

Studies on Populations Exposed to Polychlorinated Biphenyls

by Kathleen Kreiss*

Mean serum levels of polychlorinated biphenyls (PCBs) in U.S. population groups without occupational exposure to PCBs are usually between 4 and 8 ng/mL, with 95% of individuals having serum PCB measurements of less than 20. Subpopulations consuming fish taken from contaminated waters, such as Lake Michigan and near Triana, AL, have mean serum PCB levels several times those found in other general population groups and ranges that extend into concentrations found in industrial populations involved in capacitor manufacture. Two studies of general populations and several studies of industrial workers have demonstrated associations of PCBs with various serum lipids and liver enzyme levels. Six groups of investigators have found associations between PCB or chlorinated pesticide levels and blood pressure. Research efforts are needed in clarifying determinants of serum-adipose partition ratios; the utility of urinary porphyrins as a measure of subclinical hepatic effects; human metabolites and excretion of chlorinated hydrocarbons; and the relation, if any, between blood pressure and organochlorine compounds when controlled for confounding variables. Established cohorts, such as those in Triana, Lake Michigan sportsfishers, the Michigan PBB cohort, residents of farms with PCB-lined silos, and occupational groups, could all be studied further with attention to these research questions.

In 1966, Jenson (1) first described the contamination of wildlife by polychlorinated biphenyls. Since that time, many investigators of human populations have documented the presence of PCB residues in human populations which are not known to have occupational exposure to this family of compounds. The sources of general population exposure in the past were diverse. Inattention to adequate disposal or destruction of PCB-containing materials led to ambient air, water, and soil pollution. In addition to ambient pollution by discarded transformers, capacitors, and industrial PCB wastes, such PCB-containing materials as carbonless duplicating paper contributed to population exposure by reuse in cardboard used in packaging food stuffs. PCB-containing coatings of silo interiors also led to food contamination when dairy and other cattle ingested PCBs that had leaked from silo walls into their silage feed. These two sources of human food contamination have been eliminated for the most part.

At the present time, general population exposure to PCBs is limited primarily to the consumption of fish (2). Levels of PCBs in fish taken from contaminated waterways reflect the successive bioconcentration of these widespread contaminants in the food chain. Fish taken for personal consumption by sportsfishers on Lake Michigan invariably have PCB concentrations which exceed the 5 mg/kg tolerance set by the Food and Drug

Administration for fish sold in interstate commerce. Whether the PCB body burdens accumulated by sportsfishers, or the lower burdens accumulated by the general population, have health implications is an inquiry of substantial public health interest.

General Population Levels of PCBs

No cross-sectional data concerning serum PCB levels exist for a representative sample of the U.S. population. Various groups of persons have had serum PCB measurements performed in the course of investigations of pesticide residues, food chain contamination, hazardous waste sites, and occupational exposures in which a nonexposed comparison population was necessary (Tables 1 and 2).

Conclusions from these reports concerning background population PCB levels are limited because of differences in analytical methodology, method of population selection, and method of data reporting. For example, the first report of PCB levels in a large number of persons (3) found measurable PCB residues in only 43% of 616 volunteers from Charleston County, SC, who gave blood samples in 1968. However, no detection limit for the analytical method was specified, and the 4.9 ng/mL mean of measurable samples remains difficult to interpret. In addition, most published investigations report arithmetic means for PCB concentrations despite the invariable documentation of a skewed distribution by comparison with the reported range. The geometric

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Table 1. Serum polychlorinated biphenyl (PCB) concentrations in U.S. populations without occupational exposures, 1968–1983.

