Arch. Environ. Contam. Toxicol. 14, 547–553 (1985)

Archives of Environmental Contamination and Toxicology

Low Dietary Iodine and Thyroid Anomalies in Ring Doves, *Streptopelia risoria*, Exposed to 3,4,3′,4′-Tetrachlorobiphenyl

Philip A. Spear[1] and Thomas W. Moon

Department of Biology, University of Ottawa, Ottawa, Ontario, Canada K1N 9B4

Abstract. Ring doves, *Streptopelia risoria*, were raised to adult size on either low iodine or normal iodine semi-purified diets. Insufficient iodine elicited thyroid hyperplasia comparable to that previously reported in Great Lakes herring gulls, *Larus argentatus*. This condition was reversed within seven days following a single dose (60 μg/g body weight) of the PCB congener 3,4,3′,4′-tetrachlorobiphenyl (TCBP) in which group the thyroid weight plus colloid diameters were consistent with the development of large-colloid goiter. TCBP exposure also decreased the core body temperature, serum TT_4, and TT_3, indicating that low iodine euthyroidism changed to mild hypothyroidism. Acute exposure of the normal iodine doves did not cause hypothyroidism or affect thyroid histology, although serum TT_4 and TT_3 decreased significantly. In a second study, doves raised on the experimental diets received three TCBP doses (3 × 20 μg/g body weight) over a 28-day period. The only significant effect associated with TCBP was decreased serum TT_4 which occurred in both dietary groups. The major conclusions are i) thyroid hyperplasia caused by low iodine was not enhanced by TCBP, ii) this effect is presumably due to opposing influences upon the thyroid-stimulating hormone (TSH) feedback system, and iii) this work in addition to previous studies indicate that PCB elicits large-colloid goiters in avian species generally, which is an inherently different response to hyperplastic goiter produced in mammals exposed to PCBs.

Histopathologic examinations of fish populations in the Great Lakes of North America have shown a relatively high incidence of thyroid anomalies (Black and Simpson 1974; Drongowski *et al.* 1975; Sonstegard and Leatherland 1976). Recent investigations have revealed similar thyroid anomalies in herring gulls, *Larus argentatus*, sampled from the Great Lakes (Moccia *et al.* 1985). The most pronounced anomaly is hyperplastic goiter comprising the enlargement of the follicle epithelia and reduction of the colloid. The occurrence of this goiter-like condition is tentatively linked to environmental contamination by organochlorine chemicals. Among the organochlorines which have accumulated in Great Lakes' biota, DDT, DDE, mirex, toxaphene PCBs and dioxin (2,3,7,8-TCDD) are known to elicit thyroid effects under laboratory conditions (Hurst *et al.* 1974; Jefferies 1975; Bastomsky and Murthy 1976; Bastomsky 1977; Leatherland and Sonstegard 1979, 1980). When fish were collected from the Great Lakes and incorporated into diets fed to fish and rats, thyroid effects were elicited (Leatherland and Sonstegard 1980, 1982; Villeneuve *et al.* 1981; Hilton *et al.* 1983).

Upon closer inspection, the thyroid effects elicited during laboratory toxicity studies with fish do not include the histologic profile observed in Great Lakes fish. That is, fish which received diets containing PCB and mirex (Leatherland and Sonstegard 1977, 1978, 1979, 1980) or diets containing contaminated Great Lakes fish (Leatherland and Sonstegard 1982; Hilton *et al.* 1983) failed to develop hyperplastic goiters. Historically, low iodine has been considered responsible for endemic (hyperplastic) goiters in humans and fish in the Great Lakes region and the hyperplasia in fish prior to organochlorine contamination could be reversed by the administration of either thyroid preparations or iodine (Marine and Lenhart 1914; LaRoche 1952).

