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A summary of PCB technical literature from 1972 to present.

MONS 200872

BIBRA INFORMATION BULLETIN

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Issue no.3
April 1975

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E. P. Wheeler

ARTICLES OF GENERAL INTEREST

LIVING WITH POLYCHLORINATED BIPHENYLS

The widespread occurrence of polychlorinated biphenyls (PCBs) throughout the environment, their relatively high toxicity and their exceptional resistance to biodegradation have all served to draw attention to these unwelcome companions and to dictate a careful watch on their progress in natural ecosystems. We have already taken a broad view of the challenge posed by PCBs and have noted that the prompt action of the Monsanto group, the sole manufacturer in the USA and UK, in restricting the use of PCBs to closed systems such as transformers and capacitors, has alleviated the natural anxiety of toxicologists and ecologists (RIBRA Bull. 1972, 11, 323). About this time, Maugh (Science, N.Y. 1972, 178, 368) summarised reports of the distribution of PCBs in the biosphere. They had appeared in the tissues of polar bears and seals in Canada, in 54·3% of 2189 samples of human adipose tissue collected throughout the USA, in nearly 20% of some 3500 samples of fish, milk, eggs and cheese investigated by the FDA, and (at levels as high as 3·2 ppm) in the bottom sediments of lakes, which were, in some cases, far from likely industrial sources.

Concentrations of about 1 ppm seem to be generally accepted as offering no toxic hazard to man, and indeed the FDA has adopted interim tolerance limits for foods ranging from 0·2 ppm in infant foods to 5 ppm in the edible parts of fish (Federal Register 1974, 39, 42747). There is, however, no guarantee that other animal species can withstand similar concentrations of PCBs without harm. Mink farmers have had reason to deplore the high susceptibility of their animals to the levels of PCBs found in some types of fish from the Great Lakes, while some PCBs (32-54% chlorine) adversely affect hatchability in chicks. Many planktonic organisms, which play an essential role in the food chains of both fresh- and salt-water fish, may be susceptible to low concentrations of PCBs and may serve to concentrate them in the food chain (Maugh, loc.cit.).

Occurrence of PCBs

Finklea et al. (Am. J. publ. Hlth 1972, 62, 645) has remarked that PCBs of industrial importance are complicated mixtures of many of the 210 theoretically possible halogenated biphenyls plus possible contaminants. They have been used in synthetic rubbers, paints, plastics, insulating materials, caulking materials, flame retardants, cutting oils, synergists for pesticides, adhesives, sealants, printing inks, duplicating papers and heat-transfer media, uses for which their high boiling point, low water-solubility, miscibility with organic solvents, high dielectric constant, thermal stability and high resistance to chemical and biological degradation render them particularly suitable. Many of these properties, however, also ensure their place among the serious and persistent environmental pollutants. Thermal destruction, for example, occurs only above about 950°C, which means that waste oils burnt at ordinary furnace temperatures, and solid wastes containing PCBs, form a ready source of atmospheric contamination (Jensen, Ambio 1972, 1, 123).

Maugh (Science, N.Y. 1973, 180, 578) has reported that PCBs can be produced by irradiation of DDT vapour with ultraviolet light of wavelengths present in sunlight in the lower atmosphere (290-310 nm). This throws new

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light on the problem of contamination with other organochlorine compounds, a situation which for so long led to the overlooking of PCBs in analyses of a wide variety of samples from the environment. It may also help to explain the discrepancy between, on the one hand, the degree of accumulation of DDT and DDE to be expected in the biosphere from the known use levels of DDT and its assumed resistance to atmospheric degradation and, on the other, the amounts that can actually be accounted for by current methods of monitoring and calculation. DDE is an intermediate in the photodegradation of DDT to PCBs. Fortunately, photodegradation may be expected to increase environmental levels of PCBs only in respect of the less chlorinated homologues, which are probably less troublesome in biological systems and less persistent. Sewage treatment is a further source of PCBs, significant quantities of which were found in the effluent from a plant which took in waste from a textile mill using biphenyl as a dye carrier (Gaffney, ibid 1974, 183, 367). This waste was treated with chlorine, and a suspension of filter scrapings was found to contain 18 ppm PCBs, which interfered with normal sewage-treatment processes.

