		< 5		

TABLE 2. Mean Concentration of Total Cholesterol and Its Fractions in the Blood Serum of Rabbits Receiving Lead*

Experimental conditions	No. of rabbits	Cholesterol (in mg%)				
		total composition	protein-bound			not combined with protein
			total	loosely combined	firmly combined	
Before administration of lead	5	25.5 ± 3.6	21.7	18.7 ± 5.7	3	3.9 ± 1.3
After 25 doses of lead	5	33.2 ± 11	27.9	25.3 ± 2.2		5.3 ± 2.4
After 37 doses of lead	5	31.9 ± 3.3	26.4	26.4 ± 3	0	5.4 ± 1.3

* The only arithmetical mean to be not significant. After 37 doses of lead it became significant.

with lead, the difference between all the indices of cholesterol metabolism in this group and in the group receiving the same amount of cholesterol without lead was much greater and was statistically significant. After 150 doses of which 70 were combined with lead, the increase in the total and loosely combined cholesterol and the cholesterol not combined with protein was more marked in the rabbits receiving cholesterol with lead.

The results of the investigation of the rabbits receiving lead without cholesterol are given in Table 2. A noteworthy feature is the complete disappearance of the cholesterol firmly combined with protein after administration of lead alone. After 37 doses of lead all the cholesterol was loosely combined with protein. The concentration of total cholesterol and the cholesterol not combined with protein showed a slight tendency towards an increase by comparison with the initial values, but the difference was not significant.

In the two rabbits which we also investigated after 70 doses of lead, the cholesterol firmly combined with protein disappeared completely, and the total cholesterol concentration rose slightly. The cholesterol not combined with protein rose considerably in one animal, but remained essentially unchanged in the other.

Hence, in experimental lead poisoning there is an obvious disturbance of the cholesterol metabolism. In rabbits treated with lead alone, this disturbance takes the form of a decrease in the strength of the bond between cholesterol and protein, and a slight tendency for the concentration of total cholesterol and of cholesterol not combined with protein to increase. In rabbits receiving cholesterol together with lead acetate, the concentrations of total cholesterol, cholesterol loosely combined with protein, and cholesterol not combined with protein were significantly higher than in the rabbits receiving the same dose of cholesterol without lead. It may be concluded from these results that the first stage of the disturbance of the cholesterol metabolism during the action of lead is a decrease in the stability of the bond by which cholesterol is combined with protein.

SUMMARY

Disturbance of cholesterol metabolism occurred in experimental lead intoxication. In rabbits subjected to the action of lead alone this derangement was manifested in reduced stability of the cholesterol-protein bond and some tendency to the rise of the total cholesterol and protein-nonbound cholesterol content. In rabbits which received cholesterol in combination with lead acetate, the content of total cholesterol, protein-nonbound, and loosely protein-bound cholesterol is much greater than in rabbits which were given the same amount of cholesterol without lead. The results obtained led to an assumption that reduced stability of the cholesterol-protein bond represented the first stage of cholesterol metabolism disturbance under the effect of lead.

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