Bull. Environ. Contam. Toxicol. 31 183–187 (1983)

Onset of Hepatomegaly in PCB (Aroclor 1254)-treated Rats

John W. Carter

Department of Anatomy, School of Medicine, Oral Roberts University, 7777 South Lewis, Tulsa, OK 74171

In the mid-1960's JENSEN (1966) reported that a new class of environmental pollutants, polychlorinated biphenyls (PCBs), had been discovered in Swedish wildlife. Subsequently, PCBs have become recognized as ubiquitous compounds of the global ecosystem (RISEBROUGH and DELAPPE, 1972).

Morphological changes in the liver of rats fed PCBs were reported in 1973 (ALLEN and ABRAHAMSON). They described a liver hypertrophy attributable to (1) proliferation of the smooth endoplasmic reticulum, (2) development of large membranous concentric arrays, and (3) an increase in lipid droplets within the cytoplasm of the affected hepatocytes. Numerous investigations of the toxic effects of PCBs on the liver have enhanced the body of knowledge concerning the biochemical and morphological changes induced by many PCB mixtures and individual isomers. However, information regarding the time necessary for the liver to respond morphologically to the dietary exposure of PCBs is lacking. Therefore, this study was conducted to determine the onset of hepatomegaly (liver hypertrophy) in rats fed a dietary concentration of PCBs which is minimally toxic.

METHODS

Male Fischer rats 34 days old (Charles River COBS/CDF) were divided into 10 groups of five animals each. The rats were individually housed in wire-bottom cages with food and deionized water available ad libitum, and acclimated to controlled lightening (from 0700 to 1900) and temperature (26°C ± 2°C) for five days. All groups were fed diets (Table I) which contained either 0 or 20 PPM of Aroclor 1254. The animals were assigned according to a randomized block design to the following groups: control with either one, two, four, eight or 14 days of dietary treatment or PCB-treated with either one, two, four, eight or 14 days of dietary treatment. Food intakes and body weight gains were recorded daily. The rats were sacrificed with diethyl ether anesthesia. 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 Scheffe's test.

