Chronic Toxicity of Three Polychlorinated Biphenyls in Beagle Dogs

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Running Title: Chronic Toxicity of 3 PCB's in Beagle Dogs

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ABSTRACT

Chronic Toxicity of Three Polychlorinated Biphenyls in Beagle Dogs. Fancher, Otis E., Keplinger, M. L., Lindberg, D. C., Wheeler, E. P., and Calandra, J. C. (0000). Toxicol. Appl. Pharmacol. 00, 00 -00. Two year toxicity studies were conducted in beagle dogs with 3 polychlorinated biphenyls (Aroclors 1242, 1254 and 1260) at dietary levels of 1, 10, and 100 ppm. Decreases in weight gains of questionable significance were experienced by male animals fed 100 ppm of Aroclor 1254 or 1260 and by female animals fed 10 or 100 ppm of Aroclor 1254 or 100 ppm of Aroclor 1260. Moderate increases in serum alkaline phosphatase activity and increases in liver/body weight ratios for both males and females resulted from feeding 100 ppm of Aroclor 1260. No other changes indicative of toxic effects were observed.

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INDEX TERMS

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Aroclor 1242

Aroclor 1254

Aroclor 1260

Polychlorinated biphenyls

Chronic toxicity of, in beagle dogs

Effects of, on SAP activity in beagle dogs

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Two year toxicity studies were conducted in beagle dogs with 3 polychlorinated biphenyls (Aroclors 1242, 1254 and 1260) at dietary levels of 1, 10, and 100 ppm. Decreases in weight gains of questionable significance were experienced by male animals fed 100 ppm of Aroclor 1254 or 1260 and by female animals fed 10 or 100 ppm of Aroclor 1254 or 100 ppm of Aroclor 1260. Moderate increases in serum alkaline phosphatase activity and increases in liver/body weight ratios for both males and females resulted from feeding 100 ppm of Aroclor 1260. No other changes indicative of toxic effects were observed.

Background information has been presented by Fancher et al.(0000) in the introducory paper of this series. The present study was conducted in order to determine the chronic effects of 3 polychlorinated biphenyls of variable chlorine content in beagle dogs.

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METHODS

The animals used in these studies were purebred beagle dogs from the BIO-TEST colony. The animals were all eligible for A. K. C. registration and had been immunized against rabies, distemper, infectious canine hepatitis and leptospirosis. All dogs were re-immunized and cleared of any detectable parasitic infestation during a two week observation period prior to initiation of treatment.

During the study, the animals, whose age at the start of the study ranged from 4.5 to 6.8 months, were housed in kennels equipped with outside runs, 4 dogs of the same sex and group being accomodated in one kennel.

A control group and 9 treatment groups, each consisting of 4 male and 4 female animals, were employed, 3 treatment groups for each of the 3 Aroclors studied.

All diets were prepared fresh each week by mixing the appropriate Aroclor at levels of 1, 10 and 100 ppm with Purina Dog Meal (Ralston Purina Company, St. Louis, Missouri) in a Hobart Mixer. Weighed quantities of diet, in excess of anticipated consumption, were distributed into self-feeding units, one such unit being available to the dogs in each kennel for 3 hours each day, during which times food was consumed ad libitum. At the end of each 7-day period, all unconsumed food was collected and weighed and average food consumption was calculated. Water was available at all times.

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The initial body weight of each dog was determined and weighings were made weekly thereafter for the duration of the study. All dogs were observed daily for behavioral effects and for clinical signs of toxicity.

Hematologic studies included erythrocyte count, hemoglobin concentration, hematocrit and total and differential leukocyte counts. Urine was examined for albumin, glucose, pH, specific gravity and microscopic elements (leukocytes, erythrocytes and crystals). Blood chemistry studies included determinations of blood urea nitrogen (BUN), serum glucose, and serum alkaline phosphatase (SAP), serum glutamic-oxalacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) activities. All parameters were determined for each dog just prior to initiation of treatment and after 1, 3, 6, 12, 18 and 24 months on test.

At the conclusion of the investigation, animals were sacrificed by electric shock and all major tissues and organs were examined grossly. The weights of the following organs were obtained: liver, kidneys, heart, brain, spleen, gonads and adrenal, thyroid and pituitary glands.

Microscopic examinations were conducted on 34 tissues and organs from each dog following fixation in 10% formalin and staining with hematoxylin-eosin.

RESULTS

A. Body Weights and Weight Gains

Male animals treated with 100 ppm of Aroclor 1254 or 1260 and

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female animals treated with Aroclor 1254 at levels of 10 and 100 ppm or with Aroclor 1260 at 100 ppm had slightly lower overall weight gains than did control animals or those of other dietary groups. A summary of the body weight data is presented in Table 1. Interpretation of these data is made uncertain by the highly variable nature of body weight gains of dogs of the age employed. All animals gained weight and appeared to be healthy.

B. Food Consumption

Food consumption was not adversely affected by any level of any of the test materials. The differences in weight gains, cited above, could not be related to differences in food consumption.

C. Mortality and Reactions

No abnormal behavioral reactions were noted among animals of any group.

Six animals died during the study. Mortality data are summarized in Table 2. Histologic examination of tissues from these animals revealed no abnormalities which could be related to ingestion of the test materials.

D. Hematologic Studies and Urine Analyses

Values for all parameters were within the normal range for the beagle dog. No significant differences between values for the control group and those for any test group were observed.

E. Blood Chemistry Studies

Moderate increases in serum alkaline phosphatase activity were

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noted at the 12, 18 and 24 month determinations among animals receiving 100 ppm of Aroclor 1260. These data are presented in Table 3. No other abnormalities were noted among animals of any other group.

