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Effects of Dietary PCBs (Aroclor 1254) on Serum Levels of Lipoprotein Cholesterol in Fischer Rats

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In 1971, the first report was published describing an increase in liver and serum cholesterol in PCB-treated rats (Nagai et al.). Although this phenomenon has been confirmed in subsequent studies, little data is available on the other lipoproteins associated with serum cholesterol.

The aim of this investigation was to determine the effects of dietary PCBs (Aroclor 1254) on serum levels of lipoprotein cholesterol in weanling Fischer rats. Within this overall goal two important factors were considered. The dietary PCB concentrations were selected to reflect minimally toxic doses (Carter, 1984) and the number of days of dietary treatment were specified to produce hypercholesterolemia (Carter, 1984).

MATERIALS AND METHODS

Male Fischer rats 28 days old (Charles River COBS/CDF) were divided into four groups of 12 animals each. The rats were individually housed in wire-bottom cages with food and deionized water ad libitum, and acclimated to controlled lighting (from 0700 to 1900) and temperature (26°C ± 2°C) for eight days. All groups were fed diets (Table 1) that contained the following concentrations of PCBs: 0, 4, 8, or 16PPM Aroclor 1254. The rats were assigned according to a randomized block design and fed the diets described above for four days. Food intakes and body weight gains were recorded at the end of the study. The animals were sacrificed with diethyl ether anesthesia, and blood samples were obtained from the abdominal aorta.

Serum was then obtained from each blood sample by centrifuging at 1,000 X G for 20 minutes at 4°C and used within 48 hours for the fractionation of the major lipoprotein classes by a slight modification of the procedure described by Bronzert and Brewer (1977). The VLDL fraction was separated from the LDL and HDL fractions by ultracentrifugation using a Beckman Airfuge with an A-100 fixed-angle rotor. The HDL fraction was obtained by selective precipitation of VLDL and LDL fractions from the whole serum with Mg^{++}/phosphotungstic acid (Lopes-Virella et al. 1977). Cholesterol concentrations in the whole serum and lipoprotein fractions were

determined using a Kem-O-Lab Autoanalyzer based on the enzymatic methods described by Allain et al. (1974) and Bucolo and David (1973).

The liver was removed and its wet weight determined. Results were analyzed by one-way analysis of variance with multiple comparisons of group means for statistical significance using Duncan's New Multiple Range test.

Table 1. Composition of Diet

Constituents	% in Diet
[1]Vitamin Mix (A.I.N. Vitamin Mix 76)	1.00
[2]Alpahcel (Non-nutritive Bulk)	5.72
[3]Salt (A.I.N. Mineral Mix 76)	3.50
[4]Cornstarch	57.00
[5]Vitamin-Free Casein	25.00
[6]Choline Chloride	0.20
[7]d,1-Methionine	0.08
Fat (Mazola Corn Oil)	7.50

[1-7]I.C.N. Nutritional Biochemicals, Cleveland, Ohio 44128

RESULTS AND DISCUSSION

The terminal body weight, total food consumption, and relative wet liver weight data are listed in Table 2. No significant differences were observed in final body weight or in total food consumption. However, relative wet liver weight was significantly elevated in the 8PPM (6.9%) and the 16PPM (9.3%) groups. Until now, no other reports have documented a significant increase in relative wet liver weight with a dietary concentration less that 10PPM PCBs (Aroclor 1254). Linear regression analysis revealed a positive correlation for relative wet liver weight versus dietary PCB concentration as seen in Table 3.

Table 2. Effects of Dietary PCBs (Aroclor 1254) on Final Body Weight, Total Food Intake and Relative Wet Liver Weight*.

	DIETARY PCBs (PPM)			
	0	4	8	16
Body weight (G)	96.2±1.7	96.7±1.0	99.0±1.5	101.7±2.6
Food Intake (G)	49.9±1.2	47.5±0.4	48.8±0.5	47.7±2.1
Liver Weight (%)	3.78±.03	3.80±.03	4.04±.07[a]	4.13±.05[a]

*Mean ± S.E. for 12 animals per group. Superscripts indicate statistical significance at $p < 0.01$.