[1] To whom correspondence should be addressed

The lack of a hyperplastic effect in the recent feeding studies (Leatherland and Sonstegard 1980, 1982; Hilton *et al.* 1983) may be related to the use of hard, well water and mineral-supplemented diets which would assure a high iodine intake. Moccia *et al.* (1981) rebut the involvement of iodine deficiency by noting that sufficient iodine occurs in the Great Lakes to meet the biosynthetic requirements for thyroid hormones. Sonstegard and Leatherland (1976) argue that the incidence of goiters does not correspond with inter-lake differences in iodine levels. Also, the between-lake incidences of hyperplastic goiters in birds (Moccia *et al.* 1985) parallel those determined in fish (Moccia *et al.* 1981) indicating that physiological responses of fish involving the pituitary-thyroid axis during the spawning migration may be of minor significance.

The present studies were designed to investigate possible interactions between low iodine intake and the goitrogenic effects of organochlorine contaminants. Previous laboratory studies have revealed a variety of thyroid disorders in organochlorine exposed birds (Jefferies 1975) but the interaction with iodine insufficiency has not been examined in fish, birds, or mammals. A PCB congener was selected for these studies, because PCB levels in the Great Lakes' ecosystem have been predominant among the bioaccumulative organochlorine chemicals (Gilman *et al.* 1979; Durham and Oliver 1983) and are of particular concern with respect to natural avian populations (Roberts *et al.* 1978).

Materials and Methods

Ring doves, *Streptopelia risoria,* generously supplied by the Canadian Wildlife Service, were held under controlled aviary conditions of 19–23°C and 14L:10D photoperiod. Birds of approximately four weeks of age and weighing 80–100 g were removed from parental cages and raised for five months on semi-purified diets plus distilled-deionized water, *ad libitum*. The diets were formulated according to the standard reference diet for poultry (US, NRC 1977) with the exception that reagent grade NaCl replaced iodized salt. The antioxidant ethoxyquin was omitted to circumvent possible effects on hormone metabolism. Fresh diets were prepared monthly in order to minimize degradation in the absence of the preservative. The basic diet mixture was divided into two parts and supplemented with either the minimum iodine requirement, 300 μg/kg, or a low concentration of iodine, 3 μg/kg, as KI. Preliminary studies demonstrated normal growth and reproduction on the full complement, semi-purified diet. The semi-purified diets were deemed to be free of naturally-occurring goitrogens which may occur in commercial and practical-type formulations.

Doves which had been raised to adult size, *i.e.*, approximately 160 g, on the experimental diets were given I.P. injections (0.16 ml) of corn oil or corn oil plus 3,4,3′,4′-tetrachlorobiphenyl (TCBP, Analabs, New Haven, CT) as a suspension. An acute study was conducted by dosing on day one with 0 or 60 μg TCBP/g body weight and sacrificing the birds seven days later by CO_2 inhalation. A 28-day study was conducted by dosing on days 1, 10, and 20 with 0 or 20 μg TCBP/g body weight. Using a complete block design, the experiment was conducted with three doves per replicate and two replicates per treatment.

Metabolic rate was estimated by direct calorimetry on days 21–26 of the 28-day study. The calorimeter consisted of a 32 × 32 × 60 cm stainless steel cage placed inside a thermally insulated chamber. Windows permitted behavioral observations and the maintenance of a normal photoperiod. Metabolic heat produced by the birds was transferred to water flowing at 10–12 ml/min through copper tubing located in the chamber ceiling. Thermistor probes monitored the inflowing (*i.e.*, approximately 12°C) and outflowing water and these temperatures were automatically recorded at 2-min intervals over a 24-hr period. Food and water were supplied *ad libitum* and air was exchanged at 100 ml/min. The calorimeter was not adiabatic and, consequently, the efficiency varied from 62% to 145% depending upon room temperature, water flow rate, and heat production rate. All data were corrected to 100% efficiency. A group of three doves were tested simultaneously in a given trial, and two trials were conducted for both the control and TCBP-exposed groups. Data for the period 2:00 am to 6:00 am were taken to represent the standard metabolic rate, because the doves were in a post-absorptive, inactive state under thermoneutral conditions.

