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Effects of Organochlorine Insecticides on Serum Proteins in Occupationally Exposed People

H. J. Miller, Ita Aronovski, Simi Cucos, Dora Wassermann, and M. Wassermann
Department of Occupational Health,
The Hebrew University-Hadassah Medical School, Jerusalem, Israel

Organochlorine insecticides (OCI) and other organochlorine compounds (OCC) have become current constituents of the environment in recent decades (WASSERMANN and Wassermann 1966).

DDT was brought into use toward the end of the second world war. The pesticidal action of DDT and other OCI were found to be accompanied by important unwanted biological effects upon man and his biological environment. The unwanted biological effects of these compounds threw a shadow over their future in spite of the succesful role they play in preventive medicine and agriculture.

The storage levels of OCI in the human body have been assessed in the general population of a large number of countries as well as in people occupationally exposed (WASSERMANN et al. 1975). The latter have been found to have a higher storage level (WASSERMANN et al. 1970) and were therefore considered a suitable study group for the assessment of biological effects of these compounds in man.

Studies carried out in occupationally exposed peole as well as in animal experiment and in wild life, have shown that OCI affect various parameters of the internal environment, an expression of changes occuring in function and structure of organs in the animal and human body.

This paper reports serum protein level changes in people occupationally exposed to OCI.

MATERIALS AND METHODS

Serum proteins were determined in two groups of persons occupationally exposed to OCI and in a group of controls, non occupationally exposed to OCI. The groups of persons occupationally exposed to OCI, were selected for this study from a larger group, whose DDT level had been previously assessed. Group 1: People occupationally exposed to OCI having DDT plasma levels of more than 100 ppb. (n = 43) and Group 2:people occupationally exposed to OCI with DDT plasma levels of less than 40 ppb (n = 23). Group 3: selected from a control group was composed of people non occupationally exposed to OCI with DDT plasma levels of less than 40 ppb (n = 20).

The large range of OCI plasma levels in occupationally and non occupationally exposed people was the reason for arranging the groups in the above way. The relatively low DDT plasma level in a

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number of occupationally exposed people may be due to a lower grade of exposure, to a prolonged intake of drugs or of other compounds, the metabolization of which interfere with that of OCI, or to an individual increase in the metabolization of xenobiotics. We have chosen a low DDT plasma level group in controls in order to eliminate those persons with high DDT exposure in household practices.

Venous blood was collected in test tubes and allowed to clot. The serum was separated and kept at -20^{0}, until used. Total proteins were assessed using the biuret reaction and protein electrophoresis was performed using the Beckman Model R-101 microzone cell. The relative concentration of protein components obtained from the analytical chart papers were refered to the total protein values and thus the absolute values of individual protein components were estimated.

RESULTS AND DISCUSSION

Table 1. summarizes our findings regarding the serum proteins levels in people occupationally and non occupationally exposed to OCI.

Total serum proteins were lower in group 1 when compared to group 2 and 3. ($p < 0.01$ and $p < 0.05$, respectively).

A variety of findings, regarding serum protein changes, have been reported amongst workers chronically exposed to OCC. In one study moderate hyperproteinemia was found (KRASNIUK 1968), in another hypoproteinemia (BARSEL'IANTS 1969), whilst yet in a further study, levels considered as normal were revealed (JAGER 1971). Since total serum protein levels vary with a large gamut of conditions one cannot compare the mentioned studies without additional data regarding state of health, diet, etc.

In our present study the mean albumin plama level was higher in group 2 than in controls. This difference was not statistically significant.

In experiments carried out in our laboratory, in which animals were exposed to individual OCC (DDT, dieldrin, lindan, polychlorinated biphenyls (PCB_s) significant changes in serum proteins levels were obtained when compared to controls, matched for sex, age, diet, housing etc. (WASSERMANN et al. 1969, 1972, 1973) In rats exposed to DDT (WASSERMANN 1969) and in rabbits exposed to dieldrin and lindane (WASSERMANN 1972) plasma albumin levels were found to be higher than in controls, but not in rats exposed to PCBs (WASSERMANN 1973)

The decrease of serum proteins levels in the groups 1 and 2, occured at the expense of globulins since the albumin serum levels did not show significant differences when compared to the control group.

The alpha-1 globulin plasma level was lower in the low DDT plasma level group of people occupationally exposed to OCI than in the high DDT plasma level group and in controls. The difference

Table 1. Total serum proteins and serum protein fractions (g/100 ml).