Area and sampling method	Number of subjects	Year	PCB level, ng/mL				95% confidence interval	Range	Reference
			Arithmetic mean	Geometric mean, median ^a	Arithmetic standard deviation				
Charleston County, SC, volunteers	616	1968	4.9	—	—	—	0–29	Finklea (3)	
Lake Michigan random nonfish eaters	29	1973	17.3	15 ^a	—	—	< 5–41	Humphrey (4)	
Bloomington, IN, volunteers and controls	110	1977	18.8	—	10.8	17–21	6–79	Baker (5)	
Michigan PBB cohort	1631	1978–9	7.7	6.4	—	—	< 1–57	Kreiss (6)	
Billings, MT, random packinghouse workers	17	1979	7.5	5.8	6.8	4–11	2–30	CDC (7)	
Franklin, ID, volunteers	105	1979	—	—	—	—	< 5	CDC (7)	
Random unexposed workers	19	1979	12	—	—	—	10–27	Chase (8)	
Newton, KS, volunteers	7	1979	4.9	4.2	3.1	2–8	2–11	CDC (9)	
Lake Michigan random nonfish eaters	418	1980	—	6.6 ^a	—	—	< 3–60	MI Dept. Health (10)	
Canton, MA, volunteers	10	1980	7.1	5.2	5.2	3–11	1–18	MA Dept. Health (11)	
Old Forge, PA, volunteers	138	1981	3.6	—	—	—	< 3–43	PA Dept. Health (12)	
Jefferson, OH, volunteers	59	1983	5.8	4.4	6.5	4–8	1–45	CDC (13)	
Fairmont, WV, volunteers	40	1983	6.7	5.0	5.3	5–8	1–23	CDC (13)	
Norwood, MA, volunteers	990	1983	4.9	4.2	3.5	4–6	2–30	MA Dept. Health (11)	

^aMedian.

Table 2. Serum polychlorinated biphenyl concentrations in U.S. populations consuming PCB-contaminated fish.

Area and sampling method	Number of subjects	Year	PCB levels, ng/mL				95% confidence interval	Range	Reference
			Arithmetic mean	Geometric mean, median	Arithmetic standard deviation				
Lake Michigan volunteer sportsfishers	90	1973	72.7	56 ^a	—	—	25–366	Humphrey (4)	
Triana, AL, volunteers	458	1979	22.2	17.2	22.3	20–24	3–158	Kriess (14)	
Lake Michigan volunteer sportfishers	572	1980	—	21.4 ^a	—	—	< 3–203	MI Dept. Health (10)	
New Bedford, MA, volunteers	11	1981	31.4	23.6	29.3	13–50	5–101	MA Dept. Health (11)	

^aMedian.

mean or, in some instances median, is a better measure of central tendency in this circumstance. Finally, few conclusions can be drawn about the population from which volunteers come forward unless the volunteers represent a large portion of the available population or volunteer for reasons independent of factors influencing PCB levels.

The studies which are most valuable in reflecting general population PCB levels are those in Michigan residents: large numbers of persons ($N = 1631$) in the PBB cohort, chosen independent of exposure to PCBs, had a geometric mean PCB level of 6.4 ng/mL in 1978 or 1979 (6). More recently, a sample of 418 persons con-

tacted through random digit dialing of several Michigan telephone exchanges (who consumed less than 6 lb of fish per year), had a median serum PCB level of 6.6 ng/mL (10). Small groups of randomly chosen workers without occupational exposure to PCBs corroborate these low average levels. Chase et al. (8) found a mean level of 12 ng/mL in a group of 19 workers in the eastern U.S. A Centers for Disease Control (CDC) investigation (15,16) found that 17 randomly selected packing house workers in Billings, MT, without exposure to materials contaminated by a leaking transformer, had an average level of 7.5 ng/mL.

Some nonurban or nonindustrialized populations may

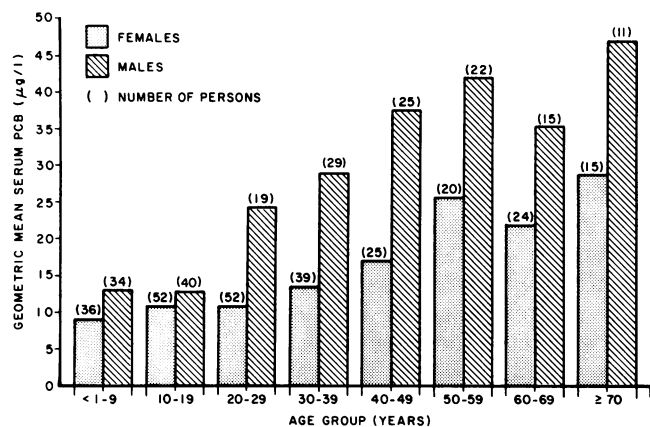


FIGURE 1. Polychlorinated biphenyl (PCB) levels in serum specimens, by age group and sex, Triana, AL, May 1979.

