PCB's AND THEIR ENVIRONMENTAL EFFECTS

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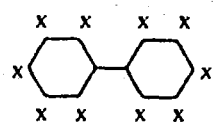
1. INTRODUCTION

Hutzinger et al. recently reviewed the chemistry of PCB's. In their preface these authors state, "Opinions on the importance of these ubiquitously distributed industrial compounds, however, still vary greatly. The authors do not wish to enter this discussion." In this article, an attempt is made to assess the biological impact of these materials, both on man and other creatures that inhabit this planet. The information on the production and usages of these materials is briefly reviewed, followed by a more detailed look at levels found in various types of organisms in various parts of the world. This information is used to consider the routes and rates of transfer of these materials through the ecosystem and their biological magnification during these processes. The physiological effects of PCB's are then considered, and their likely importance is assessed by comparison with existing environmental levels.

The picture is complicated by the fact that we are not dealing with a single compound. The basic structure of PCB's is:



where any of the positions marked with x can be substituted by chlorine. The physical properties of PCB's have been described in detail elsewhere.[1] In brief, they are chemically inert, are not hydrolyzed by water, and resist alkalies, acids, and other corrosive chemicals. They have low volatility, their boiling points ranging from 278°C for Aroclor 1221 to 415°C for Aroclor 1268.[2] All are stable to prolonged heating at 150°C. The solubility of PCB's in water is very low, and is high in hydrocarbon solvents. The degree of chlorination is expressed by the number following the trade names. For the Aroclor series the last two digits give the percentage of chlorine. The Japanese and American equivalents are given in Table 1.

2. PRODUCTION OF PCB'S

Detailed figures on production and usages of PCB are only available for the U.S. (Table 2) and Japan (Table 3). Additionally, PCB's are known to be manufactured in Germany (Bayer), France (Prodelec), Italy (Caffaro), U.S.S.R. (Sovol) and Czechoslovakia (Chemko), although production figures are not available.[1] In 1970 the combined production of Japan and the U.S. was 107 million pounds, and the total world production can be estimated at 150 to 200 million pounds. This is

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TABLE 1

American and Japanese Trade Names of PCB's and Their Degree of Chlorination

American trade name	Japanese trade name	% Chlorine	Main components
Aroclor 1232	Kanechlor-200	32	dichlorinated
Aroclor 1242	-300	42	trichlorinated
Aroclor 1248	-400	48	tetrachlorinated
Aroclor 1254	-500	54	pentachlorinated
Aroclor 1260	-600	60	hexachlorinated

probably half the maximum production of DDT that occurred in the late 1960s.

The figures in Table 2 reflect the restrictions placed on the usages of PCB's by Monsanto, and currently PCB's are sold only to the electrical industry for use in closed systems as a dielectric fluid in transformers and capacitors.

3. TRANSPORT OF PCB'S IN THE ENVIRONMENT

The basic document for this section is the analysis made by Nisbet and Sarofim,[3] although an attempt is made to update in the light of more recent research and the restrictions placed on the usage of PCB's. These workers made the following assumptions on the useful life of objects containing PCB's:

A. The rate at which capacitors are discarded, primarily into landfill dumps, is equal to half the rate of production.

B. Ten percent of sales of transformer fluid is to replace scrapped oil.

C. The rate of vaporization of plasticizer amounts to 10 to 20% of sales.

D. The rate of disposal of plasticizers into dumps is equal to the residual 80 to 90% of sales.

Using these assumptions Nisbet and Sarofim calculated gross estimates of the rates of input and accumulation of PCB's in North America in 1970 (Table 4). Starting in 1970, restrictions were placed by Monsanto (the sole U.S. producer) to reduce the environmental input of PCB's. The use of PCB's in pesticide formulations was discontinued in early 1970 although evidence suggests that this was a minor use. Later in 1970, sales of PCB's for plasticizers, surface coatings, and adhesives were stopped. The main uses now are in sealed electrical transformers and capacitors and in heat transfer systems. Monsanto has made arrangements to destroy spent PCB fluid and destroyed 2.2×10^3 metric tons in 1973 and 1.2×10^3 metric tons in 1974.[4] On the basis of these changes in use patterns, the inputs and accumulations have been recalculated for 1974 (Table 4). Since PCB's have not been used as plasticizers for three years, the input from the vaporization from this source should now be negligible. Vaporization from open burning is dependent on the amount of PCB's reaching the site, and it is arbitrarily assumed that this is decreasing at a rate of 20% per year.

Nisbet and Sarofim[3] estimated that 1.5 to 2×10^3 metric tons per year of PCB's were vaporized into the atmosphere in 1970. Now it is likely that the amount has decreased by an order of magnitude since the major source, vaporization from plasticizers, has been removed.

Maugh[5] reported on the possibility that PCB's could be formed from DDT under the influence of UV light. It was pointed out earlier[6] that this would only be expected to lead to dichlorobiphenyls which are not normally found in environmental systems.

Nisbet and Sarofim[3] calculated that the total input of PCB's into the seas around North America, mainly into the Atlantic, has been 1.5×10^4 tons. This figure can be compared to the global value calculated for DDT of 5×10^5 tons.[7] On an annual basis, the fluxes into the North Atlantic would be 5×10^3 tons for PCB's and 25×10^3 tons for DDT. Using the latter figure, the SCEP (Study of Critical Environmental Problems) calculates a figure of 5 ng/l for DDT in the surface mixed layer assuming a residence time of 5 years. These calculations are based on the production and usage patterns of the late 1960s, and in North America these have changed considerably in the last 5 years. Seba and Corcoran[8] measured levels of organochlorine pesticides in surface slicks and sea water in 1968. They found values ranging from

TABLE 2

PCB Production and Usage in the U.S. (Metric Tons)

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PCB Production and Usage in the U.S. (Metric Tons)

	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Domestic use by category																	
Heat transfer	–	–	–	–	–	78	291	464	618	883	1,131	1,264	1,525	1,979	1,530	376	–
Hydraulics/lubricants	806	775	1,342	1,262	2,055	1,957	1,973	2,187	2,308	2,129	2,322	2,883	4,020	3,701	776	–	–
Miscellaneous industrial	352	378	784	779	1,057	847	764	846	920	889	713	642	540	813	577	–	–
Transformer	6,478	2,859	2,992	3,960	3,147	3,992	3,645	3,998	4,328	4,455	5,535	5,792	6,052	6,914	5,567	12,828	18,871
Capacitor	8,514	7,050	8,250	8,483	7,968	7,691	7,803	9,770	11,874	14,442	14,851	14,775	12,511	13,354	7,070		
Plasticizer applications	*	1,969	2,286	3,722	4,549	4,462	4,590	5,168	5,848	6,740	6,680	7,202	8,230	9,768	1,630	–	–
Petroleum additives	–	–	–	–	–	–	–	–	–	–	–	–	719	–	–	–	–
Domestic use by PCB grade																	
Aroclor 1221	11	8	127	52	47	70	181	298	185	264	221	68	254	738	1,107	85	18
Aroclor 1232	98	57	120	77	120	112	6	6	4	8	12	45	136	130	85	–	–
Aroclor 1242	9,111	5,222	6,799	9,098	9,973	10,327	9,255	11,785	15,762	19,778	21,527	22,427	22,745	24,294	10,990	364	3,100
Aroclor 1248	889	1,279	1,692	1,414	2,072	1,731	2,506	2,619	2,782	2,507	2,352	2,447	2,825	2,036	106	404	–
Aroclor 1254	2,230	3,345	3,377	3,044	3,147	3,162	2,955	3,740	3,864	3,517	3,348	4,445	4,911	6,210	2,330	1,747	3,988
Aroclor 1260	3,793	2,997	3,370	3,665	3,270	3,297	3,813	4,267	2,915	2,937	3,208	2,626	2,220	2,445	864	152	–
Aroclor 1262	76	92	179	163	180	276	207	223	279	384	420	360	356	512	1	–	–
Aroclor 1268	–	36	51	94	79	105	142	95	98	142	144	140	150	165	–	–	–
Aroclor 1016	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1,667	10.451	11,765
Production	*	*	*	18.960	18.257	19,176	22,367	25,416	30,240	32,924	37,654	62,427	38,194	42,527	17,497	19,300	21,089
Domestic sales	16,149	13,030	15,655	17,604	18,769	19,021	19,066	22,434	25,898	29,539	31,233	32,558	33,597	36,530	17,150	13,204	18,87
Export	**	**	**	**	**	**	1,823	2,048	2,117	3,426	4,062	5,615	5,312	6,825	–	3,194	4,173

*Production figures and plasticizer applications figures available during year indicated.
**U.S. export sales figures unavailable during year indicated.

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TABLE 3

PCB Production and Usage in Japan (Metric Tons)

Domestic use by cagetory	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
Electrical apparatus	760	740	1,060	1,320	1,860	1,640	1,270	1,920	1,990	2,600	2,370	2,830	4,220	5,960	4,560
Heat transmitter	80	100	120	170	180	240	240	400	450	660	730	720	1,290	1,890	1,920
Copy paper	–	–	–	–	–	10	30	100	170	300	390	780	1,320	1,920	350
Other uses	30	40	80	150	180	200	170	210	240	270	270	260	330	360	100
Production	820	980	1,260	1,640	2,220	2,190	1,810	2,670	3,000	4,410	4,480	5,130	7,730	11,110	6,780
Imports	–	–	–	–	–	–	–	–	–	–	60	100	110	150	170
Exports	–	–	–	–	–	100	100	40	160	580	720	540	590	1,000	730

Adapted from Fujiwara, K., *Report, Department of Hygienic Chemistry*, Kyoto City Institute, Kyoto, Japan, 1974.

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TABLE 4

Estimates of Rates of Input and Accumulation of PCB's in North America in 1970* and 1974** (Metric Tons)

	1970	1974	
Vaporization of plasticizers	$1-2 \times 10^3$	Negligible	Mainly 1248 to 1260
Vaporization during open burning	4×10^3	1.5×10^3†	
Leaks and disposal of industrial fluids	$4-5 \times 10^3$	$4-5 \times 10^3$††	
Destroyed by incineration and open burning	3×10^3	1.2×10^3†	
Disposal in dumps and landfills	1.8×10^4	7×10^3	
Accumulation in service	7×10^3	4×10^3	

*From Nisbet, I. C. T. and Sarofim, A. F., *Environ. Health Perspect.*, 1, 21, 1972.
**Calculated from the assumptions of Nisbet and Sarofim, see text.
†Assuming 20%/year decrease in PCB reaching open burning.
††Assumed to have decreased an order of magnitude. Partially due to collection by Monsanto and partially due to greater awareness and many fewer firms handling the material.

80 ng/l some 25 miles off the Florida coast to a maximum of 12.7 μg/l in Biscayne Bay. No DDT compounds were detected in sea water, limit of detection was 1 ng/l. PCB's were not mentioned and presumably not examined for. Hartung and Klingler[9] found that the partitioning coefficient for p,p'-DDT between oil and water is around 10^6. Finding that the level in sea water was below 1 ng/l is not surprising in view of the levels in oil slicks even though equilibrium may well not be complete. The data in Table 4 confirm the low levels of DDT in the upper mixed layer, although by 1971 the usage of DDT had markedly declined in North America.

Current evidence suggests that the bulk of DDT transferred to the ocean is not dissolved in the upper mixed layer, nor is it present in aquatic organisms. It appears that DDT is sedimented, degraded beyond DDD or DDE, or co-distilled back into the atmosphere. At present there is little evidence on which to evaluate the relative importance of these mechanisms.

The levels of PCB's are most interesting. The values for 1971 and 1972 (Table 5) are much higher than would be predicted by calculation along the lines of the SCEP report. If one multiplies their value for DDT by the ratio of estimated amounts of transfer of PCB and DDT, one comes up with a figure of 1 ng/l ($5 \text{ ng/l} \times \frac{5 \times 10^3}{25 \times 10^3}$). Then the figures show a rapid decline to about 1/30th of the earlier values. This shows that the levels in the upper mixed layer are in much more rapid equilibrium with atmospheric values than was previously indicated. In making these calculations one has to bear in mind that these measurements are close to the limit of analytical capability, and suggestions have been made[10] that many substances as yet unidentified may be included in the analysis and may introduce serious errors. The basic question is the accuracy of these figures. While it is not possible to check the actual determinations, it is possible to calculate the implications of accepting figures. If an area for the North Atlantic is 5,000 km^2, then the volume of the upper mixed layer (100 m) would be 25×10^{20} ml. Assuming Harvey et al.'s value is 30×10^{-12} g/ml,[28] then the amount in this layer of the North Atlantic would be 7.5×10^{10} g or approximately 10^5 metric tons. This figure is high as compared with the calculated annual flux to the total production of PCB's. The PCB found in sea water is of the 1254 pattern; the maximum annual usage of which is only 6×10^3 metric tons. Even if higher Aroclors are included, the figure would be 10^4 metric tons. Thus, the indications are that the determinations of Harvey et al. are too high.