Immediately following sacrifice, a pre-warmed thermistor probe was inserted under the keel into the liver-cardiac region and the maximum temperature recorded. Cardiac blood was collected and the serum stored at −100°C until analysis. Total thyroxine (TT_4) and total triiodothyronine (TT_3) were determined with Quantimune radioimmunoassay kits (Bio Rad Laboratories, Mississauga, Ontario, Canada), and T_3 resin uptake was measured with a Bio-Ria (Montreal, Quebec, Canada) radioimmunoassay kit. Standards provided with the TT_4 kit were diluted 50% with serum devoid of thyroid hormones in order to increase sensitivity. Hormone standards consisted of six serum concentrations in the ranges 0–100 ng/ml and 0–10 ng/ml for TT_4 and TT_3, respectively. The T_3 uptake standards were 25.6%, 31.9%, and 41.3%. A single RIA kit was used for each type of assay to circumvent possible inter-assay variation. The intra-assay coefficient of variation on ten replicate samples was 4.8%, 5.1%, and 5.9% for TT_4, TT_3, and T_3 uptake, respectively.

The condition of the thyroid glands was assessed by light microscopy. The glands were excised, weighed, fixed in Bouin's solution, embedded in parrafin, and 4μ sections stained with haematoxylin and eosin. Colloid diameters were measured in all follicles of three sections randomly selected from each gland. (Epithelia cell heights could not be accurately measured due to epithelial flattening in the normal iodine control doves). Body weights and food consumption were measured every 2–3 days. Food consumption was estimated by offering a specified weight of food to the doves and measuring the unconsumed portion 2–3 days later.

The data were first evaluated by 2-factor (diet X toxicant) analysis of variance in which the significance criterion was $P \leq 0.05$. When variance was significant, specific comparison of means was accomplished by a Dunnett's test (Zar 1974) at $P \leq 0.05$. No significant deviations from normality were detected in the data following analysis by the Kolmogorov-Smirnov test (Campbell 1974).

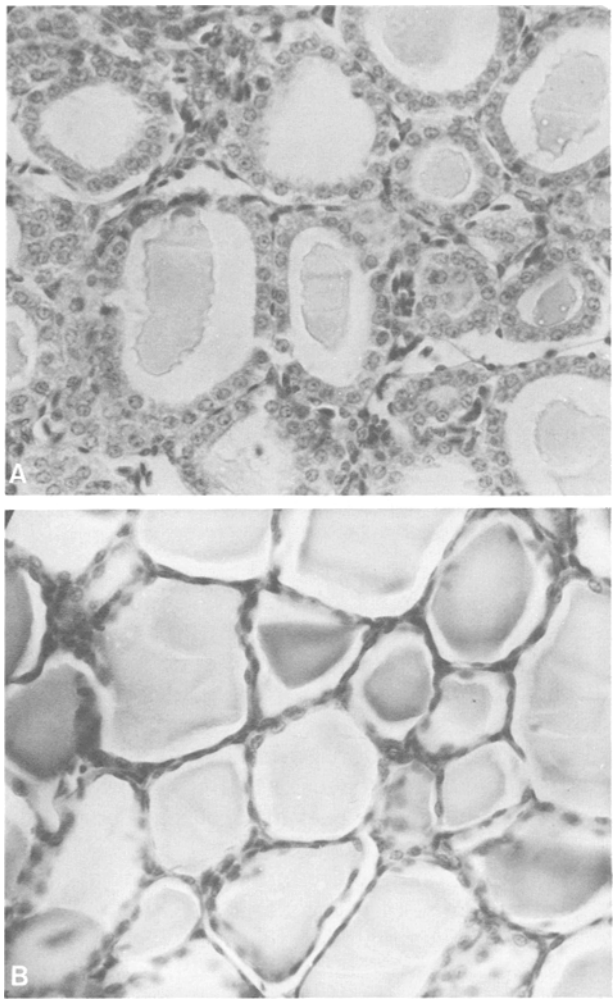

Fig. 1. Thyroid follicles from doves fed a low iodine, semi-purified diet. Controls **(a)** were mildly hyperplastic with cuboidal or slightly elongated epithelia and small colloid diameters. Exposure to 60 μg/g TCBP at 7 days **(b)** resulted in larger colloid diameters and low cuboidal or flattened epithelia. Magnified 340×.