PCBs in human tissues and milk

In a study of human perirenal fatty tissue obtained from 32 post-mortem samples taken in the Vienna district, Pasendorfer et al. (Wien. klin. Wschr. 1973, 85, 218) found a mean concentration of 3·5 ppm PCBs, ranging from 0·3 ppm in a woman aged 81 to 8·5 ppm in a male aged 76. Associated with the PCBs was a mean fatty tissue content of 5·8 ppm total DDT and DDE. In view of the fact that, when body fat is consumed, stored organochlorine derivatives are liberated into the circulation, an investigation by Hesselberg & Scherr (Bull. env. contam. & Toxicol. (U.S.) 1974, 11, 202) is relevant. Nine patients suffering from severe wasting disease were studied and compared with apparently normal subjects. DDE residues in the blood were much higher in these patients than in the controls, the mean levels for the two groups being 21 and 3 ppb ($b = 10^9$), respectively. The cachectic patients also showed a mean blood concentration of 47 ppb PCBs, which were not detectable in the controls. The authors dismiss the DDE residues in the cachectic patients as being less than those found among apparently healthy workers in a DDT plant, but they suggest that the levels of circulating PCBs may have been high enough to be harmful, although the patients' multiple symptoms would probably have masked any such effects.

In contrast to the figure reported from Vienna, a survey of human fatty-tissue samples analysed in Japan (Curley et al. Nature, Lond. 1973, 242, 338) showed that while all the tissues analysed were positive for PCBs, the level in 80% of the samples was less than 1 ppm and the overall range was 0·3–1·48 ppm. The tissue levels of PCBs in ordinary persons in Japan and in others suffering from 'Yusho' disease, attributed to the consumption of rice oil contaminated with PCBs, have been compared by Masuda et al. (Bull. env. contam. & Toxicol. (U.S.) 1974, 11, 213). The average concentration of PCBs in the fatty tissue of the Yusho patients was 2·5 ppm (6·3 ppm in isolated fat) compared with 0·9 ppm (2·6 ppm in fat) in the controls. The livers of Yusho patients contained 0·1 ppm PCBs (6·5 ppm in fat). The gas-chromatographic (GLC) patterns of the tissue samples and of the PCBs present in the rice oil suggest that while the overall PCB levels decreased substantially during the year following the accident, this largely reflected a decrease in the PCBs of lower chlorine content; retention of the hexa- and heptachlorobiphenyls was more prolonged, apparently for as much as 4 years or more.

The long retention of PCBs in body fat raises the question of how much may be excreted into breast milk and passed on to the infant. Masuda et al.

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(loc.cit.) reported an average of 0·014 ppm and a maximum of 0·02 ppm PCBs in milk from 12 normal Japanese women; milk samples from another group of 19 normal women showed an average level of 0·03 ppm and a range of 0·01–0·06 ppm. The sample available from the one appropriate Yusho patient also contained 0·06 ppm PCBs and gave a GLC pattern similar to residues from the liver and adipose tissues of the patients. Siyali (Med. J. Aust. 1973, 2, 815) detected DDT and other common pesticide residues in the milk of 45 women in a metropolitan area of New South Wales but did not find any PCBs, and suggested, therefore, that the human food chain in that region was possibly not contaminated by PCBs. Savage et al. (Bull. env. contam. & Toxicol. (U.S.) 1973, 9, 222) reported low concentrations of PCBs in milk from some of a group of 39 women in rural Colorado. Only eight of the samples contained PCBs, six at a level of 0·04 ppm, one at 0·05 ppm and one, from a 25-year-old woman who had spent her entire life in Colorado, at 0·1 ppm.