have serum PCB levels that are even lower: more than 100 volunteers in and near Franklin, ID, had PCB levels below the 5 ng/mL detection limit of the Idaho state laboratory (7). This finding is reminiscent of the early work in South Carolina, as is the finding that 58% of 138 residents around a contaminated electric company site had PCB levels below a detection limit of 3 ng/mL (12). Other unpublished data from the Centers for Disease Control concerning serum PCB levels in volunteers with residential proximity to hazardous waste suggests average levels of 4 to 7 ng/mL with 95% of serum values falling below 20 ng/mL (13). In investigations of such volunteers in Jefferson, OH (13); Fairmont, WV (13); Canton, MA (11); and Newton, KS (9); no plausible route of exposure to PCBs was apparent, and the few persons with serum PCB levels higher than 20 ng/mL usually had occupational or food chain exposure. In Norwood, MA, the Commonwealth's Department of Public Health (11) found 90 volunteers near a hazardous waste disposal site to have an average serum PCB level of 4.9 ng/mL, with 95% of values being less than 10 ng/mL.

Serum PCB Levels among Fish eaters

Since fish consumption is the major source of general population exposure to PCBs, special attention to sportfishers catching from heavily contaminated fish populations has been justified. In 1973, Humphrey drew blood samples from 90 persons who consumed 24 lb/year or more of fish taken from Lake Michigan (4). The mean PCB level was 73 ng/mL, more than 4-fold the level in persons who consumed no fish, with a range of 25 to 366 ng/mL. An expanded study (10) of 572 Michigan sports fishers (consuming more than 24 lb of fish/year, median 38 lb) in 1980 showed a considerably lower median level of 21.7, with a range of < 3 to 202.7 ng/mL. This median value was 3.2-fold higher than that for a comparison group of persons consuming less than 6 lb of fish/year. Unfortunately, the analytical methods for PCBs in the two studies did not give comparable results and comparison of serum PCB measurements for individuals who participated in both 1973 and 1980 surveys

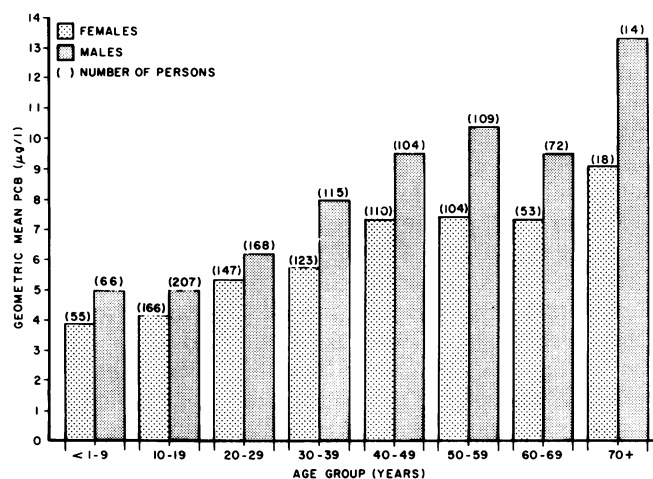


FIGURE 2. PCB levels in serum specimens, by age group and sex, Michigan, 1978-1979.

is not possible. Nonetheless, the identification of this large cohort of fish eaters and randomly selected controls provides future opportunities for important clinical work regarding health implications of such food chain exposure with its preponderance of higher chlorinated biphenyl homologs.