Results and Discussion

Classical histologic investigations in avian species have demonstrated that iodine deficiency causes a hyperplastic appearance of the thyroid gland (Creek *et al.* 1957). In the acute study, the thyroid follicles from the low iodine doves were mildly hyperplastic with cuboidal or elongated epithelia and small colloid diameters (Figure 1a). This profile is typical of an active avian thyroid (Astier 1980) and was interpreted to mean that iodine intake was insufficient for the storage of substantial amounts of thyroglobulin colloid. The histologic profile is also consistent with mild hyperplasia due to increased thyroid-stimulating hormone (TSH) activity (Collins and Capen 1980). The condition of the low iodine doves may be described as euthyroidism, because the diet did not alter growth rate core body temperature, serum TT_4, TT_3 or $\%T_3$ uptake (Table 1).

The thyroid glands of doves receiving the low iodine diet and exposed to TCBP were observed to have large colloid follicles while the epithelial cells were dramatically diminished and in some cases flattened (Figure 1b). The follicle enlargement was statistically significant and explains the significant increase in thyroid weight (Table 1). The histology of the low iodine exposed group is characteristic of the inactive, or slightly active, avian thyroid (Astier 1980). These histologic changes were accompanied by a small but significant decrease in core body temperature, and significant decreases in serum TT_4 and TT_3 (Table 1). Thus, the low iodine euthyroidism changed to hypothyroidism in the exposed doves presumably owing to decreased conversion of thyroglobulin to T_4 and T_3. The condition of the exposed doves is consistent with large-colloid goiter as occurs with decreased TSH influence on the thyroid (Turner and Bagnara 1976).

On the normal iodine diet, the thyroid glands were significantly larger than those of the low iodine controls owing principally to larger colloid diameters (Table 1, Figure 2). Epithelia were flattened, such that the nuclei protruded from the cell surface toward the follicle centers. Thyroid sections from normal diet controls and normal diet exposed groups were virtually indistinguishable, although serum TT_4 and TT_3 were significantly less in the exposed group (Table 1). Core body temperature showed a tendency to decrease, but the change was not statistically significant (Table 1).

In the 28-day study, thyroid follicles from both the normal and low iodine diet controls were as described for the acute study. Thyroid weight and colloid diameters were significantly different between the diets, but no effect of the toxicant could be distinguished histologically. The only significant effect associated with TCBP exposure was decreased serum TT_4 at both dietary levels of iodine (Table 2). Body weight and food consumption were unaffected. The fact that TCBP did not significantly alter core body temperature or metabolic rate (Table 2) indicates that a hypothyroid condition did not develop despite the TT_4 decrease. One may speculate that the doves compensated for decreased TT_4 over the 28-day period, or that toxicant-related oxidative metabolism was thermogenic to the point of balancing the decreased TT_4 activity.

The present experiments have demonstrated that

Table 1. Effect of acute, 7-day exposure to 3,4,3′,4′-tetrachlorobiphenyl on the thyroid status of doves maintained on semi-purified diets

	Normal iodine diet		Low iodine diet	
	Controls	Exposed	Controls	Exposed
Serum thyroxine (ng/ml)	38.8 ± 1.2[a]	24.6 ± 0.6[b]	32.8 ± 3.4	23.0 ± 2.5[b]
Serum triiodothyronine (ng/ml)	3.05 ± 0.10	2.28 ± 0.09[b]	3.10 ± 0.11	2.23 ± 0.15[b]
Triiodothyronine resin uptake (%)	49.6 ± 1.5	41.6 ± 1.8	49.3 ± 1.7	41.2 ± 5.6
Thyroid weight (mg)	8.6 ± 0.5	9.8 ± 1.3	6.3 ± 0.5	9.6 ± 1.1[c]
Core body temperature (°C)	41.82 ± 0.08	41.54 ± 0.14	41.75 ± 0.08	41.34 ± 0.12[c]
Colloid diameter (μ)	81.0 ± 3.6	79.7 ± 4.2	56.6 ± 3.1	78.3 ± 4.4[c]