Bidleman and Olney[11] show that the levels of PCB's in the surface microlayer (150 μm) is

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TABLE 5

PCB and DDT Concentrations in North Atlantic Surface Waters, 1971 to 1974

Date	Mean PCB ng/l	Mean DDT ng/l	DDT/PCB	Area	Reference
August 1971	25	n.s.	–	Iceland – Newfoundland	Olney and Quinn cited in Harvey et al., 1973.[28]
July 1972	41	< 1	< 0.02	Newfoundland – Portugal	Harvey et al., 1973.[28]
August 1972	36	< 1		Portugal – Norwegian Sea	
September 1972	30	< 1	< 0.03	Massachusetts – Bermuda	
April 1973	1	< 0.15	< 0.15	Sargasso Sea	Olney and Quinn, 1974.[29]
September 1973	2	< 1	< 0.5	Azores to Barbados	Harvey et al., 1974.[30]
September 1973	0.8	n.s.	–	Sargasso Sea - New York	
February 1974	0.8	n.s.	–	New England continental shelf	

n.s. – not stated.

substantially higher than subsurface water (30 cm). The surface, even in the absence of visible slicks, is an area of high concentration of organic materials.[16] The information on PCB levels in sediments is confined to areas near sources of direct contamination. Hom et al.[13] made an analysis of PCB and DDE in a dated core from the Santa Barbara Basin of the coast of California. They found that PCB deposition started about 1945, and that the rate of deposition in 1967 was 1.2×10^{-4} g/m^2/year. Holden[14] and Halcrow et al.[15] have found PCB's in sludge and marine sediments near to dumping areas off the coasts of Great Britain. Linko et al.[16] found residue levels of 0.01 ppm in sediments in the Baltic, and Dexter and Pavlou[17] found residue levels* up to 0.7 ppm in sediments near Athens. An experiment of great interest would be to examine dated core samples from the North Atlantic remote from direct sources of contamination. Such measurements would enable us to balance the transport figures for both PCB's and DDT in the environment. The higher DDT/PCB ratios in the Pacific correlate with the findings of Bevenue et al.[18] who found DDT in all rain water samples collected on Hawaii during 1971–1972 but did not detect any PCB's. However, it should be pointed out that the sensitivity of PCB detection is considerably less than for DDT. Bidleman and Olney[11] measured the levels of PCB's and DDT in air, the surface microlayer, and subsurface water in the Sargasso Sea. The DDT/PCB ratios were low, typically 0.1 to 0.004, which is in line with the low levels reported in zooplankton over a wide area of the North Atlantic,[19] which was considered by Nisbet and Sarofim to be the major discrepancy of the DDT/PCB ratio data.

A recent review[20] points out that degradation products have not been identified for PCB's in aquatic systems, and the relative importance of degradation and sedimentation remains to be assessed.

Soedergren[21] examined the levels of chlorinated hydrocarbons collected in nylon nets at several sites in southern Sweden in 1970 and 1971. The geographical distribution of PCB and DDT was distinctly different, with PCB's showing high levels (up to 10,510 ng per m^{-2} per $month^{-1}$) in western Sweden and much lower levels (620 to 2190 ng per m^{-2} per $month^{-1}$) in eastern areas, whereas DDT shows little variation between sampling points. The higher residues in southwest Sweden presumably come from local Swedish industry with likely additions from Denmark and industrialized districts of West Germany.

Bidleman and Olney[11] tackled the problem of the relative importance of particulate matter and free molecular form. They found that filter-retained PCB were less than 2% from Bermuda of samples analyzed in 1973. A similar situation is found with the authors' values from Rhode Island[22], although Bidleman cautions that re-evaporation from the filter may increase the free value. Bidleman and Olney found values of 2.1 to 9.4 ng/m^3 for Rhode Island, 0.21 to 0.65 ng/m^3 for Bermuda, and 0.72 to 1.6 ng/m^3 for the Sargasso Sea. Their values are higher, by two orders of magnitude, than earlier work on organo-

*Residue levels are cited in parts per million (ppm) following usual convention. This is equivalent to μg/g.

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chlorines in this area,[23] but these workers collected samples using hanging nylon screens which only trapped PCB's attached to particulates. Eiichi and Ito[24] found values around 3 ng/m^3 in Nagoya, an industrial city in Japan. Current findings suggest that the atmospheric levels are higher and residence times shorter than suggested by previous work.

These findings do not invalidate the general conclusion[3,25] that the aerial route is much more important than run-off in transport of PCB's into the ocean. Recent studies have frequently failed to detect PCB's in rivers, i.e., Greve[26] in the Rhine, and Sampson[27] in major rivers and the Great Lakes of North America.

4. RESIDUE LEVELS

The aim of this section is to tabulate the levels of PCB's at various trophic levels in different parts of the world. No attempt at completeness is made, but selection is made to cover a range of trophic levels and as wide a geographic area as possible. Unfortunately, studies outside Europe, Japan, and North America are compartively few.

The environmental levels in five major groups of organisms are examined. These are: (1) plankton, (2) fish, (3) oceanic birds, (4) aquatic mammals, and (5) top avian predators. Additionally, levels in human food and in human beings are considered.

The levels of PCB's tend to parallel those of DDT and its major metabolite DDE. In the previous section on transport the movement of DDT was considered as a basis for comparison with PCB. A widely used expression of the relevant concentration is the ratio ΣDDT/PCB where ΣDDT is the sum of DDT and its metabolites.

A. PCB Levels in Planktons

Stringent precautions are necessary in the collection of plankton in order to achieve accurate results. Grice et al.[31] point out that as any ocean-going vessel is an abundant source of pollutants such as petroleum hydrocarbons and pesticides, the collection of uncontaminated samples for analysis is difficult. These workers give a list of precautions and consider that the internal consistency of the data should be carefully examined. Jensen et al.[32] clearly showed that samples collected in the wake of the boat are strongly contaminated with PCB's from the bottom paint. Additionally, these workers showed that the chromatographic pattern of PCB's of wake samples resembled the pattern of PCB's extracted from the paint, whereas the samples from the bow showed a different pattern. Harvey and Teal[33] have shown that plankton can extract absorbed hydrocarbons from the net, and further that the net is in equilibrium with hydrocarbon materials in the water, detritus, and plankton. A sweep of a net thus samples the entire system rather than the individual components. Ware and Addison[34] studied the effect of particle size on PCB concentration of plankton collected in the Gulf of St. Lawrence. They found that there was a linear relationship between the surface to volume ratios of the different size fractions and their PCB content. The levels of PCB's in the 73 to 102 μm particles ranged as high as 22 ppm on a wet weight basis and are easily the highest PCB concentrations reported in plankton. The values for composite samples (plotted on Figure 1) are more in line with values for other areas.

While carefully standardized procedures are essential for monitoring of residue levels in plankton, there is no doubt that a global system of monitoring would add to our knowledge of the rate of transfer of pollutants to the open ocean. The current knowledge of levels in plankton are summarized in Figure 1. The values for the open North Atlantic are remarkably similar to those from such polluted areas as the Baltic and the Firth of Clyde. The values for the South Atlantic are considerably lower; unfortunately no values are available for the Pacific.

B. Residue Levels in Fish

Europe – The data on levels in herring are summarized in Figure 2. The highest levels are found in the Mediterranean and in the Baltic. The Baltic has been particularly well-studied and for additional information the reader is referred to Jensen et al.[35,36] and Westöö and Noren.[37]

North America – Reinke et al.[38] examined the organochlorine levels in fish caught in 78 locations in Canada in 1970. Good coverage was obtained in Alberta, Saskatchewan, Manitoba, and Southern Ontario. Nine localities in the Northwest Territories were sampled, but none in British Columbia, Quebec, or the Maritimes. Values for levels of PCB are not given but authors state "PCB's were quite prominent throughout the

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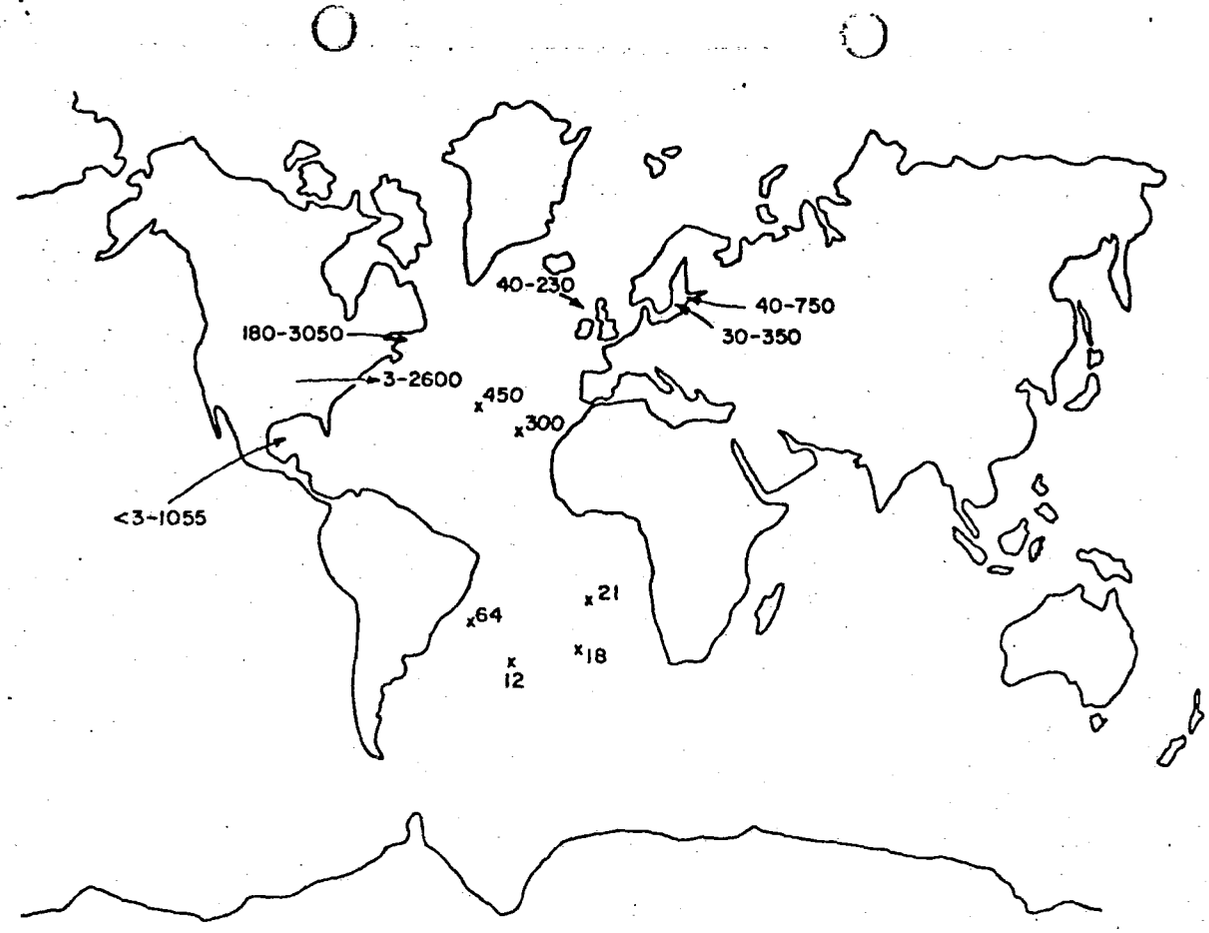

FIGURE 1. Global PCB's levels in plankton. Values are in ppm (lipid).

Great Lakes and appeared to a lesser degree in southern Lake Winnipeg in Manitoba and in the Bow River in Alberta."[38]

In the U.S., the first major survey of PCB levels in fish was made by Henderson et al.[39] Their data are mapped in Figure 3 and the averages include those samples in which PCB's were not detected by plugging in the value of the limit of detection, viz., 0.10 ppm. They found that PCB's are a major contaminant in fish, and, in two thirds of the samples, the PCB residues were higher than those of total DDT. The majority of the high values are found in the northeast, especially the Great Lakes, whereas Gulf coast and west coast values are generally low so that the pattern is different from that of DDT. There is no suggestion of concentration around the site of production, viz., St. Louis. This survey was made in the fall of 1969, and no more recent national survey has yet been reported.

Carr et al.[40] examined organochlorine residues in six species of fish from many sampling points in Lake Erie in 1970 and 1971. Average values for the 6 species ranged from 0.8 to 4.4 ppm PCB, considerably higher than those for total DDT which were 0.18 to 0.90 ppm. These findings are in agreement with those of Henderson et al.[39] For the Atlantic coast Zitko and Hutzinger[41] found that most marine fish had 0.2 to 0.5 ppm. Zitko[42] has examined levels in herring in the Maritimes in 1972 and 1973 and compared them to the levels found by Addison et al.[43] in 1968 and 1969. There are some difficulties in that the data are not always strictly comparable, but the major finding was that PCB levels have remained constant while DDT levels have decreased over this period.

Caribbean – Giam et al.[44] sampled a number of different species of fish in the Caribbean from Florida, around the Gulf of Mexico to Yucatan. The levels were low, most below 0.1 ppm (wet weight), with the highest value 0.5 ppm near the Mississippi Delta. Giam et al.[45] examined levels in the coral-reef dwelling Groupers and only 2 fish out of 18 exceeded 0.1 ppm; the maximum value recorded was 0.2 ppm.

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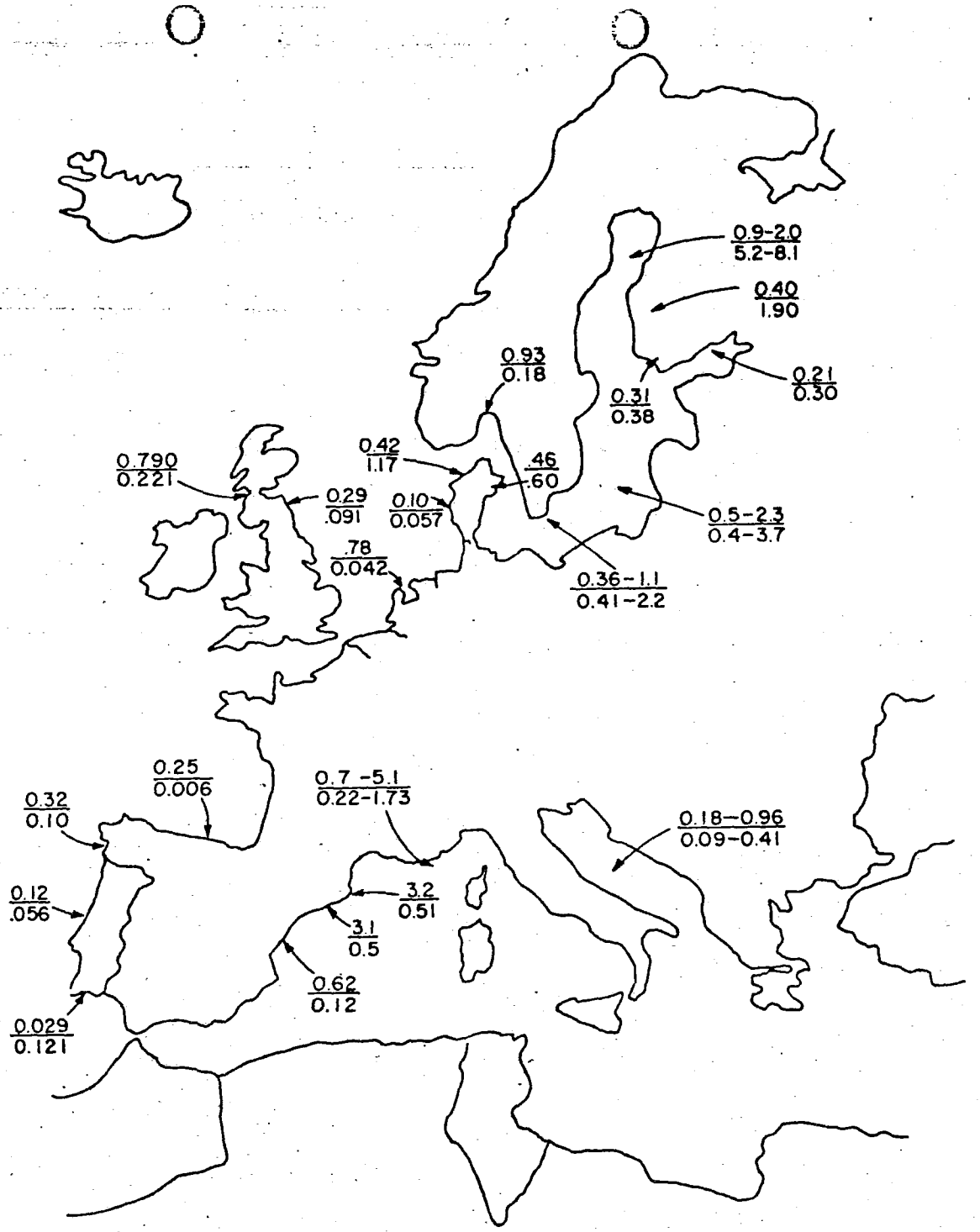

FIGURE 2. Levels of PCB's in herring or similar species in Europe. Top values are total DDT, bottom values PCB; both are on wet weight basis.