Routes of entry into the food chain

Seas and lakes are known to contain low concentrations of PCBs. In a study of North Atlantic waters, Harvey et al. (Science, N.Y. 1973, 180, 643) found that open surface water contained a mean concentration of 35 ng/litre, while water from 200 m down contained 10 ng/litre. The surface waters of the Sargasso Sea showed slightly lower concentrations (27 ng/litre) but there was no observed relationship between PCB concentration and the proximity of land masses, and it seems that the atmosphere must be the predominant mode of transport of these contaminants. The same group of workers recently published some encouraging data derived from subsequent studies of North Atlantic surface waters (idem, Nature, Lond. 1974, 252, 387). These results indicated that by the end of 1973 the levels of PCBs in these waters were some 40 times lower than those found in 1972. In the Sargasso Sea, a rapid decline in concentration to 1 ng/litre in April 1973 had levelled off at 0·8 ng/litre by the end of the year. These reductions in surface-water concentrations roughly coincided with a tenfold decrease in PCB contamination of the atmosphere over the North-west Atlantic during 1973 (Harvey & Steinhauer, Atmos. Environ. 1974, 8, 777) and a fivefold decrease in the PCB content of mixed plankton from this area between 1972 and September 1973 (Harvey et al. J. mar. Res. 1974, 32, 103).

Ware & Addison (Nature, Lond. 1973, 246, 519) have described how the concentration of PCBs in plankton from the Gulf of St. Lawrence varies with the mean size of the plankton species and the time of year. PCB concentrations were inversely proportional to particle size, even with a 34-fold difference in residue levels between composite plankton samples, and the acquisition of organochlorine contaminants from the environment therefore appears to bear a direct relationship to the surface area of the particles. Plankton particles in the 73–202 μm group contained what was thought to be the highest PCB concentration ever reported for natural plankton, namely 31 ppm (wet weight) in June. Overall PCB concentrations in the plankton varied greatly, from 93×10^{-9} g/m^3 at the beginning of June to 2×10^{-8} g/m^3 at the beginning of August, showing an irregular incremental pattern indicating that PCBs entered the plankton in discrete pulses, largely from the air and rainwater. This explanation was supported by the observed correlation between PCB contamination and the cumulative rainfall during the 10–20 days preceding the sampling. During periods of light precipitation the disappearance of PCBs by small-plankton biomasses would account for the low PCB residues afterwards. Ware & Addison (loc.cit.) were careful to eliminate the interfering effect of PCBs in the antifouling paint on the hulls of their sampling vessels by checking the water of the wake. Jensen et al. (ibid 1972, 240, 358) had

previously reported that in sampling plankton in Stockholm harbour they found that samples from the wake could be heavily contaminated with PCBs and other lipophilic organochlorine compounds derived from the bottom paint. It seems likely that inshore water may regularly be contaminated with PCBs from shipping in this way, and that plankton may thereby acquire high concentrations of PCBs.

The effect of PCBs on plankton communities was described by Moore & Harrise (ibid 1972, 240, 356), who studied the effects on photosynthesis of different concentrations of PCBs added to heterogeneous plankton samples taken from the Gulf of Mexico. Radiocarbon uptake by the samples was more depressed by the PCB mixtures, Aroclor 1242 and 1254, than by equivalent amounts of p,p'-DDT or pure 2,4'-dichlorobiphenyl. Inhibition indicating toxicity was evident with 1-2 ppb in the case of the Aroclors, whereas DDT and 2,4'-dichlorobiphenyl caused comparable inhibition at 5 and 7 ppb respectively. These effects on total plankton communities were more marked than those previously observed with isolated laboratory cultures of selected species.

From plankton, PCBs enter fish and seabirds. As regards marine mammals, Sanchenbrecker (Can. J. comp. Med. 1973, 37, 203) has remarked that it is not known whether whales ingest PCBs in their planktonic diet or absorb them directly from the water; but widespread oil pollution of the North Atlantic may produce an enriched surface stratum from which lipid-soluble contaminants, including PCBs, might be absorbed. Blubber tissue from 12 North American fin-back whales, collected in 1970 and 1971, showed a maximum of 0·185 ppm PCBs, compared with levels of DDT metabolites of up to 2·557 ppm.