[a] Mean ± SEM; n = 6 doves per treatment group
[b] Significantly less than pair-fed controls; Dunnett's t-test; one-tailed; $P \leq 0.05$
[c] Significantly different from pair-fed control; Dunnett's t-test; two-tailed; $P \leq 0.05$

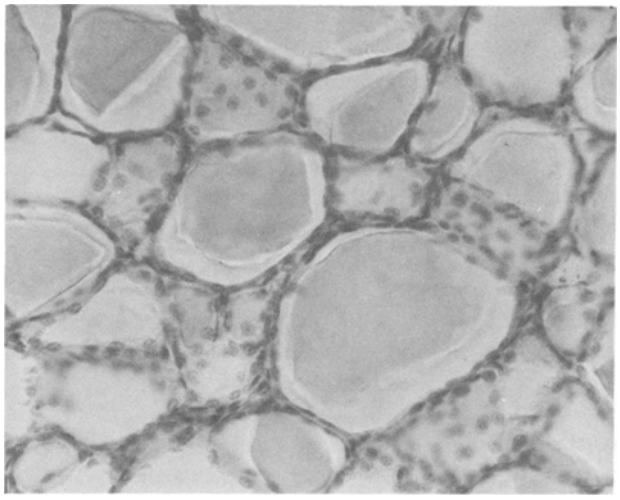

Fig. 2. Thyroid follicles from control doves fed a normal iodine, semi-purified diet were composed of large colloid areas and flattened epithelia. Magnified 340×.

mild thyroid hyperplasia produced by insufficient iodine was reversed within seven days following acute exposure to the PCB congener. The combined action of TCBP and low iodine upon thyroid histology was therefore antagonistic, presumably due to opposite influences upon the TSH feedback system. Extrapolating from these experiments, one may predict this type of antagonism in the case of any organochlorine chemical which potentially causes large-colloid goiter. Conversely, one may predict that hyperplasia caused by any organochlorine chemical would be more severe under conditions of low iodine intake.

A summary of organochlorine effects upon thyroid histology reveals that PCBs caused large-colloid goiters in species closely related to the herring gull (Table 3). Therefore, it is unlikely that PCBs, or the combined influences of PCBs and low iodine, are responsible for thyroid hyperplasia reported in Great Lakes herring gulls by Moccia *et al.* (1985). Table 3 shows that the literature pertaining to birds is contradictory in the cases of DDT and DDE which have accumulated to relatively high levels in Great Lakes herring gulls (Gilman 1979; Mineau *et al.* 1984). The only study conducted using dieldrin in an avian species demonstrated thyroid hyperplasia. Thus, low dietary iodine might be expected to enhance hyperplasia if it were caused by dieldrin. Significant levels of dieldrin have accumulated in herring gulls of the Great Lakes (Gilman 1979; Mineau *et al.* 1984).

Organochlorine chemical effects on fish thyroid histology have not been demonstrated in laboratory studies (Table 3).

In the case of mammals, the situation is distinct from that in birds. Studies with rats using a variety of organochlorine compounds have consistently resulted in thyroid hyperplasia (Table 3). Accordingly, mammalian species exposed to organochlorine mixtures may develop more severe hyperplasia under conditions of low iodine intake compared with iodine sufficiency. Qualitative differences in response to goitrogens between birds and mammals have been noted by other investigators (Newcomer 1967; Leung and March 1975) but the reason for these differences is unknown at present.