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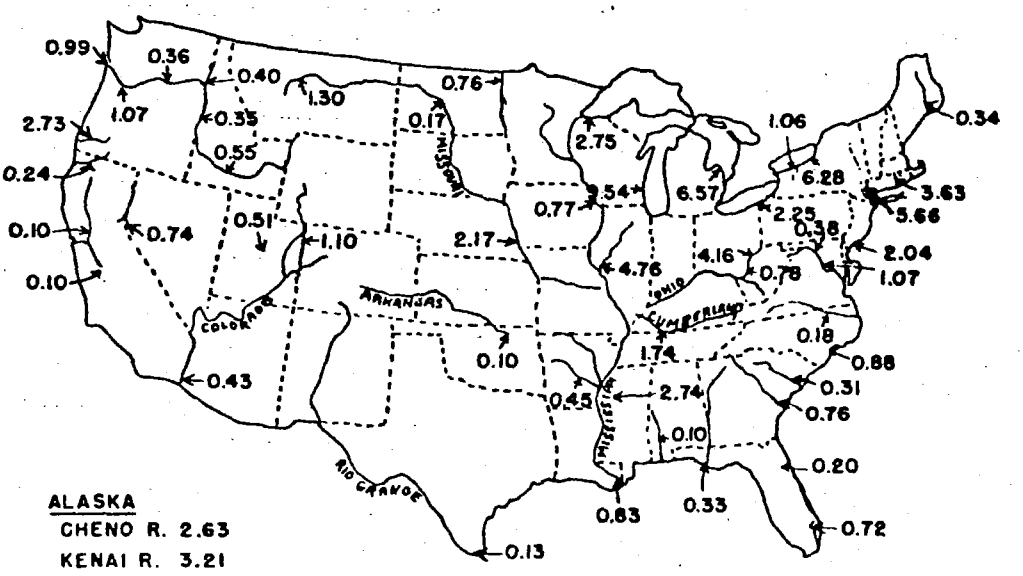

AFTER HENDERSON, INGLIS & JOHNSON, 1971

ESTIMATED PCB CONTENT OF FISH IN PPM. DETECTION LIMIT 0.10 PPM.

FIGURE 3. Levels of PCB's in fish in the U.S. Values are in ppm, on wet weight basis.

Japan – High levels have been found in both fresh and salt water fish in Japan.[46,47] Based on 599 samples, Fujiwara[47] reported that 16% of the samples exceeded 1 ppm and 3% exceeded 3 ppm. The latter value is standard regulatory value in Japan. Doguchi[46] summarizing results on 2,826 samples found that 141 or 5% exceeded the 3 ppm limit. They concluded "that the pollution by PCB's is dangerously advanced in the aquatic environment around the megalopoles such as Tokyo and Osaka and other industrial districts, and some species of fish in these areas are unfit for human consumptions."

Southern hemisphere – Solly and Harrison[48] did not detect any PCB's in any species of fish, crustaceans, and mollusks from both fresh and coastal waters of New Zealand. Neuhaus et al.[49] examining for residue levels of organochlorines in several species of fish in Australia, did not comment on the presence or absence of PCB's.

C. PCB Residue Levels in Sea Birds

The residue levels in sea birds, a diverse group of birds, have been the subject of many papers (Table 8). The information on two species for which there is clear evidence of reproductive failure in some areas where organochlorine residues are high are given in some detail. These species are the herring gull and brown pelican. The possible causes of reproductive failure are considered later in this review (Section 5). Additionally, data on pelagic sea birds, mainly shearwaters and storm-petrels (Procellariiformes), are summarized as for this group the widest geographical information on residue levels is available. One difficulty in building up a global picture of the residue levels is the highly migratory nature of some species. The sooty shearwater, for example, breeds on remote islands in the southern Pacific and then migrates around the basin of the Pacific passing close to such industrial areas as California and Japan. Other species, such as the snow petrel, remain all the year in Antarctic waters. In some cases, notable sea bird kills have been examined to assess the likelihood that organochlorines have been involved.

Herring gulls – This species is closely associated with man, particularly in winter when scavenging in garbage dumps is a way of life. Not surprisingly, high residue levels have been found in some areas, especially those from the Great Lakes of North America. Reproductive success in some colonies in Lake Ontario have been very low.[50] (These findings are considered in more detail in Section

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5). The residue levels in eggs of this species are summarized in Table 6. Bjerk and Holt[51] examined the levels of PCB's in 10 colonies in Norway. The variation was small, the mean values ranging from 1.58 ppm in southern Norway to 0.63 ppm halfway up the Atlantic coast. The value for a colony in the extreme north was 0.74 ppm. In all cases the ΣDDT/PCB were between 0.44 and 0.87. The residue levels are higher on the Atlantic coast of North America, but the levels of the colonies on the Great Lakes showing marked reduction in breeding success have levels an order of magnitude higher.

Brown pelican – The dramatic failure of the reproduction of this species off the coast of California, first noted in the late 1960s, was one of the clear-cut cases of a man-made chemical having an effect in the environment. In this case, the levels of DDE are much higher than PCB's (ratio of circa 0.2) compared with ratios of 2 to 3 in Florida, (Table 7). In the failing colony at Anacapa the levels of PCB's are well below those of the herring gulls in the Great Lakes. The DDE levels are considerably higher and the main cause of failure, egg shell thinning followed by breakage, is outside the scope of this review. Similarly Blus et al.[52] considered that DDE was the main agent in the failure of brown pelican nesting in South Carolina.

Sea bird kills -- Several large kills of sea birds, especially alcids, in the Irish Sea have been associated with high residues of PCB's in the bodies.[68,69] Parslow and Jefferies[68] found that the mean total body burden of PCB's in guillemots was 4,660 μg (body weight 580 g) in birds found dead, about twice that found in apparently healthy birds collected in the same area. Due to loss of much of their body weight (the healthy birds weighed about 1 kg), the levels in organs were much higher in the birds found dead than in those collected. These authors conclude that PCB residues may have contributed to but not been the initial cause of mortality. Lloyd et al.[69] examining a later kill, also concluded that no definite cause of mortality could be established. Lincer and Peakall[70] reduced the food intake of ring doves preloaded with Aroclor 1254 such that the birds were losing 10% body weight per week. No differential mortality was noted with controls and the liver levels of PCB's were some 20 times higher

TABLE 6

Residue Levels in the Eggs of Herring Gulls

Location	Year of collection	n	DDE(ppm)	PCB(ppm)	Reference
Norway	1969	80*	1.53 (W)	1.00 (W)	Bjerk and Holt[51]
New Brunswick	1969–72	5	14.1 (D)	25.4 (D)	Gilbertson and Reynolds[53]
Bay of Fundy	1971	13	2.51 (W)	5.3 (W)	Zitko[43]
	1972	15	1.32 (W)	3.3 (W)	
	1973	15	2.10 (W)	3.7 (W)	
Quebec	1969–72	16	32.1 (D)	65.2 (D)	Gilbertson and Reynolds[53]
Lake Ontario	1973	15	134 (D)	420 (D)	Teeple[54]
	1972	16	131 (D)	565	Gilbertson and Reynolds[53]
Lake Erie	1972	6	48.0 (D)	300 (D)	
Lake Huron	1972	5	110 (D)	368 (D)	
Lake Superior	1973	6**	15.9–33.9 (W)	40.6–64.1 (W)	Ryder[56]
Southern California†	1973	12	11.8 (W)	5.1 (W)	Hunt et al.[57]

*Summary from 10 colonies. (For details see text.)
**Six pooled samples from three colonies.
†Closely related western gull.
n – Sample size.
W – Wet weight basis.
D – Dry weight basis.

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TABLE 7

Residue Levels in Brown Pelican Eggs

Location	Year	Sample size	DDE(ppm)	PCB(ppm)	Reference
Florida (Gulf coast)	1969	27	1.37 (W)	0.89 (W)	Blus et al.[58]
Florida (Atlantic coast)	1969	22	2.24 (W)	2.81 (W)	
South Carolina	1969	11	5.24 (W)	2.81 (W)	
California (Anacapa)	1969	10	71.7 (W)	3.6 (W)	
South Carolina	1971/72	11*	1.87 (W)	5.50 (W)	Blus et al.[58]
		26**	3.23 (W)	7.94 (W)	
Florida	1969	14	37 (L)	120 (L)	Risebrough[35]
	1970	21	26 (L)	69 (L)	
Florida (five colonies)	1969 and 1970	87	26 (L)	71 (L)	Risebrough[35]
California (Anacapa)	1969 and 1970	65	1176 (L)	210 (L)	
(Los Coronados)		28	1109 (L)	266 (L)	
(San Martin)		6	429 (L)	72 (L)	
(San Benitos)		10	128 (L)	39 (L)	
(Gulf of California)		4	11 (L)	4 (L)	

*Successful nests.
**Unsuccessful nests.
W – Wet weight.
L – Lipid weight.
Ratio W:L circa 1:20.

TABLE 8

Residue Levels of Seabirds and Their Eggs

Location	Species	Tissue	DDE(ppm)	PCB(ppm)	Reference
Ascension Island Central Atlantic	Sooty tern	Liver	n.d.	0–9.2 (L)	Johnston[59]
		Fat	n.d.		Johnston[59]
	Fairy tern	Liver and fat	n.d.	Trace	Johnston[59]
Mauritius Central Indian	Trinidad petrel	Eggs	1.4–2.5 (D)	n.d.	Temple and Peakall[60]
Hallett Island Antarctica	Wilson's petrel	Whole body	2.2 (L)	11.0 (L)	Risebrough and Carmignani[61]
	Snow petrel	Whole body	0.11 (L)	0.34 (L)	
Palmer Station Antarctica	Wilson's petrel	Whole body	45.8 (L)	185.3 (L)	
Ross Island Antarctica	Adelie penguin	Fat	0–0.18 (W)	n.e.f.	George and Frear[62]
South Orkneys Antarctica	Chinstrap penguin	Fat	0.013–0.048 (W)	n.e.f.	Tatton and Ruzicka[63]
	Skua	Fat	5.8 and 26.0 (W)	n.e.f.	
		Liver	4.0 and 0.9 (W)		
Palmer Station Antarctica	Skua	Eggs	8.7 (L)	45.2 (L)	Risebrough and Carmignani[61]
Greenland	Brunnich's guillemot	Fat	3.5 (D)	12.9 (D)	Braestrup et al.[64]
			1.2–8.7 (D)	3.9–39.6 (D)	

W – Wet weight.
D – Dry weight.
L – Lipid weight.
n.d. – Not detected.
n.e.f. – Not examined for.

Location

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Faroes

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California

New Zealand
South Island
New Zealand
Cook Strait

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TABLE 8 (continued)

Residue Levels of Seabirds and Their Eggs

Location	Species	Tissue	DDE(ppm)	PCB(ppm)	Reference
Davis Strait		Fat	–	0.5, 1.7 (W?)	Bourne and Bogan[65]
		Liver		0.03, 0.2	
Faroes	Puffin	Liver	–	0.1–0.6	
	Common guillemot	Liver	–	0.6–1.1	
60°N 4°W	Fulmar	Liver	–	1.2–5.9	
		Fat		32–103	
Trinidad	Great shearwater	Liver	–	0.5, 0.7	
California	Fulmar	Whole body	–	0.4,3.4,17.5 (W)	Risebrough et al.[33]
	Sooty shearwater	Whole body	–	2.3,10.3,12.3 (W)	
New Zealand South Island	White-fronted tern	Egg	4.4–5.3 (L)	1.4–1.6 (L)	Bennington et al.[66]
New Zealand Cook Strait	Fairy prion	Whole body	5.5–3.9 (L)	0.6–3.3 (L)	
	Diving petrel	Breast muscle	1.6–2.9 (L)	2.1–3.3 (L)	
New Zealand Snares Island	Diving petrel	Whole body	0.03–0.25 (L)	0.5–0.14 (L)	
	Sooty shearwater	Egg	0.5–1.2 (L)	0.8–2.2 (L)	
New Zealand Auckland Island	Sooty shearwater	Egg	7.3 (L)	7.4 (L)	
New Zealand	Sooty shearwater	Fat, adult	10.6–19.2 (L)	1.1–2.7 (L)	Dacne[67]
		Fat, chick	1.30,1.22 (L)	0.05,0.11 (L)	

than those found in sea bird kills. Thus no strong evidence exists to link PCB levels with sea bird mortality.