Groups / Compounds	People occupationally exposed to OCI				3. Control		Statistical Evaluation
	1. High DDT plasma level		2. Low DDT plasma level				
	Range	M ± SD	Range	M ± SD	Range	M ± SD	
Total proteins	5.84 - 7.94	6.70 ± 0.43	6.14 - 8.65	7.25 ± 0.49	6.61 - 8.05	7.41 ± 0.21	1 vs. 3 $p < 0.01$
Albumin	3.68 - 4.98	4.44 ± 0.36	3.81 - 5.66	4.62 ± 0.46	4.05 - 5.15	4.52 ± 0.28	1 vs. 2 $p < 0.05$
Globulins: Alpha-1	0.10 - 0.27	0.19 ± 0.04	0.10 - 0.26	0.17 ± 0.04	0.16 - 0.25	0.19 ± 0.03	1 vs. 2 $p < 0.05$
Globulins: Alpha-2	0.40 - 0.85	0.65 ± 0.10	0.45 - 0.89	0.63 ± 0.10	0.53 - 1.01	0.70 ± 0.13	
Globulins: Beta	0.52 - 0.86	0.65 ± 0.09	0.55 - 0.90	0.68 ± 0.09	0.46 - 1.02	0.77 ± 0.12	1 vs. 3 $p < 0.01$ 2 vs. 3 $p < 0.02$
Globulins: Gamma	0.76 - 1.41	1.06 ± 0.18	0.64 - 1.77	1.14 ± 0.25	0.83 - 1.82	1.24 ± 0.26	1 vs. 3 $p < 0.01$

for the alpha-1 globulin serum level between the low DDT plasma level group and the high DDT plasma level group was significant ($p < 0.05$)

In animal experiments (carried out in our laboratory) a statistically significant decrease in alpha-1 globulin was found in rats exposed to p.p'- DDT (WASSERMANN et al. 1969). The alpha-1 peak of the electrophoresis pattern consists of several proteins including, alpha-1 - antitrypsin, alpha-1 - acid glycoprotein, alpha-1 - lipoprotein and others. The alpha-1 - antitrypsin forms about 90% of the alpha-1 globulin electrophoretic peak in normal persons (LARSON 1974). It is clear therefore that changes in the pattern of this peak will almost certainly be due to changes in the quantity of alpha-1 - antitrypsin. Cases with decreased or even absent alpha-1 - antitrypsin are known to occur as an inborn error of metabolism (HEIDLEBERGER 1976). Even a slight environmentally induced decrease in the alpha-1 - antitrypsin in serum levels, in persons already bearing an hereditary disturbance in their alpha-1-antitrypsin synthesis, may be of consequence.

The alpha-2 globulin plasma levels were lower in the occupationally exposed groups, but the differences were not statistically significant. The same finding was obtained in our rats given p.p'-DDT (WASSERMANN et al. 1969).

There was a highly significant lowering in the serum beta globulin concentrations in both the high and low OCI exposed groups of men, when compared to the control group ($p < 0.01$ and $p < 0.02$ respectively). The major components of the beta globulin electrophoretic peak are the very low density lipoproteins (VLDL), transferin, the low density lipoproteins (LDL) and C'3. Lipoproteins are primarily concerned with triglyceride transportation, and since OCI are known to produce an increase of triglycerides (lipid droplets) in liver parenchymatous cells, we may presume that the decrease of the beta globulin peak takes place at least partially at the expense of lipoproteins. It goes without saying that only a study of the concentration of the individual lipoproteins would confirm or refute this assumption. This is because an accumulation of triglycerides may occur in the presence of a normal amount of lipoproteins, in the case of an impairment in the synthesis of lipid acceptor protein, or of an ineffective coupling with the lipid acceptor protein.

A change in serum iron concentration may confirm a lowering of serum transferin. A C'3 decrease will point to an effect on the immunological defense.

In beagles receiving hexachlorobenzene(HCB), a significant decrease in the beta lipoproteins was found (LUTHRA et al. 1977), but not in our p.p'- DDT receiving rats (WASSERMANN et al. 1969).

The gamma globulin levels were lower in group 2 than in controls, and still lower in the high DDT plasma level persons (group 1). The difference between the values of gamma globulins in group 1 and the controls was highly significant statistically ($p < 0.01$).

Plasma levels of gamma globulins were found to be lower also in animals exposed in our laboratory to DDT (rats - WASSERMANN et al. 1969, rabbits - WASSERMANN et al. 1973, antigen treated rabbits - WASSERMANN et al. 1971), to dieldrin (antigen treated rabbits - WASSERMANN et al. 1972), to lindan (antigen treated rabbits - WASSERMANN et al. 1972), and dieldrin or lindan given together with salmonella antigen to rabbits, prevented the expected increase of 7 S gamma globulin serum levels. These facts point to the problem of the effect of some OCC on the immunological defence system.

Changes in the immunological defence system like atrophy of the spleen in birds (DUSTMAN et al. 1971), thymus atrophy and lymphopenia in rabbits (VOS and BEEMS 1971), increased mortality rate from hepatitis virus in ducklings (KOEMAN et al. 1969) and a lowering of the gamma globulins in guinea pigs (VOS and ROIJ 1972) were reported following PCBs administration.

The changes in serum protein levels, induced by OCC, are the expression of biological effects of these compounds on a number of tissues and organs involved in serum protein synthesis.

Reduction of exposure in industry, agriculture and the household may prevent such and other unwanted effects in man and his biological environment.

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