F. Pathologic Studies

1. Aroclor 1242

a. Organ weight data:

No abnormalities were observed

b. Gross and histologic findings:

No changes attributable to the test material were observed among animals sacrificed at termination of the study.

The female animal which was sacrificed in extremis after 60 weeks of treatment at 100 ppm showed severe chronic peritonitis on the serosal surface of all of the gastrointestinal tract, consisting of a thick layer of scar tissue, granulated tissue and a limited degree of cellular infiltration. There was no evidence of ulceration or mucosal injury. The cause of the lesion was undetermined.

The presence of chronic pneumonitis and chronic pleuritis was confirmed histologically for the male animal which died after treatment at a level of 10 ppm for 82 weeks.

2. Aroclor 1254

a. Organ weight data

One male animal treated at a level of 100 ppm showed a slightly elevated liver/body weight ratio and both female animals which died during the study showed elevated liver/body weight ratios,

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attributable to depressed body weights rather than to increases in liver weights.

One male at 10 ppm and 3 at 100 ppm showed depressed testes weights and testes/body weight ratios. These findings were judged to have resulted from a chronic testicular inflammation, as discussed below.

b. Gross and histologic findings:

None of the sections from any of the dogs revealed a compound or dose related pattern. The mild to moderate non-specific inflammatory changes observed in various tissues were considered to be incidental findings, frequently observed in clinically normal, untreated dogs. There was histologic evidence of testicular inflammation for one animal at 10 ppm and 3 at 100 ppm. This was judged to be the result of an infectious condition of undetermined etiology.

Chronic peritonitis was evident on the serous surfaces of the stomach, intestines and bladder of the female animal which died after treatment for 37 weeks at a level of 10 ppm.

3. Aroclor 1260

a. Organ weight data:

Animals receiving 100 ppm of Aroclor 1260 exhibited elevated liver/body weight ratios. While the elevations for those animals which died prior to termination of the study can be explained in part by the weight losses experienced prior to death, a majority of the animals of this group displayed real elevations as compared to control animals or to those at lower treatment levels. These data are presented in Table 4. No other

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effects were observed.

b. Gross and histologic findings:

No changes were observed among animals sacrificed at termination of the study except for mild focal inflammation of various tissues such as is frequently seen in clinically normal untreated dogs.

The existence of chronic peritonitis was confirmed histologically for the female animal which died after treatment for 29 weeks at a dietary level of 100 ppm.

DISCUSSION

Aroclor 1242 caused no effects in beagle dogs at dietary levels of 100 ppm or lower.

Except for a slightly elevated liver/body weight ratio for one male animal at 100 ppm and a questionable depression in weight gain for males at 100 ppm and for females at 10 and 100 ppm, Aroclor 1254 caused no effects at dietary levels of 100 ppm or lower.

Moderate elevations in serum alkaline phosphatase activity, elevated liver/body weight ratios and a questionable depression in body weight gains resulted from feeding Aroclor 1260 at a level of 100 ppm in both male and female beagle dogs. Levels of 1 and 10 ppm caused no detectable effects.

No histologic changes which could be related to the Aroclors were observed among animals of any treated group.

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TABLE 1

Weight Gains of Beagle Dogs Treated with

Aroclor 1242, 1254 or 1260

Test Material	Dietary Level (ppm)	Terminal Group Mean Weight Gain (kg)	
		Male	Female
None	—	3.7	3.7
Aroclor 1242	1	5.6	3.8
	10	3.1	3.4
	100	4.6	3.7
Aroclor 1254	1	4.3	3.8
	10	4.8	2.1
	100	2.0	2.4
Aroclor 1260	1	3.9	3.0
	10	2.9	2.7
	100	2.3	2.3

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TABLE 2

Mortality Data for Beagle Dogs Treated with

Aroclors 1242, 1254 and 1260

Test Material	Dietary Level (ppm)	Number and Sex of Animals	Time of Death (Wks)	Cause of Death
Aroclor 1242	10	1 M	82	Chronic pneumonia
	100	1 F	60[a]	Chronic peritonitis
Aroclor 1254	10	1 F	37	Chronic peritonitis
	100	1 F	33	Physical injury
Aroclor 1260	100	1 M	33	Acute pneumonitis; elevated total leukocyte count
	100	1 F	29	Severe chronic peritonitis; elevated total leukocyte count and elevated SGPT

[a] Sacrificed in extremis

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TABLE 3

Serum Alkaline Phospatase Activity for Beagle Dogs Treated with Aroclor 1260, King-Armstrong Units/100 ml

(Group Mean Values)

Dietary Level (ppm)	Sex	Months 6	12	18	24
None	M	5.8	5.7	4.2	5.7
	F	3.6	4.1	4.1	6.6
1	M	4.7	4.2	3.7	4.7
	F	4.4	4.2	4.6	6.6
10	M	4.1	4.2	3.7	4.8
	F	4.7	3.6	4.5	5.2
100	M	6.5	28.7	36.9	36.4
	F	5.1	11.4	15.5	22.0

Note: Colorimetric method of Babson (1965)

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TABLE 4

Liver Weights and Liver/Body Weight Ratios for Beagle Dogs Treated with Aroclor 1260

(Group Mean Values)

Dietary Level (ppm)	Sex	Liver Wgt. (g)	Liver/Body Wgt. Ratio (g/kg)
None	M	373.8	34.5
	F	387.2	34.8
1	M	444.4	33.8
	F	384.3	41.5
10	M	411.4	40.0
	F	337.1	34.7
100	M[a]	490.4	55.4
	F[b]	418.3	45.1

[a] Excludes one animal which died after 33 weeks
[b] Excludes one animal which died after 29 weeks

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FOOTNOTES

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