D. Levels in Marine Mammals

A good deal of information is available on levels in marine mammals. These species are long-lived and most are at the top of marine food chains. The levels of PCB follow expected patterns (see Table 9). Levels in the ringed seal, for example, range from a hundredth of a ppm in the high arctic to 20 ppm in the Baltic. The values for the grey seal show high values near industrial sources in England. The ΣDDT/PCB ratio shows considerable variation. Values about unity were found by Holden[71] for both sides of the Atlantic by Addison et al.[72] and Frank et al.[73] in eastern Canada, and Bowes and Jonkel[74] in the Canadian arctic. However, Clausen et al.[75] found very low ratios in western Greenland and Jensen et al.[35] found very high ratios in the Baltic. The small amount of data from the southern hemisphere confirms the low levels of PCB's found in pelagic sea birds and fish (Figure 2, Table 8).

Both Frank et al.[73] and Addison et al.[72] have found a distinct increase of PCB levels with age in seals.

E. Residue Levels in Birds of Prey

The birds of prey have been extensively studied in connection with contamination with organochlorine compounds. Studies are particularly detailed on the peregrine falcon. This species breeds on all the continents except Antarctica and, being highly prized by falconers, there is a good deal of background information on this species. A technique for eluating the membranes of eggshells from museum collections[84] has enabled studies to be made on residue levels from the time of first usage of the persistent organochlorines. This data, together with that obtained by analysis of the egg contents, is summarized in Table 10. Although levels in the southern hemisphere are a good deal lower than in the northern hemisphere, appreciable levels are present in the eggs of this top bird-eating predator throughout its range.

The bald eagle of North America and the white-tailed eagle of Europe are similar species which feed largely on fish.

In Europe, Koeman et al.[86] report residue level in eagle eggs as 6 to 97 ppm (wet weight) in 22 eggs collected from 1969 to 1971 in Germany. The range of values of DDE was 1.2 to 17 ppm. A single dead eagle had 35 ppm PCB and 4 ppm DDE in its liver. Even higher values, viz., 157 ppm PCB's

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TABLE 9

Levels in Seals and Other Marine Mammals

Species	Locality	Residues, ppm (blubber) PCB	ΣDDT	Number	Reference
Ringed seal	Arctic Canada	3	2.7	3	Holden[71]
	Arctic Norway	1.5	2.4	3	
	Baltic	22	23.8	1	
	Gulf of Bothnic	13	130	-	Jensen et al.[35]
	Western Greenland	0.9	0.15	5	Clausen et al.[75]
	James Bay	1.0	1.3	1	Bowes and Jonkel[74]
	Western Greenland	0.16	0.18	1	
	Arctic Ocean	0.01–1.9	0.16–2.8	17	
Harp seal	Gulf of St. Lawrence	8.2	6.3*	56	Pearce et al.[76]
	Newfoundland/Labrador	1.2	0.58*	6	Holden cited in Pearce et al.[76]
	Jan Mayen	1.5	0.50*	7	
	Barent Sea	1.7	0.94*	5	
	Gulf of St. Lawrence	2.6–8.0	4.5 10.6	24	Frank et al.[73]
	Newfoundland/Labrador	1.2–26	2.0–50.0	54	
	Gulf of St. Lawrence	2–22	3.1–22.6	18	Addison et al.[72]
Hooded seal	Gulf of St. Lawrence	3	10.2	1	Holden[71]
	Western Greenland	2.7	0.29	5	Clausen et al.[75]
Grey seal	Baltic	30	130	–	Jensen et al.[35]
	Gulf of Finland	6.5	42	–	
	Stockholm Archipelago	13	130	–	
	Orkney, Scotland	18	13	8	Holden[71]
	Western Scotland	16–30	9.8–13	7	
	Eastern Scotland	38	20.1	16	
	Eastern England	123	39.7	2	
	Wales	212	17.5	3	
	Gulf of St. Lawrence	27–32	45–49	7	
	Western Scotland	14.4	7.4	6	Heppleston[77]
	Fames Island	31.0	10.7	7	
	Eastern England	152	15.5	4	
Bearded seal	Western Greenland	1.8	0.47	5	Clausen et al.[75]
Harbor seal	Maine	92.5	65.4	6	Gaskin et al.[78]
	New Brunswick	41.0	31.0	4	
		PCB + ΣDDT**			
	California	610		–	Anas[79]
	Oregon	62		–	
	Washington	862		–	
	Alaska	11		–	
		PCB	ΣDDT		
	Holland (juvenile)	240	2	3	Koeman et al.[80]
	Holland (adult)	1,470	9.5	5	
	California	Not stated	18 and 158	2	Shaw[81]
Bottle-nosed dolphin	Holland	35	20.5	2	Koeman et al.[80]
Common dolphin	New Zealand	Not detected	83	4	Koeman et al.[80]

Species

Surinam dolphin

Harbor porpoise

Sea lion

Finback wh

Pilot whale

*DDE only
**Only one
†Giving bir

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TABLE 9 (continued)

Levels in Seals and Other Marine Mammals

Species	Locality	Residues, ppm (blubber) PCB	ΣDDT	Number	Reference
Surinam dolphin	Dutch Guiana	Not detected	2.7	1	Koeman et al.[80]
Harbor porpoise	North Sea	88	41	7	Koeman et al.[80]
	Western Greenland	6.7	0.3	2	Clausen et al.[78]
Sea lion	California	112 17	824 103	6 4	De Long et al.[82]
Finback whale	North Atlantic	0.01–0.18	0.66–2.56		Saschenbrecker[83]
Pilot whale	Caribbean	0.69–5.00	1.25–7.38		Gaskin et al.[84]

*DDE only.
**Only one sample analyzed for individual compounds; this gave 2,100 ppm DDE, 96 ppm DDT, and 572 ppm PCB.
†Giving birth to premature pups; other sample going full-term.

TABLE 10

Organochlorine Levels in Peregrine Eggs

Locality	Date and sample size	DDE (ppm, w)	PCB (ppm, w)	Technique	Reference
Amchitka, Aleutians	1971–73; 10	2.5–7	5–80	Whole egg	Peakall et al.[90]
Interior Alaska	1971–73; 10	41–80	32–60	Whole egg	
Greenland	1972; 1	36	40	Whole egg	Walker et al.[91]
California	1948–49; 3	3–9	n.d.	Membrane	Peakall[85,92]
	1950; 2	4, 30	n.d., 15	Membrane	
Colorado	1973; 4	33	5.8	Whole egg	Enderson and Craig[93]
Great Britain	1962–66; 12	4.4–21.4	not determined	Whole egg	Ratcliffe[94]
	1967–71; 54	2.3–10.1	1.0–4.0	Whole egg	
Chile	1966; 1	1.5	4.0	Membrane	Peakall and Kiff[95]
Southwestern Africa	1970; 1	10	8.0	Membrane	Peakall and Kiff[96]
Australia	1949; 1	1.7	n.d.	Membrane	
	1951; 1	3.1	n.d.	Membrane	
New Zealand Auckland Island*	1973; 1	3.8	4.9	Whole egg	Bennington et al.[66]

*Closely related New Zealand Falcon.
W – Wet weight.
n.d. – Not detected.

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and 1.72 ppm DDE, were recorded for two white-tailed eagle eggs from the Gulf of Bothnia.[87]

These levels are high compared to those of the bald eagle from the U.S. Alaskan Eagles in the Kodiak area averaged 2.2 ppm (range 1.4 to 5.4 ppm), and those from the Admiralty Island only 1.1 ppm (0.4 to 2.3). From the continental U.S. values ranged from 2.2 (Minnesota) to 27.7 in Michigan. Five eggs out of 11 exceeded 10 ppm. Residues of DDE were distinctly higher.[88] Brain levels in adult bald eagles ranged from trace to 65 ppm in 1969 (n = 28) and trace to 230 ppm in 1970.[89] Levels of DDE were similar, but median values were lower.

F. Levels of PCB's in Humans and Their Food

In considering the problem of contamination of human food by PCB's, it is necessary to separate occasional accidents leading to serious but local problems from the "normal" background level. In Japan, PCB's leaking from a pipe in a food processing plant led to rice bran oil containing up to 1,500 ppm of organic chlorine compounds. The main findings of this occurrence, termed "Yusho," were described in a special issue of *Fukuoka Acta Medica* in 1969.[96-99] In the same year contamination of some two million chickens occurred in Japan[100] at a level high enough to cause symptoms similar to chick edema disease. Over a million chickens were destroyed in the U. S. in 1972 after accidental contamination.[101] While these accidents produce the most serious cases of PCB poisoning on record, they are the result of carelessness and the main concern of this review is to evaluate the effects of overall environmental contamination.

The question of the role of chlorinated dibenzofurans, which occur as impurities in PCB's causing effects ascribed to PCB's, is a difficult one to evaluate. The chlorinated dibenzofurans are much more toxic than PCB's. Severe and lethal liver damage in rabbits has been caused by 0.5 to 1.0 mg/kg.[101A,101B] Thus, the chlorinated dibenzofurans are some orders of magnitude more toxic than the chlorinated biphenyls. The chlorinated dioxins are even more toxic with LD_{50} values as low as 0.6 μg/kg reported for guinea pigs.[101C] Vos et al.[227] found 5 ppm of pentachlorodibenzofurans in Clopen A60 and 20 ppm in Phenoclor P60, but less than 1 ppm in Aroclor 260. These differences in furan levels were correlated with differences in toxicity.[226] Attempts to detect dibenzofurans and dioxins in wildlife samples have failed,[101D,101E] but these studies were carried out in Canada and the U. S. Studies in Europe, where the levels of chlorinated dibenzofurans are higher, would be of interest. Recent studies in which PCB levels up to 100 ppm were fed to ducks resulting in tissue levels up to 3,000 ppm, failed to reveal chlorinated dibenzofurans.[101F] In this study the initial levels of furans was about 1 ppm. The possibility that highly toxic impurities are involved in actions ascribed to PCB's is real, but has rarely been definitely demonstrated.

A sampling of levels of PCB's in food are given in Table 11. As might be expected, levels are highest in fish (see also Section 3.3). In other foods the levels detected are low. The tentative acceptable daily intake in the U. S. has been set at 150 to 300 μg/day[102], whereas the average intake has been calculated to be only 7 μg/day.[103] However, a study by Price et al.[104] on the diet of 8 girls in Virginia found that while 4 had only traces of PCB (i.e., less than 0.001 ppm), 4 contained 200, 420, 580, and 840 μg/day. In certain areas, viz., northeast U. S., Japan, and much of Europe, persons eating considerable amounts of fish would be expected to exceed the FDA guidelines.

Levels of PCB's have been measured in human adipose tissue and in human milk (Tables 12 and 13). Where possible, the residue levels of PCB's are compared to those of total DDT. In general, the levels of PCB's are lower than total DDT and in some cases PCB's were not detected, viz., adipose tissue and milk from Texas.[105,106] In the southern hemisphere PCB's were not detected in humans from either New Guinea[106] or Australia[107], despite the fact that DDT and its metabolites were detected in both groups.

Finklea et al.[108] examined the level of PCB's and total DDT in 723 plasma samples from persons in South Carolina in 1968 (see Table 14). They found marked differences in the levels of both compounds by both race and residence. The PCB levels ran from a low of 0.3 ppb for rural blacks (with less than 5% positive) to 3.1 ppb in rural whites (with over half positive). No significant variation was found by either age or sex. Considerably higher levels have been reported from Japan, where healthy persons were found to average 10.6 ppb and PCB-intoxicated patients averaged 18.3 ppb.[109]

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TABLE 11

Levels in Human Food

Food	Area	PCB level	Reference
Fish (various species)	U.S. (Atlantic and Gulf coast)	Values ranging up to 0.65 ppm, 66% positive	Markin et al.[114]
Herring oils	Eastern Canada	1.7 to 10.9 ppm	Addison et al.[43]
Crabs	–	Values up to 0.13 ppm, 66% positive	–
Beef fat	U.S.	Occasionally present (10% positive), maximum value 0.64	Ford et al.[115]
Cheese	Canadian European	0.01 to 0.27 ppm* 0.02 to 0.08 ppm	Villeneuve et al.[116]
Chicken eggs	Canada	Mean value 0.008 ppm, 100% positive	Mes et al.[117]
	Japan	n.d. – 0.08 ppm	Fujiwara[47]
Butter	Norway	0.01 to 0.08 ppm	Bjerk[118]
	Japan	n.d. – 0.02 ppm	Fujiwara[47]
Marine products	Japan	0.003 to 5 ppm	Fujiwara[47]

*Only one value above 0.6 ppm.
n.d. – Not detected.

"Kanemi Yusho" was found by Inoue et al.,[110] although the actual values were lower. These workers found a mean value for rural persons of 2.7 ppb, urban persons of 4.5 ppb and "Yoshi" patients of 7.0 ppb. The elevation of PCB levels in patients over the normal population is relatively small, but these measurements were made five years after the initial poisoning. This group also examined the correlation of adipose tissue levels and blood plasma levels.[111] They found mean values (n = 17) of 1.6 ppm in adipose tissue and 4.9 ppb in plasma. No correlation was found in levels for individuals, and it was concluded that equilibrium had not been reached. The ΣDDT/PCB ratio for adipose tissue was 3.8 and 4.9 for plasma.

Hesselberg and Scherr[112] examined the levels of PCB and DDE in patients suffering from various carcinomas and from apparently healthy adults. They found an average level of 3 ppb DDE in nonpatients and failed to detect PCB's in these persons. The corresponding values in cachetic patients were 21 ppb DDE and 47 ppb PCB. The increase in patients suffering from cancer is likely to be due to loss of body fat and hence to increasing circulating levels of organochlorines. The change in the ratio of DDT to PCB from nonpatients to patients is surprising, and the final level of PCB's in the blood is high in the latter group.

No PCB's could be detected in human embryos from Japan and levels in fetuses were only in the parts per billion range (2 to 28 ppb) at term.[113] Again in this study the levels of total DDT were higher than those of PCB's. The ΣDDT/PCB ratios in humans are typically above unity and thus different from most other top predators.