Table 2. Effect of a 28-day exposure to 3,4,3′,4′-tetrachlorobiphenyl on the thyroid status of doves maintained on semi-purified diets

	Normal iodine diet		Low iodine diet	
	Controls	Exposed	Controls	Exposed
Standard metabolic rate (KJ/hr)	4.75 ± 0.05[a]	4.85 ± 0.05	4.83 ± 0.06	4.83 ± 0.09
Serum thyroxine (ng/ml)	36.8 ± 3.2	27.8 ± 2.1[b]	33.4 ± 3.4	25.8 ± 1.7[b]
Serum triiodothyronine (ng/ml)	3.00 ± 0.23	2.69 ± 0.22	3.06 ± 0.10	2.81 ± 0.21
Triiodothyronine resin uptake (%)	48.1 ± 3.5	51.8 ± 1.2	49.0 ± 1.3	48.8 ± 4.2
Thyroid weight (mg)	9.2 ± 0.5	8.3 ± 1.4	6.6 ± 0.7[c]	6.9 ± 0.9[c]
Core body temperature (°C)	41.79 ± 0.09	41.98 ± 0.14	41.73 ± 0.09	41.66 ± 0.88
Colloid diameter (μ)	82.5 ± 4.7	80.3 ± 5.2	52.7 ± 3.9[c]	58.3 ± 7.0[c]

[a] Mean ± SEM; n = 6 doves per treatment group
[b] Significantly less than pair-fed controls; Dunnett's t-test; one-tailed; $P \leq 0.05$
[c] Significantly different from corresponding normal iodine groups; Dunnett's t-test; two-tailed; $P \leq 0.05$

Table 3. Comparison of organochlorine chemical effects on thyroid histology between animal classes

Class	Species	Chemical[a]	Thyroid histology	Source
Osteichthyes	Rainbow trout *Salmo gairdneri*	PCBs	No effect	Leatherland and Sonstegard (1979, 1980)
	Rainbow trout *Salmo gairdneri*	Mirex	No effect	Leatherland and Sonstegard (1979, 1980)
Aves	Rock doves *Columbia livia*	DDT	Hyperplastic	Jefferies and French (1969, 1971)
	Quail *Coturnix coturnix*	DDT	Large-colloid	Richert and Prahlad (1972)
	Quail *Coturnix coturnix*	DDE	Large-colloid	Richert and Prahlad (1972)
	Rock doves *Columbia livia*	DDE	Hyperplastic	Jefferies and French (1972)
	Quail *Coturnix coturnix*	DDA	No effect	Richert and Prahlad (1972)
	Rock doves *Columbia livia*	Dieldrin	Hyperplastic	Jefferies and French (1972)
	Black backed gull *Larus fuscus*	PCBs	Large-colloid	Jefferies and Parslow (1972)
	Guillemots *Uria aalge*	PCBs	Large-colloid	Jefferies and Parslow (1976)
Mammalia	Rats	Dieldrin	Hyperplastic	Wassermann *et al.* (1972)
	Rats	PCBs	Hyperplastic	Collins and Capen (1980)
	Rats	PBBs	Hyperplastic	Akoso *et al.* (1982)
	Rats	Photomirex	Hyperplastic	Chu *et al.* (1981)
	Rats	2,3,7,8-Dioxin	Hyperplastic? (loss of colloid, exfoliated epithelia)	Gupta *et al.* (1973)

[a] PCBs = polychlorobiphenyls; PBBs = polybromobiphenyls
Mirex = Dodecachlorooctahydro-1,3,4-metheno-2*H*-cyclobuta(cd) pentalene
Photomirex = a toxic breakdown product of mirex formed by exposure to sunlight
DDT = Dichlorodiphenyltrichloroethane
DDE = 2,2-bis-(*p*-chlorophenyl)-1,1-dichloroethylene
DDA = Bis-(*p*-chlorophenyl) acetic acid
Dieldrin = 1,2,3,4,10,10-hexachloro-*exo*-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo*-*exo*-5,8,-dimethanonaphthalene
2,3,7,8-Dioxin = 2,3,7,8-tetrachlorodibenzo-*p*-dioxin

Acknowledgments. The authors express their gratitude to Dr. D. B. Peakall and G. A. Fox of the Canadian Wildlife Service for interest in this project and to R. D. Moccia for his enthusiastic encouragement. Special thanks to S. Barleban for technical assistance and Dr. J. C. Fenwick (University of Ottawa) for providing comments on the manuscript. The research was funded by Environment Canada Contract #KN107-2-4173 awarded to T. W. Moon.

