

The Effect of Organochlorine Insecticides on Serum Cholesterol Level in People Occupationally Exposed

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Recent studies have revealed that organochlorine insecticides (OCI) present in the animal body are far from inert (1). A large variety of OCI stimulates the proliferation of smooth surfaced endoplasmic reticulum (SSER) in the liver cell (2,3,4), thus increasing the level of enzymes which metabolize steroid hormones (5) and some xenobiotics (drugs (6,7) and OCI (8)).

Homeostatic body processes apparently related to biological effects of OCI have been investigated by us in workers occupationally and non-occupationally exposed to OCI. The SSER synthesizes a large proportion of liver cholesterol (9,10,11,12). The proliferation of SSER induced by the presence of OCI could thus lead to a rise in the serum cholesterol level. This paper reports on the findings obtained investigating such a hypothesis in people occupationally exposed to OCI.

Method

Serum cholesterol was determined in 206 workers in a chemical plant which synthesizes and formulates OCI and in a control group of workers non-occupationally exposed to OCI. The Chiamory and Henry method (13) was used for cholesterol estimation.

Results

Serum cholesterol level increased with age, both in control and exposed groups. This increase was more marked in the exposed group (Table 1, Graph 1), but the difference was significant only in the age group over 45 years: in the exposed workers, 250 ± 50 mg/100ml and in the control group, 214 ± 32 mg/100ml ($p < 0.01$).

The Sephardim ethnic group had lower mean values for serum cholesterol than the Ashkenazim ethnic group (Table 1, Graph 2). The difference between these groups was not statistically significant ($p > 0.10$).

Comments

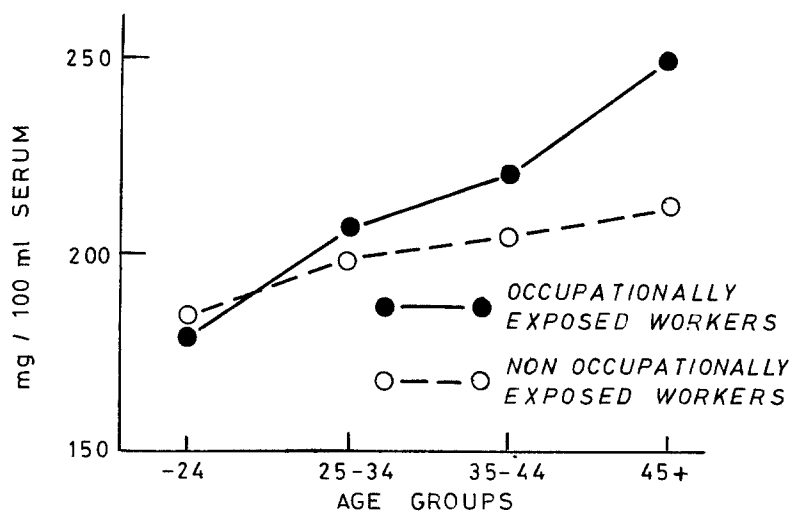
The liver is the main site of serum cholesterol synthesis. It seems that the feedback control of cholesterol synthesis is not as efficient in man as in other mammals (14). On the other hand many xenobiotics (drugs, insecticides and some of their synergists) have been proved to affect cholesterol synthesis. Thus the synthe-

TABLE 1 - Serum total cholesterol levels
(mg./100ml.)