5. PHYSIOLOGICAL EFFECTS OF PCB's

The physiological effects of PCB's are considered mainly on a class by class basis. In general, the effects are sufficiently different from mammals to birds to fish to make this the most convenient way of handling the data. In some cases, notably enzyme induction, the data lend themselves to a wider consideration. Acute toxicity is considered first, followed by effects on reproduction.

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TABLE 12

Levels of PCB's and DDT in Human Adipose Tissue

Area	Date	PCB(ppm) Mean(range)	PCB(ppm) %(number)	ΣDDT(ppm) Mean(range)	Reference
U.S. (Michigan)	1971	Negative	2.0%(4)	Not stated	Price and Welch[125]
		Trace to 1.0	55.6%(109)		
		1.0 to 2.0	36.7%(72)		
		2.0	5.6%(11)		
U.S. (Michigan, Florida, and Colorado)	1968–69	Negative	34.2%(235)	Not stated	Yobs[126]
		Trace to 1.0	33.3%(229)		
		1.0 to 2.0	27.3%(188)		
		2.0	5.2%(36)		
U.S. (Texas)	1969	Not detected		23.0	Burns[105]
	1970	Not detected		21.0	
	1971	1.7(0.6 to 9.9)		22.3	
	1972	Not detected		29.3	
Norway (Oslo) (Rikshospitalet)	1969–70	0.88(0.0 to 2.75)		1.90(0.11 to 6.72)	Bjerk[121]
		0.60(0.23 to 1.83)		3.18(0.61 to 9.40)	
Germany	1974**	6.8 to 10.0*		3.8 to 7.5*	Acker and Schulte[127]
Austria (Vienna)	1973**	3.5		4.6	Psendorfer et al.[128]
Japan (Tokyo)	1971–72	2.1(0.7 to 5.1)		Not stated	Doguchi[46]
(Kyoto)	1971	4.7(1.9 to 1.33)		9.8(4.2 to 14.8)	Fujiwara[47]
Israel	1974**	2.75		9.94	Wassermann[129]

*Means from five cities.
**Year of publication.

Notes: An early report of 200 and 600 ppm[130] in two samples is presumably in error. Additional references of data from Japan are given in Doguchi.[131] Values are similar to those cited above.

A. Acute Toxicity

Mammals – The acute toxicity of PCB's is low compared to most organochlorine pesticides. Grant and Phillips[132] found LD_{50} for rats of 1.3 to 2.5 g/kg for Aroclor 1254 with younger rats having somewhat higher values than older animals and virtually no difference between the sexes. An LD_{50} of 4.2 g/kg for Aroclor 1242 was found by Bruckner et al.[133] Values around 29 g/kg have been reported for mice,[134,135] and Clegg[136] cites values of 8 to 11 g/kg for rabbits. By comparison, the LD_{50} for rats of DDT is 0.11 g/kg, and dieldrin 0.06 g/kg.[137]

In feeding experiments, Tucker and Crabtree[138] found 100% mortality in rats fed 1,000 ppm Aroclor 1254 within 53 days. Kimbrough et al.[139] found only 50% mortality at the same dosage in an 8-month study. An anomalous situation is the high sensitivity of mink; in this species 3.6 ppm Aroclor 1254 produced 100% mortality within 105 days.[140] The reproduction of this species is also very sensitive to PCB's (see next section).

Birds – Heath[141] measured the dietary LC_{50} for several different Aroclors. Their definition of LC_{50} was the ppm of a chemical in an ad libitum diet expected to produce 50% mortality among 2-week-old birds in 8 days, with 5 days of toxic diet followed by 3 days of untreated diet. These workers studied four species of birds, viz., mallard, pheasant, bobwhite, and Japanese quail, and six Aroclors (1232 to 1264). In general, the toxicity

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TABLE 13

Levels of PCB's and DDT in Human Milk

Area	Date	PCB(ppm) mean(range	DDT(ppm) mean(range)	Reference
U.S. (Colorado)	1971-72	(0.04 to 0.10)	(0.019 to 0.386)	Savage et al.[119]
(Texas)	1971*	Not detected	Present	Dyment et al.[106]
Canada (New Brunswick)	1972	0.022(0.015 to 0.030)	0.035(0.017 to 0.068)	Musial et al.[120]
(Nova Scotia)	1972	0.018(0.011 to 0.032)	0.019(0.009 to 0.031)	
Norway (Oslo)	1969-71	0.011(0.0 to 0.03)	0.054(0.01 to 0.22)	Bjerk[121]
(Bergen)		0.011(trace to 0.02)	0.077(trace to 0.21)	
Sweden	1971-72**	0.025	0.059	Westöö and Noven[123]
Germany	1970*	0.103	0.081	Acker and Schulte[125]
Japan (Kyoto)	1971	0.05(0.01 to 0.31)	0.095(0.006 to 0.44)	Fujiwara[47]
New Guinea	1971*	Not detected	Present	Dyment et al.[106]
Australia	1973*	Not detected	0.064	Siyali[107]

*Date of publication.
**Westöö[124] states that the average PCB level in human milk in Stockholm seems to have increased from 1967 to 1972.

TABLE 14

Levels of PCB and Total DDT in Blood Collected from Humans in South Carolina in 1968

Residence, race	Mean plasma residues (ppb) PCB	Total DDT	Sample size
Rural, black	0.35	20.9	139
Urban, black	1.97	12.5	173
Urban, white	2.4	4.7	199
Rural, white	3.2	5.6	210

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of the Aroclors increased as the percentage of chlorine increased although there were some exceptions. Some species variation was noted; the Japanese quail was the least sensitive with LC_{50} values of 2,185 to 5,000 mg/kg and the bobwhite was the most sensitive with values of 745 to 3,000 mg/kg. In general the toxicity of Aroclors was less than either DDT or DDE, although there was some overlap in the case of DDE.

Subsequently these workers[142] fed Japanese quail diets containing Aroclor 1248, 1254, and 1260, such that the birds received equal amounts of chlorine in their feed. It was concluded that while toxicity was positively correlated with the degree of chlorination, it is not simply a function of chlorination.

Harris and Rose[143] found a reverse situation in chicken – a species not studied by Heath and co-workers – in that Aroclor 1242 was more toxic than 1254 which in turn was more toxic than 1260.

Fish – Wildish[144] found that the lethal threshold for *Gammarus oceanicus* was 0.001 to 0.01 mg/l for colloidal solutions of Aroclor 1254 and 0.01 to 0.1 mg/l for Aroclor 1254 solubilized in an emulsion. Hattula and Karlog[145] found a linear relationship between the time for 50% mortality and the log of the concentration of Clophen A50 for goldfish. With a concentration of 4 mg/l, the time for 50% mortality was 5 days; at 0.5 mg/l the time was 21 days. Hansen et al.[146] found that the time for 50% mortality for pinfish exposed to 0.005 mg/l Aroclor 1254 was 12 days and 18 days for spotfish. The latter species was not affected by 0.001 mg/l. Morgan[147] found that 2 mg/l Aroclor 1242 caused 100% mortality of guppies, but only 25% mortality was caused by 0.2 mg/l.

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Crustaceans -- Duke et al.[148] found that 0.1 mg/l caused 100% mortality of juvenile pink shrimp within 48 hr, whereas 0.01 mg/l did not cause mortality within this period. Complete inhibition of oyster shell growth was found at 0.1 mg/l; at 0.01 mg/l, the inhibition was 41% and at 0.001 mg/l, the value was 19%.

Insects -- Lichtenstein et al.[149] found that PCB's were 40 to 300 times less toxic than DDT to house flies and fruit flies, the toxicity decreasing as the chlorine content increased. Moriarty[150] found that the grasshopper had a low susceptibility to Aroclor 1254.

It is clear that the acute toxicity of pure PCB's is low compared to other organochlorine compounds in widespread use, such as the insecticides DDT, dieldrin, benzenehexachloride, aldrin, and endrin.

B. Liver Morphological Changes

Morphological changes in the liver have attracted a good deal of attention, starting with a study by Bennett et al.[151] Inhalation studies (0.57 and 0.93 mg/m^3 16 hr/day for up to 143 days) on rats led to livers which were pale, or slightly yellow and mottled. The most conspicuous change was hyaline degeneration, increased prominence of cytoplasmic granules and increased vacuolization. No increase in liver weight was noted. Most rats given 3 g daily (65% chlorine) died; survivors showed enlarged livers with swollen cells. At a dose level of 0.5 g on alternate days enlarged livers (33% increase) were seen, with large numbers of acidophilic hyaline globules in the cytoplasm.

Nishizumi[152] examined the fine structure of livers of mice and monkeys exposed to PCB's. The dose given to the mice was high, 0.5%, but the dose given to monkeys was 1.4 to 16 mg/day. The most marked alteration was an increase of the smooth endoplasmic reticulum and a reduction of the rough endoplasmic reticulum. It was considered that this proliferation of the smooth endoplasmic reticulum corresponds to hyaline cytoplasmic inclusions seen under the light microscope. Cytoplasmic inclusions, consisting of concentric whorls of closely packed smooth membranes, were noted in the mice. Additional findings were swelling of Kupffer's cells with an increased number of lysosomes and vacuoles.

Kimbrough et al.[139] exposed rats to a diet of 20, 100, 500, 1,000 ppm of Aroclor 1254 and 1260 for a period of 8 months. Increasing liver weight with increasing dosage was noted, but was not statistically significant for female rats at 20 or 100 ppm Aroclor 1260. In male rats exposed to Aroclor 1260, enlarged hepatocytes and inclusions in cytoplasm were commonly noted at all dosage levels; increased lipid was noted in all rats at 100 ppm and higher doses. The effect was less marked in females, with little sign of effects at 20 ppm. With Aroclor 1254, the findings were similar except that adenofibrosis was marked at higher doses. Ultrastructural changes consisted of an increase of the smooth endoplasmic reticulum and of atypical mitochondria. The epithelial component of adenofibrosis consists of goblet cells and cells similar to those of the epithelium of the bile ducts. In a later study these workers[153,154] studied rat livers for 8 months after exposure to 500 ppm Aroclor 1254 for 6 months. Liver weights decreased over this period from 6.32% to 3.34% (control values 2.44 to 2.59%). Morphological changes persisted over the recovery period with small lipid vacuoles in the cytoplasm of hepatocytes characteristic of the recovery phase. Adenofibrosis was examined in more detail and was considered likely to be a permanent lesion. The final residue levels in the liver range from 17.3 to 26.2 ppm after 8 months off dosage.

Allen and Abrahamson[155] exposed rats to a diet of 1,000 ppm of Aroclor 1248, 1254, and 1262. Approximately threefold increase in liver weight was noted, with some increase with increasing chlorination. The morphological changes - proliferation of the smooth endoplasmic reticulum, formation of large membranous concentric arrays and lipid droplets within the cytoplasm agree with other workers. There was some indication of decreased enzyme activity after six weeks as compared to four weeks, but the changes were not consistent from enzyme to enzyme, nor were the changes marked.

Hansell and Ecobichon[156] have studied the effect of a series of pure isomers, biphenyl, mono-, di-, tetra- and octachlorobiphenyls, on the morphology of rat livers. They found that biphenyl, mono, and dichlorobiphenyls caused little morphological change, but that the pure higher chlorinated isomers caused changes comparable with Aroclor 1254 and 1260. Thus for this response to PCB's, the pure isomers and commercial mixtures act in the same manner.

Litterst et al.[157] found no effect on liver

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weight at 0.5 or 5 ppm for 4 weeks with any Aroclor studied (1242, 1248, 1254 or 1260). At 50 ppm, significant increases were found for all but 1242, and at 500 ppm all Aroclors caused liver enlargement. These workers also studied the induction of hepatic enzymes, finding some enhancement as low as 0.5 ppm. The conclusion is that liver enlargement is a good deal less sensitive to PCB's than the induction of some hepatic enzymes. This conclusion is in agreement with work on other organochlorines.

Detailed studies on alterations of the liver have not been made outside those on mammals. Lincer and Peakall[158] noted an increase of cytoplasmic RNA in American kestrels exposed to a diet of 5 ppm Aroclor 1254 or 1260, an alteration that would be expected to correlate with proliferation of the smooth endoplasmic reticulum.

C. Hepatic Enzyme Induction

One of the best studied effects of organochlorine compounds has been the induction of hepatic microsomal enzymes in mammals. See for examples reviews by Conney[159] and Conney and Burns.[160]

Alvares et al.[161] found that Aroclor 1254 enhanced the activity of all hepatic enzyme systems studied (viz., benzo(a) pyrene hydroxylase, ethylmorphine N-demethylase, and cytochrome P_{450}). In this regard, PCB's have the inducing properties of both barbiturates and polycyclic hydrocarbons. Since Aroclor 1254 is a mixture, it is possible it contains one or more compounds with barbiturate type inductive properties and one or more compounds of polycyclic hydrocarbon class of inductors. Alternatively PCB's may possess the combined properties of the two classes of inductors.

Bruckner et al.[133] found that Aroclor 1242 enhanced the activity of both N-demethylation and hydroxylation enzymes. The relative induction agrees with the findings of Alvares et al.[161] that hydroxylation enzyme activity is increased to a greater extent than N-demethylation activity. A single dose of 100 mg/kg was enough to cause significant increase of enzyme activity and increase of liver weight.

Chen et al.[162] studied the effect of two pure isomeric tetrachlorobiphenyls (TCB) on hepatic enzyme systems. These workers found noticeable differences between the effects of 2,3,4,5 TCB, caused enhanced enzyme activity of ethyl morphine N-demethylase and aniline hydroxylase in both male and female rats over the dose range 5 to 40 mg/kg daily for 5 days. With the 3,3',5,5' isomer enhanced, enzyme activity was noted only for the male rats, whereas significant decreases of enzyme activity were noted for female. Even with the males, peak activity of aniline hydroxylase was noted at 5 mg/kg with small enhancement at 20 and 40 mg/kg. These findings indicate that studies of mechanism of induction may be difficult to evaluate if commercial mixtures of PCB's are used.