A large proportion of the published observations seem to have been made on freshwater fish in the lakes of North America. Bache et al. (Science, N.Y. 1972, 177, 1191) have reported that trout from Cayuga Lake in New York State showed an overall rise in PCB levels with age and maturity, the concentrations found ranging from 0·5 ppm in juvenile fish to 12-30 ppm in adults (8-12 years old). The presence of PCBs containing 54% chlorine was verified in a 12-year-old trout containing 26·2 ppm PCBs, the mass spectra of which were essentially identical with those of the isomers of Aroclor 1254. Zitko (Bull. env. contam. & Toxicol. (U.S.) 1974, 12, 406) has demonstrated the uptake of Aroclor 1254 under experimental conditions in juvenile Atlantic salmon maintained in aerated fresh water containing, in a concentration of 1 g/litre, a suspension of silica contaminated with 0·7% Aroclor 1254. In fish killed after 24, 48 and 144 hours, whole-fish analyses indicated PCB concentrations of 19·9, 28·3 and 134·0 µg/g wet weight, respectively. Under comparable conditions, the uptake of chlorinated paraffins was much lower, concentrations equivalent to 0·2-0·75 µg/g (expressed as chlorine) being obtained after 48 or 144 hours. The GLC pattern of the absorbed PCB components compared with that of an Aroclor 1254 standard indicated a relatively high uptake of components with shorter retention times, particularly after the shortest exposure time. This preferential absorption was not observed, however, when food contaminated with Aroclor 1254 was fed to juvenile Atlantic salmon for 33-181 days, although again there was a marked discrepancy between uptake of the PCB and that of similarly administered chlorinated paraffins. When Aroclor 1254 was fed at a dietary level of 10 ppm, the PCB levels in the fish reached equilibrium, at 3·8-3·9 µg/g wet weight, within 33 days, but with a dietary level of 100 ppm residues of 13·9, 24·0 and 30·0 µg/g were found after 33, 109 and 181 days, respectively.

In a study of PCBs in the Lake Poinsett and Dry Lake waters in South

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Dakota, Greichus et al. (Bull. env. contam. & Toxicol. (U.S.) 1973, 9, 321) found that the concentration of organochlorine insecticides in bottom sediments was about seven times higher than that in the water, while fish in the two lakes contained concentrations of PCBs some 12 times higher than those in bottom sediments. There is thus a concentration gradient rising into the food chain. Greichus et al. (loc.cit.) found, moreover, that adult cormorants feeding on the fish in these two lakes contained concentrations of organochlorine compounds that were 250 times higher than those in the fish, while levels in the local pelicans were 280 times higher. PCBs in these two bird species were, respectively, 60 and 30 times higher than in the fish they fed on, and PCBs were detected in the cormorants' eggs. In both types of bird, the highest PCB concentrations were in the body fat (22·4 and 31·4 ppm wet weight on average in cormorants and pelicans, respectively) and paralleled the body-fat concentrations of total organochlorine compounds. Bogan & Bourne (Nature, Lond. 1972, 240, 358) reported relatively low concentrations (0·1-1·0 ppm) of organochlorine residues in auks and shearwaters from the North Atlantic and higher levels (1-10 ppm) in more pelagic birds, such as kittiwakes, fulmars and storm-petrels. The highest concentrations, exceeding 10 ppm, occurred in large gulls and skuas feeding around trawlers in winter and seabird-breeding stations in summer. However, the finding that a fulmar carrying 42 ppm PCBs in its body fat had only 1·3 ppm in its stomach oil, which is fed to the chick, suggested only a low transfer from one generation to the next in food. Arctic glaucous gulls had, on average, 24 ppm PCBs in the liver, while one had 535 ppm in its body fat. One gull, observed to convulse, had a liver-PCB concentration of 311 ppm. The presence of PCBs in the Arctic, over 250 miles north of a major land mass, is somewhat disturbing.