Another fish-eating population has been more extensively characterized in Triana, AL. This population of 600 rural black residents was invited to participate in a cross-sectional health survey in 1979 because of its unusual exposure to DDT-contaminated fish taken downstream from a defunct DDT-manufacturing facility (17). Mean fish consumption among the 499 community volunteers and nearby commercial fisherman had been 4.3 fish meals per month until the extensive publicity about the DDT contamination of fish 6 months before the study. The geometric mean total DDT level in serum was 76 ng/mL (arithmetic mean 159), with individual levels ranging from <1 to 2820 ng/mL. For rough comparison, the U.S. population geometric mean total DDT concentration in serum is 22 ng/mL (18). During laboratory analysis of serum samples for DDT, excessive levels of PCBs were suspected and 458 sera were subsequently analyzed for PCB levels (14).

The geometric mean PCB level in Triana was 17.2 ng/mL, ranging from 3.2 to 158 ng/mL. The arithmetic mean was 22.2 ng/mL. Thus, the average PCB level exceeded those found in most large population studies conducted recently, although the Triana average was comparable to that found for 110 volunteers in Bloomington, IN (5,14) and the recent median among Michigan sportfishers discussed above. Comparisons of findings among specific populations are made difficult by differences in age and sex distributions among the populations studied. In the Triana data set, a striking age and sex dependence of mean values for subgroups was evident (Fig. 1). Mean PCB levels increase with age, and males have higher mean PCB levels than females in each age group in the PCB data from the Michigan PBB cohort as well (Fig. 2).

No major point source of PCBs was found for fish

taken in Indian Creek near Triana, although low levels were found in a variety of environmental samples, consistent with the receipt of drainage from Redstone Arsenal and Huntsville, a city of about 140,000 persons. PCB levels in Triana participants were related to consumption of locally caught fish. Six catfish taken in Indian Creek had an average PCB level of 3.64 mg/kg and 12 fish taken at another time had an average PCB level of 1.08 mg/kg. Despite these low levels of PCB contamination in fish, at least compared to the Food and Drug Administration's PCB tolerance of 5 mg/kg, 36% of the Triana study population had serum PCB levels higher than 20 ng/mL. Thus, long-term ingestion of halogenated hydrocarbons in fish can result in accumulation of human body burdens substantially higher than those found for most general population samples.

In summary, the best information available at this time suggests that geometric mean or median PCB levels encountered in general population samples without occupational exposure are normally less than 10 ng/mL, although age and sex standardizations are crucial. No representative weighted cross-sectional data exist for the PCB levels in the U.S. population, as are available for other chlorinated hydrocarbons such as the DDT family. Certain groups which eat large amounts of fish may have members who accumulate PCBs to levels usually associated with occupational exposure, even when the level of fish contamination by PCBs is within the tolerance set by the U.S. Food and Drug Administration.

Health Effects

Only two studies of general population volunteers have attempted to correlate serum PCB levels with health indices derived from questionnaire data and biochemical clinical laboratory measurements (5,14). Baker et al. (5) showed that plasma triglyceride levels increased significantly with serum PCB levels in both alcohol drinkers and nondrinkers. In the Triana study, serum cholesterol was positively associated with serum PCB levels, independent of other major predictors of PCB level such as age, sex, fish consumption, body mass

index, and alcohol consumption. In turn, the PCB level was a significant predictor of serum cholesterol independent of triglyceride level and age. The weak correlation between log-transformed PCB and triglyceride levels disappeared when controlled for cholesterol and γ -glutamyl transpeptidase (GGTP) levels. No relation was found between log-transformed PCB and high-density lipoprotein (HDL) cholesterol.

Workers with occupational exposure to PCBs resulting in higher average serum PCB levels and substantially greater ranges of PCB concentrations have also been evaluated for subclinical associations with serum lipids and other health indices (Table 3). Chase et al. (8) found a significant correlation between plasma PCB and serum triglyceride level independent of age but did not find a correlation with cholesterol level or cholesterol subset. Adipose PCB levels were not associated with plasma triglycerides. Smith et al. (23) found a positive correlation of serum PCB level with plasma triglycerides and a negative correlation with plasma HDL-cholesterol.