Johnstone et al.[163] studied the effects of pure biphenyl and isomerically pure mono-, di-, tetra-, hexa-, and octochlorobiphenyls on hepatic function in the rat. These workers studied the following hepatic enzyme systems: O-demethylase, N-demethylase, aniline hydroxylase, nitroreductase, in addition to conjugation of bromosulfphthalein and pentobarbital sleeping time. There were some variations from enzyme system to enzyme, but in general, little or no effect was seen with the pure biphenyl, 4-mono-Cl, 2,2',2,4',2,5,2',5', whereas marked effects were seen with 4,4', and the three hexachloro- and one octochlorobiphenyls. Increases in enzyme induction paralleled closely decreases in barbiturate sleeping time. These workers also found similar hepatic enzyme induction with the commercial mixtures, Aroclor 1254, and 1260, to those found with the pure hexa- and octochloro isomers. The marked effect of 4,4' compared with the other low chloro compounds shows the difficulty of evaluating results from mixtures.

Chen and DuBois[164] studied the effect of three different Aroclors (1221, 1254, and 1260) on three hepatic enzymes (N-demethylase, nitrophenyl phosphonothioate detoxification, and O-demethylase). In all cases, the least chlorinated PCB (1221) was the weakest inducer, and in most cases no significant induction was observed. The most marked induction was Aroclor 1260 on N-demethylase and Aroclor 1254 on O-demethylase. These workers also studied the dose response of Aroclor 1260 and its interaction with DDT. They found significant increase of the most sensitive enzyme system (N-demethylase) at a dietary level of 1 ppm Aroclor 1260 for 1 week, and the other systems were significantly elevated at this dietary level after 3 weeks. DDT at 5 ppm for 1 week stimulated all enzyme systems, and a diet containing DDT and PCB showed additive effects on N-demethylase, but not with the other 2

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enzyme systems. These workers also noted that male rats were more sensitive than females and that young males were more susceptible to enzyme induction than adults.

Litterst et al.[157] studied the effect of four Aroclors (1242, 1248, 1254, and 1260) on several hepatic enzyme systems (nitroreduction, demethylation, and hydroxylation). In general, the degree of enzyme induction increased as chlorination increased, and a dose-related increase was found in all systems. Induction was seen at the lowest level examined, viz., 0.5 ppm for 4 weeks. The level of cytochrome P_{450} was less marked than the enzyme systems.

Bickers et al.[165] found that Aroclor 1016 was a less potent inducer of hepatic enzymes than 1254. Dosage was 25 mg/kg daily, intraperitoneal, for 6 days. Hydroxylase activity was stimulated by 1254 but not by 1016. Interestingly enough, hexobarbital sleeping time was significantly reduced by 1016 (48 min vs. 100 min by controls) as well as by 1254 (24 min). N-demethylase activity and cytochrome P_{450} levels were increased by both Aroclors, although the effect was much more marked with the higher chlorinated material.

Litterst and Van Loon[166] examined the effectiveness of Aroclor 1254 as an inducing agent compared to two well-studied agents, DDT and phenobarbital. They found that PCB's were far more effective than phenobarbital and at least as effective as DDT. They found that 0.05 mg/kg/day for 30 days was not effective, but that 0.05 mg/kg/day caused a significant increase in microsomal hydroxylation enzymes and cytochrome P_{450}.

Studies of hepatic enzyme induction in birds are a good deal less detailed than those on mammals. Risebrough et al.[23] demonstrated that Aroclor 1262 at 20 mg/kg, intramuscular, caused increased metabolism of estradiol, and that this PCB was more active than either DDE or DDT in causing induction of hepatic enzymes in the pigeon. Bailey and Bunyan[167] found that a diet of 500 ppm Aroclor 1242 increased both microsomal protein levels and, more markedly, cytochrome P_{450} levels. The microsomal protein levels returned to control values after two months, but cytochrome P_{450} was still three times the control values six months after exposure to the PCB had ceased. Nowicki and Norman[168] dosed chicks, starting at 1 week of age, with 1 mg Aroclor 1254 or 1260 daily. They found enhanced metabolism of steroids and further noted that the effects of both Aroclors were similar and also equivalent to p,p'-DDT and o,p'-DDT. No data are available on the threshold levels of PCB's on hepatic enzyme induction in birds, but it is probably not markedly different from that in mammals.

The only data on PCB-induced microsomal enzymes outside mammals and birds appear to be the work of Rhee and Plapp[169] on house flies. These workers studied the effects of Aroclor 1221, 1242, and 1254 and found increasing induction with increasing degree of chlorination. They found that minute amounts, i.e., 1 μg/jar, caused measured induction and concluded that a no-effect level apparently does not exist. It is likely that this induction increases the ability of the insect to detoxify insecticide chemicals. Thus the widespread contamination of the environment with PCB's may be a factor in increasing the resistance of insects to insecticides.

There is abundant evidence that PCB's are potent inducers of hepatic microsomal enzymes. The enzyme systems studied have been mainly hydroxylases and N- and O-demethylases. In general, the degree of induction increases as the degree of chlorination increases. Threshold values as low as 0.5 ppm have been found,[157] although other workers[170,171] have found the threshold dose between 1 and 10 ppm.

The minimum dose causing an effect should be compared with calculated intake to ascertain if an effect is likely. In the case of man, the normal exposure to PCB's (see Section 4) is too low for an effect on hepatic enzymes to be observed. Only in the case of accidental exposure, such as the "Yoshi" incident in Japan, would hepatic enzyme induction be expected to occur in man. Under these conditions interactions with drugs would have to be considered. The residue levels discussed in Section 4 indicate that marine mammals and predatory birds are exposed to levels of PCB's capable of causing enzyme induction. The next question to be answered is whether this induction is of importance to the function and survival of the animal.

While the documentation of induced microsomal enzymes is extensive, the evaluation of its effects on the intact animal are much less well studied. The use of increased hepatic function to shorten barbiturate sleeping time is one technique. Indeed the field of hepatic enzyme induction by

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chlorinated hydrocarbons was discovered by alterations in barbiturate sleeping times after the cages of rats had been treated with chlordane.[172] Bickers et al.[165] found marked alterations in sleeping time with Aroclor 1016 and 1254 at a dosage of 25 mg/kg for 6 days. Johnstone et al.[163] found no effect on pentobarbital sleeping time with biphenyl, 4-mono-chloro, or 2,2′ di-chloro-, slight decreases with 2,4′ and 2,5,2′,5′, and marked decreases with 4,4′, 2,4,2′,4′ and 3 hexa- and octochloroisomers. The dosage level was 50 mg/kg/day for 3 days in rats. In some cases sleeping time was reduced by 90%. Villeneuve et al.[173] studied the effect of Aroclors 1221, 1242, 1254, and 1260 on the pentobarbital sleeping time of rats exposed to dietary levels for 20 ppm for up to 350 days. Marked effects were found only with Aroclor 1254 and 1260; both of these compounds were more effective than chlordane. Zepp et al.[174] found that 10 ppm for 12 weeks caused significantly shorter periods of sleep in rabbits. These studies show that induced hepatic enzymes, largely studied by in vitro methods, are capable of increasing the metabolization of a circulating compound enough to alter its physiological effect at comparatively low dosages of PCB's.

There is a considerable volume of work which shows that a variety of organochlorines induce hepatic enzymes which are capable of metabolizing the naturally occurring steroids. Most of these studies are on in vitro metabolism, and unlike the experiment using barbiturates, effects on circulating levels can involve a feedback mechanism. In the intact animal increased metabolism of steroids could be compensated for by increased synthesis of these agents. A consideration of this problem requires the use of data obtained on other chlorinated hydrocarbons than PCB's.

Villeneuve et al.[175] demonstrated an increase in the urinary excretion of estrogen and dehydroepiandrosterone in the boar following a single dose of 100 mg/kg Aroclor 1254. No effect was seen at 10 mg/kg. While these experiments show an effect on the intact animal, the circulating levels of steroids were not measured. Recent studies on male rats fed toxaphene have shown a rapid increase in enzyme levels, and a transient drop in circulating testosterone levels.[176] The levels of testosterone returned to normal within a few days and remained at normal levels over the next six months although hepatic enzyme levels remained elevated. Orberg and Lundberg[177] found that DDT and PCB's were able to reduce the weight of testes and seminal vesicles of castrated rats, but not of intact animals. In both castrated and intact animals, enhanced hepatic enzyme induction was found and it was concluded that the intact animal was capable of compensating for enhanced steroid breakdown, although no direct measurements of steroid levels were made.

In ring doves, Peakall[178] found that DDE caused enzyme induction, decreased circulating levels of estradiol, and a slight delay in the onset of breeding. Studies of herring gulls, collected when incubation was almost complete, have shown no differences in blood steroid levels in birds collected from Lake Ontario with high levels of PCB's and DDE and those collected in New Brunswick.[179] Actual levels in eggs are given in Section 4.

The best summation is that hepatic enzyme induction can cause a temporary decrease of circulating steroid levels. This may be reflected in delayed breeding,[178,180] but feedback mechanisms then come into play to restore normal steroid levels. No overall effect on reproduction appears to be caused by this mechanism.

D. Mammalian Reproduction

Villeneuve et al.[175] found no effect on reproduction in the rat at dosages of Aroclor 1254 up to and including 100 mg/kg/day given orally. These workers examined the number of litters, average litter size, resorption sites, average litter weight and checked for anomalies. The only alteration seen was a slight reduction in litter weight and a slight increase of litter size at the highest dosage. Keplinger et al.[181] studied the effects of Aroclor 1242, 1254, and 1260 on rats at dosages of 1, 10 and 100 ppm. The only effects noted were decreased survival of pups at 100 ppm of 1242 and 1254 and decreased mating indices with 1242. In rabbits, Villeneuve et al.[175] found no effects at dosages of 6.25 or 10 mg/kg/day, but at dosages of 12.5 to 50 mg/kg/day, fetotoxic effects were noted. Abortions, maternal death, and stillborns occurred, but no consistent skeletal abnormalities were found. Since the work was done by the same group, it is clear that the rabbit is more sensitive than the rat to PCB's.

In 1968 and 1969 the feeding of Coho salmon taken from Lake Michigan led to reproductive failure in mink.[182] In a later study Ringer et

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al.[183] found that 1 ppm of Aroclor 1254 caused a slight reduction in reproductive success (4.3 kits/female compared to 6.0 in controls, statistical significance not stated); but at 5 ppm Aroclor 1254, complete reproductive failure was found in 1 experiment, and only 0.8 kit/female in another experiment. Premature births in California Sea Lions have been associated with high organochlorine residues.[82] In this, no controlled experimental data is available to verify the relationship between premature pupping and organochlorine residues. The levels of total DDT are much higher than those of PCB's (see Table 9), but the levels of PCB's in the liver of females giving rise to premature pups is similar (5.7 ppm) to the values found in mink dying from eating Coho salmon (5.2 ppm).

E. Avian Reproduction

Eggshell thickness – Decreased eggshell thickness caused by organochlorines, especially DDE, has attracted a good deal of attention (see review by Cooke[184]). In the case of PCB's, the bulk of the evidence shows that these compounds do not affect the thickness of eggshells. The following studies have been made: mallard and bobwhite quail,[185] ring doves,[186] chickens,[187-189] Japanese quail,[190] pheasant,[191] kestrel,[192] and mallard.[205] There is an early report by Keplinger et al.[181] which mentions eggshell thinning in chickens but does not give specific data, and Call and Harrell[194] found eggshell thinning in Japanese Quail using three different Aroclors.

Egg production and hatchability – The basic data are summarized in Table 15. The overall conclusion is that egg production is often reduced although the effect is not very marked. In contrast, massive effects are seen on hatchability in most studies. In the chicken the threshold effect dosage is around 10 ppm. The depression of hatchability does not appear to be caused by lack of fertility. Briggs and Harris[195] found that while 83% of the eggs from PCB-treated chickens were fertile, only 14.8% hatched. These found that comparatively little mortality occurred during the first six days of incubation, that there was a striking increase over control values during the second week of incubation, with considerable mortality in the third week although control values were also higher for this last period. Platonow and Reinhart[196] also found no effect on fertility, although hatchability was reduced to almost zero at the higher dosage of PCB's. These workers noted that initially embryonic mortality occurred at the latter stage of development, but shifted earlier as the experiment progressed. It is likely that this was due to increasing levels of PCB's in the eggs as the experiment progressed. Lincer and Peakall[70] found an essentially linear increase in residue levels in eggs of ring doves exposed to 10 ppm PCB's for approximately 100 days when the increase began to reach a plateau. Lillie et al.,[289] studying six different Aroclors, found no effect on fertility, and that most of the deaths of embryos occurred on the 20th and 21st days of incubation. Dahlgren and Linder,[191] in their studies on the pheasant, found a significant increase in eggs that pipped but failed to hatch.

Scott et al.[187] found that hatchability was reduced to about 72% of normal when the residue level in eggs was 2.2 ppm (wet weight). At 3 ppm hatchability is down to 56% and with 4.5 ppm or more PCB hatchability is close to zero. Platonow and Reinhart[196] found that hatchability was not affected when PCB concentrations in eggs were less than 5 ppm, but that 15 ppm or more caused the majority of embryos to die. Tumasonis et al.[198] found that yolk levels of under 10 to 15 ppm have no adverse influence on embryo development in the chicken. The most detailed study of the residue levels causing embryonic mortality are those of Britton and Huston[188] (see Table 16). These workers expressed their results based on the weight of the yolk, whereas Scott et al.[187] and Platonow and Reinhart[196] apparently used whole eggs for homogenization. Since the PCB's are concentrated in the yolk, using the yolk will give higher but more meaningful values.