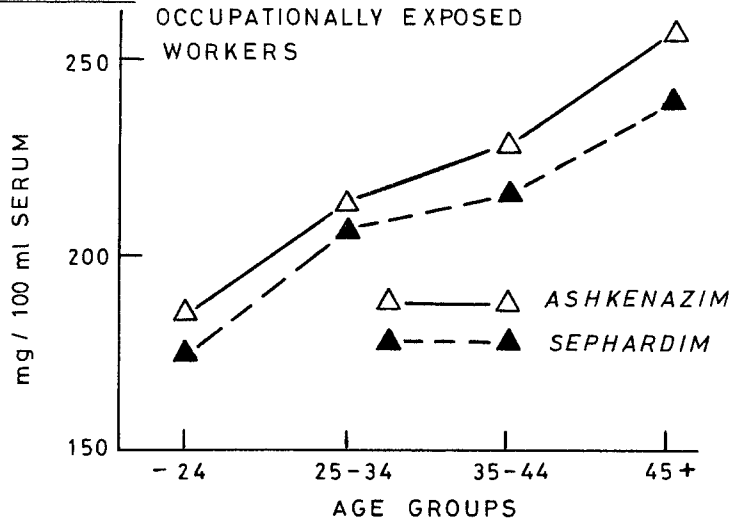
Age Group Groups of Workers	till 24		25 - 34		35 - 44		over 45	
	Cases	Mean \pm SD	Cases	Mean \pm SD	Cases	Mean \pm SD	Cases	Mean \pm SD
1. Occupationally-exposed workers (Ashkenazim)	12	185 \pm 40	19	212 \pm 42	22	228 \pm 46	25	257 \pm 50
2. Occupationally-exposed workers (Sephardim)	28	176 \pm 38	35	206 \pm 45	46	216 \pm 43	19	240 \pm 53
3. Occupationally-exposed workers (Total)	40	179 \pm 37	54	208 \pm 45	68	220 \pm 44	44	250 [*] \pm 50
4. Non-occupationally exposed workers	22	183 \pm 39	15	198 \pm 32	22	204 \pm 57	27	214 [*] \pm 32

* Statistical evaluation gr. 3 versus gr. 4 : $p < 0.01$

GRAPH 1. SERUM CHOLESTEROL LEVELS



GRAPH 2. SERUM CHOLESTEROL LEVELS IN OCCUPATIONALLY EXPOSED WORKERS



sis of cholesterol is inhibited by inhibitors of drug metabolism, hypocholesterolemic agents and insecticide synergists while microsome inducers such as phenobarbital lead to increased C¹⁴-acetate incorporation into cholesterol (15). In the case of phenobarbital, a concomitant breakdown may be supposed since serum cholesterol level does not rise (15).

Phenobarbital, like OCI, leads to the proliferation of SSER. So, an increase of cholesterol biosynthesis by OCI may therefore be expected.

The findings of this study could thus be interpreted as follows. OCI induce an increase in the synthesis of serum cholesterol. This rise is probably compensated for by a concomitant breakdown since, in the workers investigated in this study, serum cholesterol remains within normal limits and no statistically significant differences between occupationally and non-occupationally exposed workers are found except in the over 45 age group. The latter findings may be explained by a diminished response in homeostatic equilibria in the old due perhaps, in the case of cholesterol breakdown, to a state of mild hypothyroidism.

The functional state of the thyroid gland has a role in cholesterol homeostasis since in hypothyroidism catabolism of cholesterol is more depressed than biosynthesis with resultant hypercholesterolemia. On the other hand, in hyperthyroidism breakdown of cholesterol is stimulated and hypocholesterolemia follows with an increase in fecal neutral steroids and a lesser increase in bile acids (16).

Organochlorine insecticides also influence thyroxine metabolism. Danowski et al (17) reported in 1964 a decreased serum PBI level after o,p'DDD therapeutic administration and suggested that the PBI lowering effect of o,p'DDD is probably due to competition with thyroxine for thyroxine binding globuline binding sites or to a direct effect on intrathyroidal synthesis of thyroid hormone.

Marshall and Tompkins found a markedly elevated resin sponge uptake, lowered serum PBI and an euthyroid clinical state in two patients treated with o,p'DDD for metastatic adrenal carcinoma (18). These findings argue for the first hypothesis of Danowski and explain the euthyroid state of the patients by a compensated hypothyroidism. The effect of OCI on thyroxine metabolism may therefore be compensated for by an efficient feedback control.

It can be assumed that OCI increase the synthesis of cholesterol. Serum cholesterol level is, however, not increased, as a result of a concomitant breakdown. In older people (over 45 in this study) the homeostatic control of serum thyroxine drops to a lower level and thus the breakdown of cholesterol may be diminished. As a consequence, higher cholesterol synthesis induced by OCI is no longer masked by a concomitant catabolism.

Summary

Serum cholesterol was determined in 206 workers occupation-

ally exposed to organochlorine insecticides (OCI) and in 86 workers non-occupationally exposed to these chemicals.

In both groups of workers the serum cholesterol level increased with age. The increase was greater in exposed workers but the difference between the two groups was statistically significant only in the over 45 years age group.

It is thought that OCI induce an increase of cholesterol synthesis, but this process is masked by a concomitant breakdown. In the over 45 years age group a diminished reactivity of homeostatic processes may explain the finding of enhanced cholesterol synthesis which is no longer masked by concomitant catabolism.

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