The interpretation of the relationship between PCB levels and serum lipids awaits additional work. Serum levels of PCB and other halogenated hydrocarbons (17) may depend on varying serum-adipose partition as a function of blood lipid content. Alternatively, subclinical hepatic effects of PCBs may impair the liver's ability to transport or metabolize lipids in a normal fashion.

Nearly all the studies in which sensitive clinical laboratory measurements were performed have noted associations between PCB levels and hepatic enzymes. Baker et al. (5) found a relation between PCB and GGTP, which was eliminated in his small population by control of alcohol use. No relation was found with other liver function tests such as serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum lactic dehydrogenase (LDH), alkaline phosphatase, or bilirubin. Similarly, in the Triana population, only GGTP and not bilirubin or SGPT, was correlated with serum PCB levels, and this relation existed independent of alcohol consumption and age (14). Chase et al. (8) found a correlation between SGOT and plasma

Table 3. Serum polychlorinated biphenyl concentrations in populations with occupational exposures.

Facility	Number of subjects	PCB levels, ng/mL			Range	Reference
		Arithmetic mean	Geometric mean	95% confidence interval		
Railway car maintenance	86	33.4	—	—	10-312	Chase (8)
Capacitor plant	34	394 ^a	—	234-554	Trace-1700	Ouw (19)
Capacitor plants	290	124 ^b	67 ^b	98-150 ^c	6-2530 ^b	Fischbein (20)
		48 ^c	21 ^c	38-58 ^c	1-546 ^b	Wolff (21)
Capacitor plants	80	342 ^a	—	—	41-1319	Maroni (22)
Capacitor plant	221	—	119 ^b	—	1-3330 ^b	Smith (23)
			25.3 ^c		1-250 ^c	
Public utility	14	—	24 ^b	15-39 ^b	5-52 ^b	Smith (23)
			24 ^c	16-35 ^c	7-24 ^c	
Private utility	25	—	22 ^b	17-25 ^b	9-48 ^b	Smith (23)
			29 ^c	20-43 ^c	7-250 ^c	

^aBlood level.

^bLower PCB homologs.

^cHigher PCB homologs.

PCB independent of age or length of employment; adipose PCB levels did not correlate with SGOT. His group did not report correlations between plasma PCB and GGTP, SGPT, LDH, alkaline phosphatase or bilirubin. Smith et al. (21) found positive correlations between serum PCB levels and both SGOT and GGTP. Similarly, Fischbein et al. (20) found a relation between plasma PCB and abnormal SGOT levels in two by two analyses, which they could not demonstrate for SGPT, GGTP, bilirubin or LDH. Ouw's group (19) found 5 of 34 capacitor plant workers to have SGPT values above the normal range, as well as four of seven abnormal bromsulphthalein retention tests among workers with blood PCB levels between 100 and 580 ng/mL. Maroni et al. (22) also noted abnormalities of a variety of liver function tests, the prevalence of which increased with increasing blood PCB level. GGTP, transaminases, and serum ornithine carbamoyltransferase were abnormal in decreasing numbers of workers; bilirubin and alkaline phosphatase activity were normal in all workers. Thus, measures of liver enzyme induction such as GGTP are most commonly found to be associated with PCB level, independent of other inducers such as alcohol. Only occupationally exposed groups with a higher range of PCB levels have been shown to demonstrate associations with indicators of possible hepatocellular damage such as SGOT or SGPT. Indices of obstructive liver disorders have not been demonstrated even in occupationally exposed groups.

The Triana study results have introduced the hypothesis that PCBs may be related to blood pressure measurements. As dependent variables, both systolic and diastolic blood pressure measurements were predicted by PCB levels when controlled for major confounders including age, sex, body mass index, and socioeconomic class (14). The associations between serum DDT levels and blood pressure measurements were not maintained after control of these major confounding variables. However, the collinearity of DDT and PCB serum concentrations (14,17) in this rural population, exposed to both chemical families through consumption of contaminated fish, precludes any certainty regarding which family of chlorinated hydrocarbons may be correlated with blood pressure.