The serum cholesterol and lipoprotein fraction data are illustrated in Figure 1. Although there is a continuous rise in serum

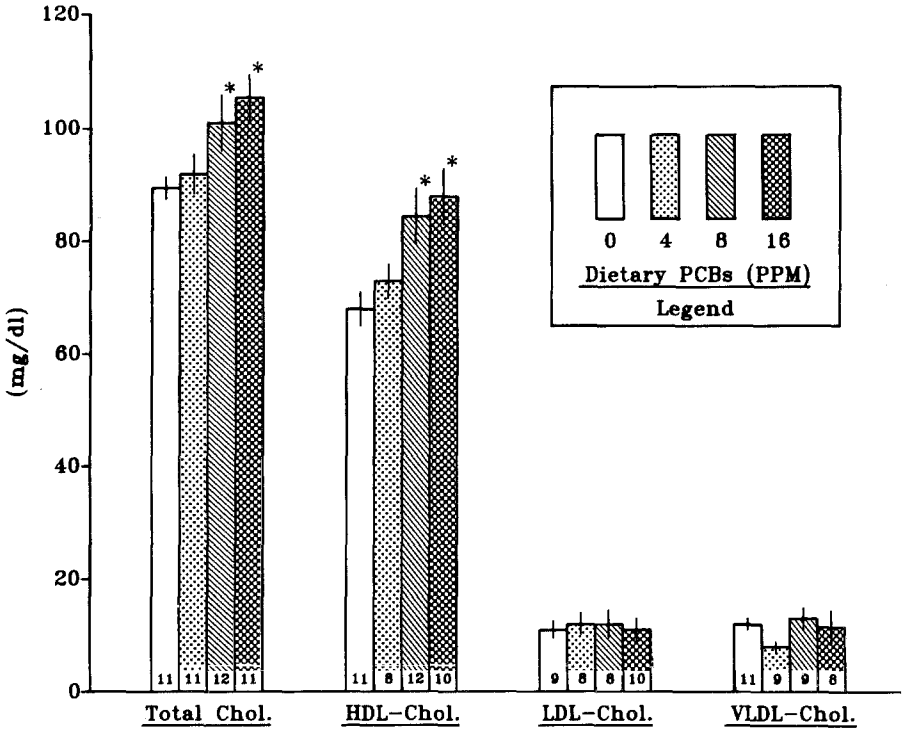

Figure 1. Serum lipoprotein-cholesterol in juvenile Fischer rats fed dietary PCBs (Aroclor 1254). Each bar represents the mean +/- S.E. with the specimens in each group indicated by the number in each bar. Asteriks indicate statistically different means at $p<0.05$.

cholesterol values with increasing dietary concentration of PCBs, only the 16PPM group is significantly elevated (18%) above the non-treated group. A positive correlation exists for serum cholesterol versus dietary PCB concentration (Table 3).

Of all three lipoprotein-cholesterol fractions measured, only HDL-Cholesterol was elevated due to dietary PCBs. This significant increase was observed in the 16PPm group which exhibited a 27.9% rise when compared to the control group (Figure 1). Here again, a continual rise is seen in HDL-cholesterol values with increasing dietary PCB concentration. And once more, a positive correlation is demonstrated for HDL-cholesterol versus dietary PCB concentration (Table 3). There were no significant increases in the LDL- or VLDL-cholesterol fractions (Figure 1), nor were any significant correlations demonstrated for these two lipoprotein fractions when compared with dietary PCB concentrations (Table 3).

An investigation reported by Carter and Koo (1948) stated that both HDL- and LDL-cholesterol were elevated in adult Fischer rats fed

Table 3. Linear Regression Analysis

Variable	Y-Intercept	Slope	r	p-value
Final Body Wt.	95.9	0.36	0.34	<0.05
Total Food Intake	49.1	-0.09	-0.12	N.S.
Relative Wet Liver Wt.	3.7	0.03	0.72	<0.001
Serum Cholesterol	89.7	1.05	0.44	<0.01
Serum HDL-Cholesterol	70.2	1.27	0.51	<0.001
Serum LDL-Cholesterol	11.4	0.0	-0.01	N.S.
Serum VLDL-Cholesterol	10.6	0.06	0.06	N.S.

50 ppm Aroclor 1254 for 14 days. However, only the HDL-cholesterol fraction remained elevated in these animals after 35 days on this diet. They reported no significant changes in VLDL-cholesterol levels.

The fact that no elevation was seen in LDL-cholesterol in the present study can be interpreted in the following manner. The dietary concentration of 16 ppm Aroclor 1254 may well have been insufficient to induce such an increase as reported earlier (Carter and Koo, 1984). Another possible explanation is that an increase in LDL-cholesterol may require more than four days dietary treatment.

The significant increase in HDL-cholesterol in this investigation is in agreement with previous studies reported by Kato et al. (1982), Ishikawa et al. (1978) and Carter and Koo (1984). This consistent elevation in HDL-cholesterol may have implications relevant to the development and progression of atherosclerosis. Epidemiological studies indicate that the incidence of coronary heart disease is directly related to elevated serum LDL-cholesterol and inversely related to serum HDL-cholesterol (Carlson and Ericsson, 1975). A study is presently being conducted in this laboratory to evaluate the effects of dietary PCBs (Aroclor 1254) on the progression of atherosclerosis in an appropriate animal model.

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