References

Akoso BT, Sleight SD, Nachreiner RF, Aust SD (1982) Effects of purified polybrominated biphenyl congeners on the thyroid and pituitary glands in rats. J Am Coll Toxicol 1:23–36

Astier H (1980) Thyroid gland in birds: Structure and function. In: Epple A, Stetson MH (eds) Avian Endocrinology. Academic Press, New York, pp 167–189

Bastomsky CH (1977) Enhanced thyroxine metabolism and high uptake goiters in rats after a single dose of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Endocrinol 101:292–296

Bastomsky CH, Murthy PVN (1976) Enhanced *in vitro* hepatic glucuronidation of thyroxine in rats following cutaneous application or ingestion of polychlorinated biphenyls. Can J Physiol Pharmacol 54:23–26

Black JJ, Simpson CL (1974) Thyroid enlargement in Lake Erie coho salmon. J Nat Cancer Inst 54:725–730

Campbell RC (1974) Statistics for biologists. 2nd Ed. Cambridge University Press, London

Chu I, Villeneuve DC, Valli VE, Secours VE, Becking C (1981) Chronic toxicity of photomirex in the rat. Toxicol Appl Pharmacol 58:268–278

Collins WT, Capen CC (1980) Biliary excretion of ^{125}I-thyroxine and fine structural alterations in the thyroid glands of Gunn rats fed polychlorinated biphenyls (PCBs). Lab Invest 43:158–164

Creek RD, Parker HE, Hauge SM, Andrews FN, Carrick CW (1957) The iodine requirements of young chickens. Poult Sci 36:1360–1365

Drongowski RA, Woods JS, Bouck GR (1975) Thyroid activity in coho salmon from Lake Oregon and Lake Michigan. Trans Amer Fish Soc 2:349–352

Durham RW, Oliver BG (1983) History of Lake Ontario contamination from the Niagara River by sediment radiodating and chlorinated hydrocarbon analysis. J Great Lakes Res 9:160–168

Gilman AP, Peakall DB, Hallett DJ, Fox GA, Norstrom RJ (1979) Herring gulls (*Larus argentatus*) as monitors of contamination in the Great Lakes. In: Nielsen SW, Migaki G, and Scarpelli DG (eds) Animals as monitors of environmental pollutants. Nat Acad Sci, Washington, DC p 280

Gupta BN, Vos JG, Moore JA, Zinkl JG, Bullock BC (1973) Pathologic effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in laboratory animals. Environ Health Perspect 5:125–140

Hilton JW, Hodson PV, Braun HE, Leatherland JL, Slinger SJ (1983) Contaminant accumulation and physiological response in rainbow trout, *Salmo gairdneri*, reared on naturally contaminated diets. Can J Fish Aquat Sci 40:1987–1994

Hurst JG, Newcomer WS, Morrison JA (1974) Some effects of DDT, toxaphene, and polychlorinated biphenyl on thyroid function in bobwhite quail. Poult Sci 53:125–133

Jefferies DJ (1975) The role of the thyroid in the production of sublethal effects by organochlorine insecticides and polychlorinated biphenyls. In: Moriarty F (ed) Organochlorine insecticides: Persistent organic pollutants. Academic Press, New York, Chapt. 4, pp 131–230

Jefferies DJ, French MC (1969) Avian thyroid: Effect of *p'p*-DDT on size and activity. Science 166:1278–1280

——— (1971) Hyper- and hypothyroidism in pigeons fed DDT: An explanation for the thin eggshell phenomenon. Environ Pollut 1:235–242

——— (1972) Changes induced in the pigeon thyroid by *p'p*-DDE and dieldrin. J Wildl Manag 36:24–30

Jefferies DJ, Parslow JLF (1972) Effect of one polychlorinated biphenyl on size and activity of the gull thyroid. Bull Environ Contam Toxicol 8:306–310

——— (1976) Thyroid changes in PCB-dosed guillemots and their indication of one of the mechanisms of action of these materials. Environ Pollut 10:293–311

LaRoche G (1952) Effets de préparations thyroidiennes et d'iodures sur le goitre ("pseudo-cancer") des salmonides. Rev Can Biol 11:439–445