Different Aroclors were used in these studies: Britton and Huston[188] used 1242; Scott et al.[187] used 1248, while Platonow and Reinhart[196] and Tumasonis et al.[198] used 1254. Carlson and Duby[199] injected Aroclors 1242, 1254, and 1260 into fertile chicken eggs. They found increased embryonic mortality with 1242 at 5 ppm with almost complete failure at 10 ppm. Aroclor 1254 showed some decrease at 5 ppm and marked decrease at 10 ppm, while 1260 was not effective in causing embryonic mortality at the highest dose, viz., 10 ppm. These results parallel those of Lillie et al.[200] who found that 1242 and 1248 caused a much larger decrease of hatchability than Aroclors with either high or lower chlorine

TABLE 15
Effects of PCB's on Egg Production and Hatchability

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TABLE 15

Effects of PCB's on Egg Production and Hatchability

Species	Dosage			Egg production	Hatchability	Reference
Chicken	10 ppm	8 weeks	1248	Decreased by 10%*	Decreased by 44%	Scott et al.[187]
	20 ppm			Decreased by 13%	Reduced to almost zero	
	5 ppm	14 weeks	1254	Decreased 82.7% to 72%	No effect	Platonow and Reinhart[196]
	50 ppm			Decreased 82.7% to 62.2%	Near zero after two weeks	
	20 ppm	9 weeks	1221	No effect	No effect	Lillie et al.[200]
			1232		93.7% to 56.5	
			1242	Significantly reduced**	to 18.4	
			1248		to 11.9	
			1254		to 80.7	
			1268		No effect	
	5 and 10 ppm	6 weeks	1242	No effect	No effect	Britton and Huston[188]
	20 ppm			No effect	91% to 75%	
	40 ppm			No effect	to 50%	
	80 ppm			No effect	to 0%	
	50 ppm	6 weeks	1254	No effect	Reduced to zero by the third week	Tumasonis et al.[198]
	20 ppm	6 weeks	1242	No effect	Zero after four weeks	Briggs and Harris[195]
	50 ppm			No effect	Zero after two weeks	
Pheasant	12.5 mg/week/bird	1254	Decreased	Slight decrease	Dahlgren and Linder[191]	Dahlgren and Linder[191]
	50 mg/week/bird		Decreased	Slight decrease		
Japanese quail	100 ppm	2 months	1242	Decreased 89% to 75%	Not studied	Cecil et al.[199]
	312 ppm	21 days	1242	0.55 to 0.45 eggs/hen/day	Not studied	Call and Harrell[194]
	5,000 ppm			0.24		
	78 ppm		1254	0.29		
	1,250 ppm			0.18		
	62.5 ppm		1260	0.48		
	1,000 ppm			0.12		

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TABLE 15 (continued)

Effects of PCB's on Egg Production and Hatchability

Species	Dosage		Egg production	Hatchability	Reference
Bobwhite quail	50 ppm	2 seasons	1254 No effect	No effect	Heath et al.[185]
Mallard	25 ppm	2 seasons	1254 No effect	No effect	Heath et al.[185]
	40 ppm	4 months	1254 Decreased on diet which also contained DDE	Not studied	Risebrough and Anderson[205]
Ring dove	10 ppm	3 months	No effect	Markedly reduced	Peakall and Peakall[204]

*No effect at 1 ppm.
**No effect at 2 ppm.

TABLE 16

Matchability and Residue Levels in Eggs of Chickens Exposed to Aroclor 1242

Dosage (Aroclor 1242, ppm)		Weeks on dosage 1	2	3	4	5	6
10	Decrease in hatchability	n.s.	n.s.	n.s.	n.s.	n.s.	16%
	Residue in yolk	0.3	0.8	1.2	1.6	2.3	3.7
20	Decrease in hatchability	n.s.	30%	26%	50%	30%	44%
	Residue in yolk	1.1	2.4	2.9	3.4	4.8	6.2
40	Decrease in hatchability	n.s.	74%	91%	97%	99%	100%
	Residue in yolk	2.4	4.6	5.4	5.8	6.7	7.7
80	Decrease in hatchability	n.s.	100%	100%	100%	100%	100%
	Residue in yolk	2.9	5.6	12.3	17.5	21.8	27.5

n.s. – Not significant

Adapted from Britton, W. M. and Huston, T. M., *Poult. Sci.*, 52, 1620, 1973.

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content. Carlson and Duby[199] found that most mortality caused by Aroclor 1242 was at the early stage of development, in contrast with most studies of the effect of dietary Aroclors. These workers also noted that growth was retarded in the chicks that did hatch after exposure to 1242 in the egg, whereas these effects were not noted for 1260.

The studies of Heath et al.[185] on bobwhite quail and mallard are in marked contrast to those on the chicken. In the latter species it is clear that a dietary level of 10 to 20 ppm for a few weeks and residue levels of 5 to 15 ppm are enough to cause severe embryonic mortality. In Heath's work no effects were seen even after the birds had been on dose for 1½ years, and residue levels of two Mallard eggs were 33 and 56 ppm (wet weight).

Effects on males – Platonow and Funnell[201] fed cockerels Aroclor 1254 as a dietary level of 250 ppm. A marked reduction in comb size was noted within six weeks, and the weight of the testes was reduced after nine weeks. No direct studies of the reproductive performance of these birds were made. Lillie et al.[200] fed cockerels Aroclor 1248 at 10 and 20 ppm for an 8-week period without finding any effect on semen or fertility.

Teratogenic effects – Carlson and Duby[199] found that 5 ppm of Aroclor 1242 injected at day 0 caused several malformations, viz., development of only one eye, hydrocephalus, incomplete abdominal closure, and nervous tremors. Tumasonis et al.[198] noted leg, toe, and neck deformities in many chicks that hatched from eggs with a yolk level of 10 to 15 ppm Aroclor 1254 or more. Cecil et al.[202] examined the effect of a diet of 20 ppm of a range of Aroclors on the production of abnormal embryos. These workers found a marked increase of abnormal embryos as a percentage of fertile eggs for Aroclor 1242 and 1248, a slight effect with Aroclor 1232 and 1254, and no effect for Aroclor 1221 and 1268. In all the treated groups, there were 843 dead embryos of which 286 were abnormal. The commonest abnormality was edema including edematous cysts and subcutaneous edema. Other abnormalities, in decreasing order of occurrence, were unabsorbed yolk, small body, external hemorrhage, skinny legs, rotated ankle, and deformed beaks.

Dahlgren and Linder[191] noted decreased chick weight in their studies on the pheasant, but no mention is made of abnormalities Peakall et al.[203] found an increase in chromosomal abnormalities in embryos of ring doves exposed to 10 ppm Aroclor 1254.

An interesting contrast can be made between the effects of PCB's and DDE on avian reproduction. This differentiation is of some importance to wildlife toxicologists since both compounds are found together in bird eggs, and the effects of organochlorines are widely considered to have had adverse effects on some avian populations. In their discussion of differing effects of PCB's and DDE on avian reproduction, Peakall and Peakall[204] considered the effects under three headings, viz., effects on the eggshell, effect of residues in the egg on the embryo, and effect on parental behavior.

F. Direct Estrogenic Effects

The geometric similarity of DDT and PCB's to the synthetic estrogen, stilbestrol, has led to the examination of the possibility that chlorinated hydrocarbons could act as synthetic estrogens.[206] These workers examined the effect of over 50 compounds on the glycogen response of the rat uterus. They found that Aroclors 1221, 1232, and 1242 had a minimum effective dose of 8 mg/rat and that Aroclors 1254 to 1268 were inactive. In contrast, the minimum effective dose of diethylstilbestrol is 0.1 μg, or a factor of nearly 100,000. Aroclors are weak estrogenic agents, but the value of 8 mg/rat should be compared to environmental levels rather than to 0.1 μg/rat of diethylstilbestrol. On a mg/kg basis, the minimum effect dose of an Aroclor in Bitman et al.'s[190] experiments was 160 mg/kg. No residue levels in the uterus were measured, but the dosage suggests that the levels would be high by environmental standards.

Nelson[207] examined the effects of several organochlorines on the binding of labeled estradiol on the rat uterine receptor. The effects of the organochlorines were compared to those of diethylstilbestrol, making possible direct comparison with the experiments of Bitman et al.'s[190] Nelson found that diethylstilbestrol was effective in causing 50% inhibition of estradiol binding at an in vitro concentration of 0.2 ppb. The most active organochlorine (o,p'-DDT) required a concentration of 0.6 ppm to produce 50% inhibition. Other organochlorines required 10 to 100 ppm to cause this degree of inhibition, with Aroclor 1221 being more active than 1254. While critical in vivo experiments have not been carried out, the data

80	Decrease in hatchability	n.s.	[illegible]	12.3	17.5	21.8	27.5
	Residue in yolk	2.9	5.6				

n.s. – Not significant.

Adapted from Britton, W. M. and Huston, T. M., *Poult. Sci.*, 52, 1620, 1973.

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presently available indicate that serious effects will not occur at environmental levels.

G. Thyroid Function

Jefferies and Parslow[208] dosed lesser black-backed gulls with Aroclor 1254 at 50, 100, 200, and 400 mg/kg/day for 8 weeks. An increase in thyroid weights (30 mg to 40 mg) was noted between the controls and dosed birds, but no dose-dependent increase was observed. Analysis of the colloid area showed a small increase. Histological changes were different from those observed with DDT.[209] DDT caused colloid loss and hyperplasia, whereas PCB caused larger follicles well filled with colloid. Hurst et al.[210] studied the effect of Aroclor 1260 at 5, 50, and 500 ppm for 1 to 4 months on bobwhite quail. Significantly different thyroid weights were found for all dose levels after four months, but this effect appears to be due to the abnormally low control value for this period. There was no actual rise in thyroid weights when compared to measurements made at one, two, and three months. There was a tendency for I^{131} uptake for the total thyroid to be higher in quail exposed to the highest dose (500 ppm), but this increase was significant for only one-time period and did not show up when expressed on per milogram of thyroid basis. Current evidence does not suggest that PCB exerts an important influence on thyroid function.

H. Vitamin A

Cecil et al.[190] studied the effect of 100 ppm DDT or 100 ppm Aroclor 1242 on liver vitamin A levels in quail and rats. After 2 months on the diet, Aroclor 1242 caused a marked reduction (approximately halved) in vitamin A in male quail, but the females were unaffected. DDT caused some reduction, but this was less marked. In rats the levels were reduced to approximately half the control values by both compounds in both sexes. No symptoms of vitamin A deficiency were noted in either species. Studies on mammals at lower doses would be desirable in view of recent findings suggesting a link between low vitamin A levels and induction of cancer.[211] Jefferies and French,[212] studying the effect of DDT on pigeons, found a marked increase in liver vitamin A levels at lower dosages (3 mg/kg/day and 36 mg/kg/day) whereas at a higher dose (54 mg/kg/day), there was a marked decrease from control values. Comparable studies with PCB's are not available.

I. Carcinogenic Effects

Studies on this topic appear to be very limited. Kimura and Baba[213] reported benign neoplastic lesions in the livers of all female rats which received more than 1,200 mg of Kanechlor-400, but no effect was seen on males. Nagasaki et al.[214] reported that 7 out of 12 mice exposed to a diet containing 500 ppm Kanechlor-500 had tumors of the liver, whereas hepatomas were not seen at 250 ppm, nor with Kanechlor-400 and Kanechlor-300. Uchiyama et al.[215] found that Kanechlor-400 was not a co-carcinogen with methylcholanthrene at either 10 or 100 ppm. A positive co-carcinogenic effect was seen with DDT at 100 ppm. Both of the direct studies on carcinogenic effects were carried out on a small number of animals for a single generation. While there is not any evidence of a strong carcinogenic effect, detailed, multigeneration studies are desirable.

Green et al.[216] found no cytogenetic effects on bone marrow and spermatogonial cells of rats treated with Aroclor 1242 and 1254. Doses of Aroclor 1242 were single doses of 1,250, 2,500, or 5,000 mg/kg, or multiple doses of 500 mg/kg. Aroclor 1254 was given in multiple doses from 75 to 300 mg/kg/day. These workers found no inhibition of mitotic division nor chromosomal abnormalities. These authors point out that their work does not exclude the possibility that point mutations occurred, but state that it is very rare for this to occur in the absence of chromosomal aberrations.

J. Immunosuppressive Activity of PCB's

Friend and Trainer[217] examined the effect of Aroclor 1254 on mortality of young mallards exposed to duck hepatitis virus. Three dose levels were used, viz., 25, 50, and 100 ppm, in the diet. At all dosages, the mortality was increased markedly over control values, but the greatest increase was at 50 ppm. The actual values were control 14.3%, 25 ppm 35.0%, 50 ppm 65%, and 100 ppm 44.4%. Vos and de Roij[218] studied the effect of 10 and 50 ppm Aroclor 1260 on the humoral immune responses of guinea pigs. Tetanus toxoid injections increased the γ-globulin levels in control animals, whereas this increase was not found in animals fed 10 ppm PCB. However, the animals exposed to 50 ppm did not vary significantly from the controls. A significantly reduced number of γ-globulin-containing cells in the lymph

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nodes were noted in the 10 ppm tetanus toxoid-stimulated group and in the unstimulated left lymph nodes of the stimulated 10 and 50 ppm groups. In a subsequent paper Vos and Driel-Grootenhuis[219] examined both the humoral and cell-mediated immunity under the influence of Aroclor 1260 and Clophen A60. These workers found that PCB's at the level of 50 ppm had immunosuppresive activity of both the humoral and cell-mediated immunity. No significant effects were seen at 10 ppm and the 250 ppm diet proved to be too toxic for these experiments to be carried out. Koller and Thigpen[220] dosed rabbits with Aroclors 1221, 1242, and 1245 150 mg/kg by stomach tube weekly for 14 weeks. All Aroclor treatments resulted in significantly lower serum-neutralizing antibody titers to pseudo-rabies virus than was found in the controls. There was little difference between the effects of the three Aroclors. Total serum γ-globulin concentrations decreased with Aroclor 1242, but increased for other groups, including controls.

The importance of the effects of PCB's on the immunosuppresive mechanisms are hard to evaluate. The lack of clear dose dependence is one problem, and interrelation with other stresses is another. The possibility of the burden of PCB's and other organochlorines[221] increasing susceptibility to disease should be borne in mind.