PCBs in human foodstuffs

Ramsey (Q. Bull. Ass. Fd Drug Off. U.S. 1973, 37, 43) has published an analysis of FDA findings during surveys of food intended for human consumption. No PCBs were found in fresh fruit and vegetables, and the most frequently contaminated food was fish, particularly freshwater fish. This was perhaps to be expected in view of the incorporation of PCBs into aquatic food chains noted above. Samples of shredded-wheat biscuits contained small concentrations of PCBs derived from paperboard dividers used in packaging. These dividers had been manufactured from recycled paper, which had included carbonless copy paper. In a survey started in 1971, about 19% of all the foods sampled contained PCBs. The overall average content of PCBs in packaged food was 0·1 ppm, and in some cases PCBs were found in the packaging materials but were not present in the food itself. Nearly 16% of the total samples of food examined contained PCB residues and were packaged in recycled materials, while contaminated food contained in virgin packaging material accounted for only 3·4% of the total samples.

Also in 1971, Shahid et al. (Bull. env. contam. & Toxicol. (U.S.) 1973, 10, 80) analysed 89 samples of paper pulp, newsprint, recycled paper and liner board and found PCB levels of more than 10 ppm in 11%, 6-10 ppm in 4% and 1-5 ppm in 25% of the samples. However, 56% of the total contained less than 0·5 ppm. The presence of PCBs in virgin newsprint and bond paper showed that recycling was not the only source and suggested that the manufacturing process might also be involved in PCB contamination. Early in 1972, Villeneuve et al. (J. Ass. off. analyt. Chem. 1973, 56, 999) studied the PCB content of 509 packaging-material samples from 120 manufacturers in Canada, finding less than 1 ppm in 8·17%, 1-10 ppm in 14·9% and more than 10 ppm in 3·4%. Of 77 foods tested, only two contained more than 1 ppm PCBs. Of 73 foods tested for polychlorinated terphenyls (PCTs) in the same study,

none contained more than 0·05 ppm. Levels of PCP residues in 445 packaging samples were reported to be less than 1 ppm in 84·5%, 1-10 ppm in 11·4% and more than 10 ppm in 4·1%.

That packaging may be carried out in such a way as to prevent any significant transfer of PCBs into the food is evident from a study by Stanovick et al. (Bull. env. contam. & Toxicol. (U.S.) 1973, 10, 101), who investigated the migration of Aroclor 1242 from treated paperboard containing this PCB at a level of 15 or 150 ppm. Food samples were stored at room temperature in jars lined with the paperboard for 2-90 days and were then assayed for PCBs. Barrier materials interposed between the paperboard liner and the food significantly reduced migration of the PCBs, the extent of the reduction being in inverse proportion to the gas-permeability of the barrier substance. Polyvinylidine chloride-coated paper prevented PCB migration for the full 90 days. Waxed glassine paper was the next most effective barrier, but polyethylene film was relatively ineffective over long periods of storage.

In his review of FDA food surveys, Ramsey (loc.cit.) stressed that, by 1973, PCB contamination of both food and packaging materials had shown some reduction compared with the findings of the 1971 studies, and it seems that this trend is continuing. In addition to possible contamination from packaging, however, PCBs may also be introduced into the human diet in meat, milk and eggs derived from farm stock fed contaminated feedstuffs, and in this situation the concentration of residues demonstrated in natural food chains may again operate.

Tooke et al. (J. agric. Fd Chem. 1974, 22, 900) found that in chicks fed from 3 days of age on a diet containing 10 ppm Aroclor 1254, the PCB residues in dissected fat and muscle, respectively, were 110·6 and 109·0 ppm after 8 weeks and 49·5 and 102·8 ppm after 32 weeks. Depletion rates of administered Aroclor indicated a biological half-life of 2·93 weeks. Fat and muscle levels of residues in chicks fed 10 ppm in the diet for 52 days from the onset of egg production were 33·4 and 70·1 ppm, respectively. PCB residues in eggs from chicks fed this diet from 3 days of age reached a peak of 9·73 ppm about 4 weeks after the onset of egg production and subsequently decreased. When PCB treatment was delayed until the onset of egg-laying, the pattern was similar but the highest residue level was only 2·54 ppm. PCB concentrations in day-old chicks closely paralleled the concentrations in the eggs. Cooking has been shown to effect a significant reduction in the PCB residues in the edible tissues of PCB-treated chicks (Zabik, Poult. Sci. 1974, 53, 1785).