Leatherland JF, Sonstegard RA (1977) On the effect of dietary mirex or PCB (Aroclor 1254®) on serum thyroxine (T_4) and triiodothyronine (T_3) levels in rainbow trout. Acta Endocrinol 212:234

——— (1978) Lowering of serum thyroxine and triiodothyronine levels in yearling coho salmon, *Oncorhynchus kisutch*, by dietary mirex or PCBs. J Fish Res Board Can 35:1285–1289

——— (1979) Effect of dietary mirex and PCB (Aroclor 1254®) on thyroid activity and lipid reserves in rainbow trout, *Salmo gairdneri*, Richardson. J Fish Diseases 2:43–48

——— (1980) Effect of dietary mirex and PCBs in combination with food deprivation and testosterone administration on thyroid activity and bioaccumulation of organochlorines in rainbow trout *Salmo gairdneri* Richardson. J Fish Diseases 3:115–124

——— (1982) Bioaccumulation of organochlorines by yearling coho salmon (*Oncorhynchus kisutch* Walbaum) fed diets containing Great Lakes coho salmon, and the pathophysiological responses of the recipients. Comp Biochem Physiol 72C:91–99

Leung P, March BE (1975) The thyroidal response to chronic goitrogenic stimulation and the persistence of effects of early goitrogenic stimulation. Can J Physiol Pharmacol 54:583–589

Marine D, Lenhart CH (1914) Further observations and experiments on goitre (so-called thyroid carcinoma) in brook trout (*Salvelinus fontinalis*). J Exp Med 19:70–88

Mineau P, Fox GA, Norstrom RJ, Weseloh DV, Hallett DJ, Ellenton JA (1984) Using the herring gull to monitor levels and effects of organochlorine contamination in the Canadian Great Lakes. In: Nriagu JO and Simmons MS (eds) Toxic contaminants in the Great Lakes. J. Wiley and Sons, New York, p 425

Moccia RD, Leatherland JF, Sonstegard RA (1981) Quantitative interlake comparison of thyroid pathology in Great Lakes coho (*Oncorhynchus kisutch*) and chinook (*Oncorhynchus tschawytscha*) salmon. Cancer Res 41:2200–2210

Moccia RD, Fox GA, Britton A (1985) Quantitative assessment of thyroid histopathology in Great Lakes herring gulls (*Larus argentatus*). J Wildl Diseases. In press

Newcomer WS (1967) Transport of radioiodide between blood and thyroid of chickens. Amer J Physiol 212:1391–1396

Richert EP, Prahlad KV (1972) Effects of DDT and its metabo-

lites on the thyroid of Japanese quail, *Coturnix coturnix japonica*. Poult Sci 51:196–200

Roberts JR, Rodgers DW, Bailey JR, Rorke MA (1978) Polychlorinated biphenyls: Biological criteria for an assessment of their effects on environmental quality. Nat Res Counc Can, NRCC No 18574

Sonstegard RA, Leatherland JF (1976) The epizootiology and pathogenesis of thyroid hyperplasia in coho salmon (*Oncorhynchus kisutch*) in Lake Ontario. Cancer Res 36:4467–4475

Turner CD, Bagnara JT (1976) General endocrinology. 6th ed, WB Saunders, London

US NRC (1977) Nutrient requirements of poultry. Nat Acad Sci, Washington, DC, p 62

Villeneuve DG, Valli VE, Norstrom RJ, Freeman H, Sangalang GB, Ritter L, Becking GC (1981) Toxicological response of rats fed Lake Ontario or Pacific coho salmon for 28 days. J Environ Sci Health, Part B, Pestic Food Contam Agric Wastes 16:649–689

Wassermann M, Wassermann D, Kedar E, Djavaherian M, Cucos S (1972) Effects of dieldrin and gamma BHC on serum proteins and PBI. Bull Environ Contam Toxicol 8:177–185

Zar JH (1974) Biostatistical Analysis. Prentice-Hall, New Jersey

Manuscript received December 18, 1984 and in revised form April 15, 1985.