K. Hydropericardium and Generalized Edema

McCune et al.[222] discovered hydropericardium when chickens were placed in a battery treated with unhardened paint. Additional studies revealed that Aroclor 1242 caused hydropericardium at dosages of 200 ppm and above. A more detailed study was made, using the same Aroclor, by Flick et al.[223] Edema formation in the pericardial sac and in the abdominal and subcutaneous areas was pronounced in the chickens exposed to 400 ppm for 3 weeks, but was much less marked at 200 ppm. Rehfeld et al.[224] observed general edema in chickens when the diet contained over 20 ppm Aroclor 1254. Chicks exposed to diets containing 50 to 150 ppm to Aroclor 1254 had extensive generalized edema. This included serious effusion into the pericardial sacs, muscles, subcutaneous tissues, and abdominal cavity.

Bayer and Bird[225] studied structural changes in the epicardium of chickens exposed for 11 weeks to a diet containing 20 ppm Aroclor 1254. They found that all the birds exposed to PCB showed morphological changes in the pericardium and three out of four birds showed large quantities of ascites fluid. Residue levels were not given, but the diet levels would suggest that the levels would not be much higher than those of fish-eating birds from highly contaminated areas. Vos and Koeman[226] studied the effects of 400 ppm of 3 different preparations of PCB's containing 60% chlorine. These were Phenoclor DP6, Clophen A60, and Aroclor 1260. The chickens were exposed to this diet for 60 days. Hydropericardium was common in the Phenoclor and Clophen group, but rare and statistically non-significant in the Aroclor group. Similarly abdominal and subcutaneous edema was observed only in the first two groups. These differences were considered to be due to the presence of chlorinated dibenzofurans in the first two preparations.[227] Nevertheless, there are considerable differences between Vos and Koeman's results on Aroclors and those of other workers. These differences may be due to the fact other workers have used lower chlorinated Aroclors (1242 and 1254) which may themselves act differently or may contain more chlorinated dibenzofurans than Aroclor 1260. Firestone[228] reviewed the etiology of chick edema disease and concluded that the chlorinated dioxins and furans were the chemical agents responsible. In view of the studies of Rehfeld et al.[224] and those of Bayer and Bird[225] which show effects at moderate levels, viz., 20 ppm, it would be useful to examine the effect of pure PCB's to clear up the question of the agent causing chick edema.

Recently hydropericardium and edema have been found in Herring Gull (*Larus argentatus*) chicks from the most contaminated areas of the Great Lakes.[229] In this case substantial levels of PCB's, DDE, mirex hexachlorobenzene dieldrin, and HCB were present. Bowes et al.[230] were not able to detect any chlorinated dibenzofuran or dibenzodioxin compounds in gull eggs from the Great Lakes.

L. Porphyria

In contrast to their findings on edema, Vos and Koeman[226] found that porphyria was induced by all preparations of PCB's studied. They found that the chickens increased fecal excretion of coproporphyrin and protoporphyrin and fluorescence (indicating the presence of porphyrins) in the liver, bile, small intestine, and bone. Subsequently, these

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workers[231] made a more detailed study using Japanese quail. Using Aroclor 1260 at 50, 100 250, and 500 ppm in the diet for 7 days on male quail they demonstrated a tenfold increase of mitochondrial δ-aminolevulinic acid synthetase in the liver of birds receiving 50 ppm, and a further increase at higher levels. Increased fluorescence of the liver only became marked at higher dosages. Lower levels were studied on female quail. A slightly but statistically nonsignificant increase of δ-aminolevulinic acid synthetase was noted at a dosage of 0.1 mg/kg/day for 7 days, but the increase was significant at a dosage of 1 mg/kg. δ-Aminolevulinic acid synthetase catalyzes (ALA synthetase) the first step in porphyrin synthesis, viz., the reaction of succinyl CoA with glycine to form α-amino-β-keptoadipic acid. Metabolic control of porphyrin formation is excreted through a feedback mechanism operating at the first two steps of the pathway, viz., ALA synthetase and δ-aminolevulinic acid dehydrase. ALA is also the precursor of the porphyrin moiety of chlorophyll and of the corrin ring of vitamin B_{12}.

The finding that ALA synthetase is stimulated by low levels of PCB's raises the possibility of a health hazard to persons suffering from acute, intermittent porphyria. Barbiturates, which also stimulate ALA synthetase, can cause a severe attack of this disorder which can result in paralysis and death.[232]

Studies on herring gull eggs collected from contaminated areas of the Great Lakes have shown markedly raised porphyria levels in the livers of embryos compared to those from less contaminated areas.[229]

M. Inhibition of Adenosine Triphosphatase (ATPases) by PCB's

The effects of PCB's on ATPases and the possible role of inhibition of these enzymes on osmoregulation in fish have been examined by a number of workers. Yap et al.[233] examined the effect of Aroclor 1221, 1254, and 1268 on the in vitro inhibition of Na^+K^+-ATPase and Mg^{++}-ATPases from several tissues of Blue Gill fish. Overall, Aroclor 1254 was the most effective inhibitor, and Na^+K^+-ATPase was inhibited to a greater extent than Mg^{++}-ATPase. Substantial inhibition was found at levels as low as 0.03 ppm in brain and muscle. In a subsequent paper,[234] these workers examined the effects of Aroclors on both oligomycin-sensitive and oligomycin-insensitive Mg^{++}-ATPase. They found that the oligomycin-insensitive Mg^{++}-ATPase was inhibited a good deal more strongly than the oligomycin-sensitive Mg^{++} ATPase. Oligomycin-sensitive Mg^{++}-ATPase is involved in the mitochondria synthesis of ATP, whereas the physiological function of oligomycin-insensitive Mg^{++}-ATPase is uncertain. In another paper,[235] this group compared the inhibition of these three ATPases in tissues of fat head minnows exposed to Aroclor 1242 and 1254 for four months. These in vivo studies failed to confirm that oligomycin-insensitive Mg^{++}-ATPase was the most strongly inhibited, and results were erratic with enhanced activity seen in some cases and a lack of clear dose-activity relationship.

Kinter et al.[236] examined the effect of both DDT and Aroclor 1221 on both in vivo and in vitro ATPase activity and on osmoregulation in teleost fish and eels. They found that both DDT and Aroclor 1221 caused inhibition of ATPase and decreased the ability of both killifish and eels to osmoregulate. The level of Aroclor 1221 required to cause an effect was much higher than DDT, in general about two orders of magnitude. Davis et al.[237] determined the degree of inhibition of ATPase in trout gill microsomes by Aroclor 1242 and 1254. They found that 1242 caused greater inhibition than 1254. For both Aroclors, 40 ppm caused significant inhibition whereas 4 ppm was not effective except on Mg^{++}-ATPase.

Sharp et al.[238] examined the effect of Aroclor 1221 and 1254 on Na^+K^+-ATPases from beef brain and rabbit kidney. They found that 10 ppm of Aroclor 1254 and 15 ppm of Aroclor 1221 caused slightly more than 50% inhibition. These workers found that phosphatidylserine and phosphatidylinositol protected the ATPase from inhibition and concluded that the phospholipids are necessary for stabilization of the enzyme and that chlorinated hydrocarbons interfere with the stabilization process.

N. Physiological Effects of PCB's on Microorganisms

Keil et al.[239] exposed the marine diatom, *Cylindrotheca closterium*, to Aroclor 1242 at 0.01 and 0.1 ppm. They found that harvest weight, chlorophyll index, and RNA levels were significantly reduced at the higher concentration. The final PCB level was 190 ppm, showing a concentration factor of 1,000.[240] Similar concentrating

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Mosser et al.[241] examined the effect of PCB's on two marine diatoms, a marine green algae and two species of fresh water green algae. One marine diatom (*Thalassiosira pseudonana*) was inhibited at 25 ppb but not at 10 ppb, whereas the other (*Skeletonema costatum*) was inhibited to some extent at 10 ppb. By contrast the marine and fresh water algae were much more resistant, one showing no inhibition at 1,000 ppb, and others only slight effects at 100 ppb. Subsequently, these workers[242] examined the effects of PCB's on the species composition of mixed cultures of a marine diatom and marine green algae. The results found were in line with those predicted from the previous experiments, viz., that the resistant algae (*Dunaliella tartiolecta*) was favored over the PCB-sensitive diatom (*T. pseudonana*) when the mixture was exposed to PCB (Aroclor 1254). A more surprising result was that competitive advantage was clearly demonstrated at concentrations much lower than the PCB concentration needed to cause inhibition of the pure culture. The minimum concentration needed to inhibit the diatom was 25 ppb, but selective advantage was found at the lowest concentration used, viz., 1 ppb. The threshold value for effects on competitive advantage have not been worked out. The complexities of interactions of various environmental contaminants on microorganisms have also been studied by this group.[243] They found interesting interactions between DDE, DDT, and PCB's on the growth of a marine diatom (*T. pseudonana*). Neither 10 ppb PCB's (Aroclor 1254) nor 100 ppb DDE caused significant inhibition of growth, but in combination growth was reduced from 6×10^6 cells/ml to 1×10^5 cells/ml. A concentration of 50 ppb PCB's caused almost complete inhibition of growth, but this inhibition was markedly counteracted by 500 ppb DDT. Interaction between DDT and DDE was slight.

Luard[244] also found considerable variation of the sensitivity of two algal species to Aroclor 1254. She found that *Dunaliella* was sensitive at 0.1 ppb, whereas *Scenedesmus* required 100 ppb to cause significant inhibition of radiocarbon uptake. Fisher et al.[245] demonstrated variable sensitivity of phytoplankton collected in various areas to PCB's.

Moore and Harriss[246] measured the effect of Aroclor 1242 and 1254 on *in situ* radiocarbon uptake by marine phytoplankton communities from the northern Gulf of Mexico. Both Aroclors showed effects on the radiocarbon uptake at 1 to 2 ppb and the LC_{50} values were 6.5 ppb and 15 ppb, respectively.

Moore and Harriss[247] have examined the effect of Aroclor 1242 on net- and nannoplankton, the latter being defined as that which is not retained by a 20 to 80 μm net. They found that nannoplankton radiocarbon uptake, which accounted for almost three quarters of the total carbon fixation, was unaffected by Aroclor 1242 at 10 or 25 ppb. In contrast, net-plankton uptake was reduced by 56% by 10 ppb and 58% by 25 ppb.

Given the high concentration factors from water to microorganisms, it is likely that PCB's entering the oceans via aerial transport will be rapidly taken up by marine phytoplankton. More detailed studies are needed to demonstrate whether or not a serious environmental effect is occurring. Studies showing marked effects on competitive advantages at 1 ppb indicate that the possibility that PCB's could alter species composition need to be taken seriously.

O. Effects of PCB's on Nonhuman Primates

Experiments on nonhuman primates are useful in the extrapolation of data from experimental animals to man. Allen et al.[248] fed rhesus monkeys diets containing 300 ppm of Aroclor 1248 for 90 days. There was a gradual loss of body weight in most of the animals receiving PCB's. The animals developed alopecia, acneform lesions of the skin, subcutaneous edema, and hypertrophy of the liver and gastric mucosa. In general, the responses were similar to those reported in the "Yusho" outbreaks in Japan.[96-99] Alterations to the liver were similar to those reported for other experimental animals (Section 5B). In another experiment this group[249] examined the absorption, distribution, and excretion of Aroclor 1248 in the rhesus monkey. They found that over 90% of the PCB was absorbed from the gastrointestinal tract, and that elimination from the body was slow. The experimental animals had slight but significant decreases in hemoglobin and hematocrit. Lesions of the gastric mucosa were considered to be unique to primates and this facet of the work was examined in another paper by this group.[250] The dietary concentration was the same as in previous experiments. It was found that the hypertrophic gastric mucosa was several times

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thicker than the control mucosa and consisted of greatly elongated hyperplastic glands containing mucus-secreting cells. The authors consider that these findings are suggestive of an eventual neoplastic transformation.

Additional experiments with lower dosages and long time periods will be necessary to assess the importance of these changes. The levels in these experiments are high by normal food standards (see Section 4E). Additional experiments by Abrahamson and Allen[251] have demonstrated that the infant rhesus monkey is more resistant to PCB's than adults. No studies covering reproduction in nonhuman primates have been reported.

6. EVALUATION OF THE ECOLOGICAL SIGNIFICANCE OF PCB's

While this is an attempt to assess the evidence already presented, it is obvious that personal bias enters into this type of an evaluation. The widely varying opinions given by trained scientists at the DDT hearings conducted by the U.S. Environmental Protection Agency emphasize this point. Opinions on the impact of DDT ranged from the viewpoint that to ban DDT was genocidal to that DDT was a universal biocide. Personally, the author dislikes the idea of any stable foreign material being released into the environment on a large scale, since ecosystem interactions are too complex for any experimentation to make certain that no serious consequences will occur.

No definite evidence is available to indicate that current PCB levels are normally a hazard to human health. In view of reproductive failure of a mammal (mink) fed fish from the Great Lakes, one would be doubtful about the safety of persons on a high fish diet in the most heavily contaminated areas, viz., the North American Great Lakes and Japan. No evidence is available that PCB's are carcinogenic or tetragenic to mammals although one could wish that the evidence was based on larger, longer-range experiments.

The reproductive failure of mink fed fish from the Great Lakes under laboratory conditions suggests the possibility of effects at current environmental levels on fish-eating mammals. No field studies have been carried out with the exception of sea lions in California. In this case, however, the predominant residue is DDE rather than PCB's. The reproductive failure of Herring Gulls in the Great Lakes is probably due, in part, to PCB's, although the relative importance of PCB's compared to other contaminants is difficult to assess. Similarly PCB's are probably involved in the declines of other top predators, i.e., Osprey, in eastern North America. Laboratory studies indicate the toxicologial effects would be expected at higher environmental levels.

The importance of PCB's and other organochlorines in selective advantage to microorganisms in the environment is difficult to assess. The possibility of alterations at environmental levels is suggested, but actual confirmation is not available and would be difficult to demonstrate.

The author's assessment of the environmental impact of PCB's is that some adverse effects have been caused to organisms high in the food chain in highly contaminated areas, such as sections of eastern North America and Japan. One lesson to be learned from the PCB story is that a stable, lipophilic compound can accumulate in significant amounts even when not deliberately introduced into the environment. The information obtained on the relationship between usage patterns and environmental levels, and the alterations following restrictions on usage, should serve as a basis for future regulations.

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