Contamination of animal feeds may result from exposure during production, processing or storage, a few severe cases involving chicken feed having been due to the leaking of PCBs from a heat exchanger (Zabik, loc.cit.). The use of spent transformer oil in herbicide sprays and of plastics containing PCBs in silos and poultry-feed wrappers may also be a source of contamination. Savage et al. (Bull. env. contam. & Toxicol. (U.S.) 1973, 10, 97) took silage samples from 21 pit silos and ten upright silos (in which PCB sealants are sometimes used) on Colorado ranches. Detectable PCB contamination involved both pit and upright silos but was limited to samples from silos on only two ranches and in no case exceeded 0·08 ppm. One of those two ranches was concerned with dairy operations, but no PCBs were detected in milk from the silage-fed cattle.

It seems therefore that the problem of PCB contamination may be less severe than it seemed a few years ago. Nevertheless, a close watch must

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clearly be kept on the situation.

[P. Cooper]

β-AMINOPROPIONITRILE AND THE FOETUS

Rats and mice treated with β-aminopropionitrile (BAPN), the toxic principle of Lathyrus odoratus, have produced offspring with both horizontal and vertical forms of cleft palate but showing no retardation in growth (BIBRA Bull. 1972, 11, 111). Further studies have been undertaken to determine the distribution of BAPN and its main metabolites in maternal and foetal tissues.

Metabolism and distribution

A study of the metabolism and teratogenicity of BAPN in rats has been published by Wilk et al. (Teratology 1972, 5, 41). Females weighing 230-260 g were given an oral dose of 106-270 mg BAPN (as BAPN fumarate) on day 14, 15 or 16 of gestation, and were killed for examination on day 20, just prior to parturition. Others were given 500 mg of the major BAPN metabolite, cyanoacetic acid (CAA), or else 75 mg β-alanine, 75 mg cyanoethanol or 250 mg fumaric acid (as the sodium salt), again on day 14, 15 or 16. Embryos and placentas and maternal tissues, serum and urine contained both BAPN and CAA after BAPN administration. Peak concentrations of BAPN were reached in serum and tissues at 6 hours, but they declined after 9 hours and became negligible after 24 hours. In these rats, tissue and serum concentrations of CAA, unlike those of BAPN, showed a gradual increase and remained high at 24 hours, by which time over 60% of a dose of 270 mg BAPN had been excreted unchanged in the urine and about 3% had been excreted as CAA.

The incidence of cleft palate in the embryos correlated with the dose of BAPN given and with the observed concentrations of BAPN in maternal and embryonic tissue, indicating that BAPN itself was the teratogen. This was supported by the finding that despite the appearance of high concentrations of CAA in maternal and embryonic tissues, direct administration of CAA failed to produce cleft palate. No abnormalities followed dosing with β-alanine or cyanoethanol, two probable metabolites of BAPN, or with sodium fumarate. Although similar tissue concentrations of BAPN were produced by doses given on any of the 3 days, a positive correlation of cleft-palate incidence with dosage and tissue levels appeared only with the dose given on day 15, when embryonic concentrations of 106, 42 and 16 μg BAPN/g tissue were associated with a cleft-palate incidence of 98, 28 and 0% respectively.

Waddell et al. (ibid 1974, 9, 211) injected BAPN labelled with ^{14}C iv into mice on day 12·5 or 15·5 of gestation. After 20 minutes, whole-body autoradiography showed the highest radioactivity to be in the salivary gland and in the urine present in the bladder. Some activity was also demonstrated in the pyloric but not the cardiac stomach. The radioactivity in foetal tissues was in general less than that in the maternal tissues, and was most intense throughout the central nervous system. After 1 hour, the foetal radioactivity exceeded that in maternal tissues, with highest concentrations in the central nervous tissue, eye, yolk sac and the tissues lining the oral cavity. After 3 and 9 hours, maternal concentrations of radioactivity were high in the eye, liver, kidney, salivary gland, intestinal wall, inner ear, aorta and vertebral ligaments. When labelled BAPN was injected sc in conjunction with a large excess of unlabelled compound, intense radioactivity

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