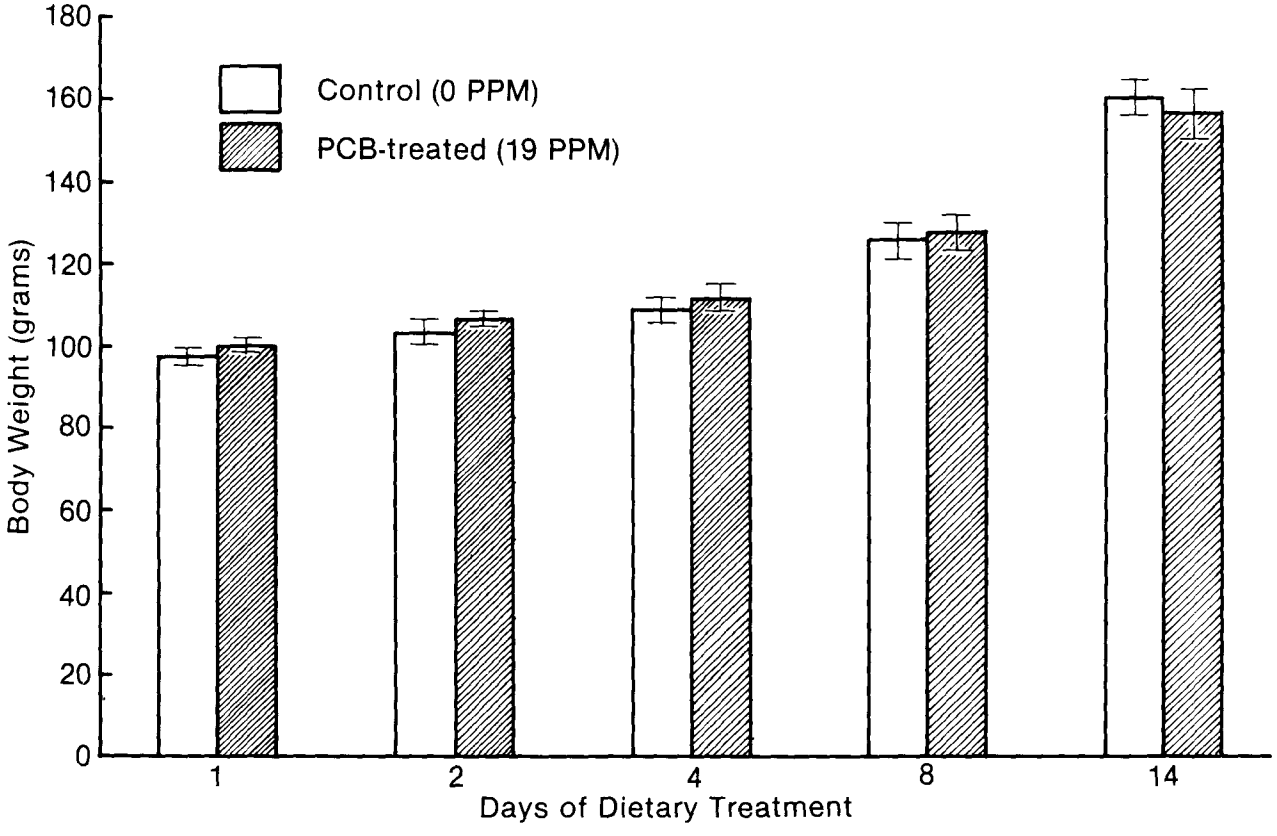

Figure 1. Effect of dietary PCBs (Aroclor 1254) on body weight (mean ± S.E.). There were five animals per group.

Table I
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,l-Methionine	0.08
Fat (Mazola Corn Oil)	7.50

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

RESULTS

The total or cumulative food consumption for both groups of rats was calculated and is presented in Table II. There were no significant differences in cumulative food consumption.

Table II
Cumulative Food Consumption (Grams)*

	Days of Dietary Treatment				
Group	1	2	3	4	5
0 PPM	2.3±.9[a]	6.3±.8[a]	13.6±1.1[a]	30.2±3.5[a]	66.1±1.8[a]
20 PPM	2.2±1.0[a]	6.9±.5[a]	13.8±1.1[a]	33.8±2.2[a]	60.8±3.8[a]

*Mean ± SEM of 5 rats per group. Values in the same column not sharing a common superscript are significantly different ($p < 0.05$).

There were no significant differences in body weight exhibited by the PCB-treated animals at any time during the study. These data are portrayed in Figure 1.

The liver, which is responsible for detoxifying these xenobiotic compounds, responded in a relatively short period of time. As can be seen in Figure 2, there is a significant increase in the relative wet liver weight beginning by four days of dietary treatment. This phenomenon continued after eight and 14 days of dietary treatment.

DISCUSSION

In order to determine the minimal time required for the liver to hypertrophy when exposed to dietary PCBs it was critical that an appropriate dietary concentration be selected. The dietary concentration which was chosen was based on the following criteria:

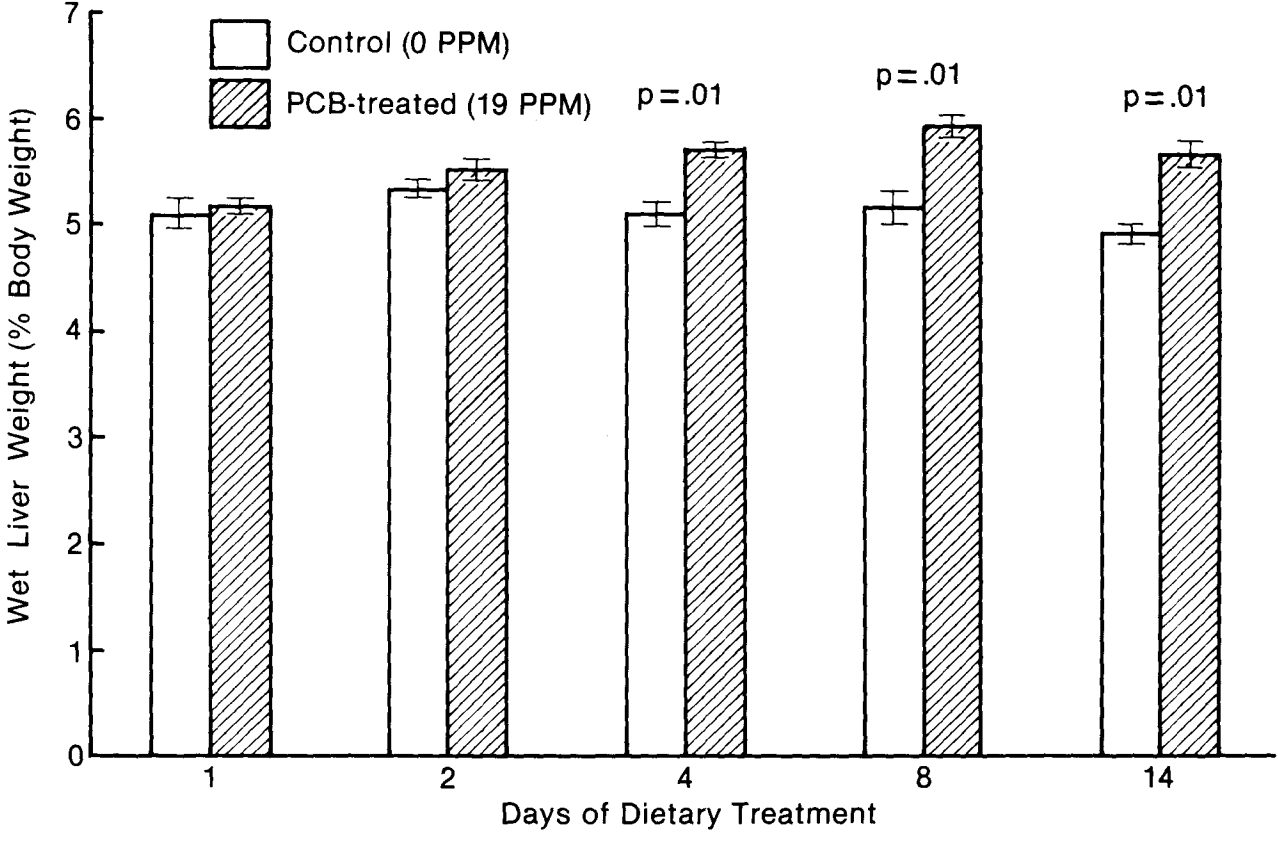

Figure 2. Effect of dietary PCBs (Aroclor 1254) on relative wet liver weight (mean ± S.E.). There were five animals per group.

(1) will this dietary concentration depress food consumption? (2) will this dietary concentration reduce body weight gain? and (3) does this dietary concentration represent a minimally toxic dose? From a previous investigation it was determined that a dietary concentration of greater than 179 PPM Aroclor 1254 is necessary to reduce food consumption and depress body weight gain in weanling male Fischer rats (CARTER and MERCER, 1983). The minimal dietary PCB (Aroclor 1254) concentration which will produce hepatomegaly in these rats is between 10-25 PPM (unpublished data).

The dietary concentration of PCBs did not significantly affect cumulative food consumption (Table II) or alter body weight at any time throughout the investigation (Figure 1). Therefore, the first two criteria stated above were met.

The dietary concentration of 20 PPM Aroclor 1254 did represent a minimally toxic dose for it produced statistically significant hepatomegaly after only four days treatment. This increase in relative wet liver weight is attributable to the toxic effects of PCBs on centrilobular hepatocytes which causes them to hypertrophy (CARTER and CAMERON, 1977).

Future studies are planned to determine if the hepatomegaly reported here is associated with increases in serum cholesterol seen in rats exposed to a diet containing 2000 PPM Aroclor 1248 for 14 days (KIRIYAMA et al., 1974).

Acknowledgments. This research was supported by an award from the Oral Roberts University School of Medicine Intramural Research Grant Program. I would like to recognize the important technical contribution made by Ms. Martha Smithson.

REFERENCES

ALLEN, J. R. and L. J. ABRAHAMSON: Arch. Environ. Contam. Toxicol. 1, 265 (1973).

CARTER, J. W. and I. L. CAMERON: Exp. Mol. Pathol. 26, 228 (1977).

CARTER, J. W. and L. P. MERCER: Nutr. Rep. Int. 27, 561 (1983).

JENSEN, S.: New Scient. 32, 612 (1966).

KIRIYAMA, S., M. BANJO and H. MATSUSHIMA: Nutr. Rep. Int. 10, 79 (1974).

RISEBROUGH, R. W. and B. DELAPPE: Environ. Hlt. Perspect. 1, 39 (1972).

Accepted May 10, 1983