Other investigators have raised the possible relation between chlorinated hydrocarbons and blood pressure. Radomski et al. (24) reported elevated DDT concentrations in adipose tissue of cases dying with hypertension, portal cirrhosis, and carcinoma; although the latter two diseases are commonly associated with cachexia, which could account for elevated adipose tissue levels, no such association was expected or found for hypertensive disease. Sandifer and Keil (25,26) found that systolic and diastolic blood pressures were elevated in 30 pesticide workers when compared to controls matched by age, race, sex, physical activity, weight, and height. Systolic and diastolic blood pressures correlated with plasma *p,p'*-DDT and *p,p'*-DDE. Morgan et al. (27) found in a 4-to 6-year followup of 2620 pesticide workers and 1049 controls that high serum organochlorine pesticide levels

were associated with the subsequent appearance of hypertension. Another group has also found a correlation between diastolic blood pressure and DDE and dieldrin levels after adjusting for racial variation and correcting for age and sex effects; these associations were observed in a Hawaiian population of 10,951 subjects (28). Finally, Wassermann et al. (29) reported that 9 of 18 cases of toxemia had high PCB levels in comparison with 12 women with normal pregnancies. The diagnosis of toxemia of pregnancy is made when a pregnant woman develops hypertension, proteinuria, and edema. Toxemia occurs predominantly in primigravidae, but seven of the nine cases with high PCB levels were multiparae. These five studies and the Triana results certainly deserve corroboration using better methodology in groups with unusual exposure to polychlorinated hydrocarbons.

Long Latency Health Effects

In light of the meager efforts to characterize the exposure and subclinical effects of PCB exposure in occupational groups and in subgroups of the population with unusual foodchain exposure, it comes as no surprise that long latency health effects of these exposures are unknown. The variety of clinical findings in Yusho patients, followed since 1968, are only indirectly relevant to known U.S. exposures, since the Japanese rice oil was contaminated with the more toxic dibenzofurans in addition to PCBs.

In the U.S., only one cohort exposed to PCBs has been investigated for mortality experience (30). Workers in two capacitor plants (2567 persons) contributed 39,018 person-years, with all-cause mortality and all cancer mortality being lower than expected. Excesses of rectal and liver cancer were observed, although neither excess was statistically significant. In one of the plants, a statistically insignificant excess of death due to liver cirrhosis was also noted. No excess of circulatory system deaths was noted. However, the small number of deaths in this cohort to date results in insufficient power to clear concerns regarding the carcinogenicity or other long latency health effects from PCB exposure (23). For example, the power of this retrospective study to detect 2-fold and 3-fold increases in risk for death from liver cancer was 13 and 33 percent respectively; in risk for death from liver cirrhosis, the power to detect 2-fold and 3-fold increases was 50% and 97%. Clearly, small cohorts, with average PCB exposures less than those typical for occupational groups, do not warrant followup for mortality experience. In contrast, longer followup of this established occupational cohort is mandatory.

Research Directions for Population Studies

Although little question remains regarding the universal low level contamination of U.S. populations by polychlorinated biphenyls, much work remains to be done to characterize the risk of special subpopulations

with unusual opportunities to accumulate PCBs via food chain contamination or occupation. Unfortunately, we know nothing about human excretion of the most persistent congeners in the PCB family, DDE, and the polybrominated biphenyl family. Profound difficulty in excretion of body burdens is suggested by many data sets in which mean levels increase with age or, more properly, duration of exposure (6,8,14,17,21). In this regard, the Michigan PBB cohort and Triana cohort offer unusual opportunities to study decrements in halogenated hydrocarbon concentrations over time. In Michigan, PBB exposure was limited to a 2-year period in 1973–1974, and median decrements in serum levels over both 1- and 2-year intervals were only 1 ng/mL. In Triana, the population's common source of DDT and PCBs was local fish, which is no longer being consumed by most residents. Since ambient pollution results in mixed accumulation of such persistent chemicals in all persons, several such populations, each with a predominant exposure, could be studied to advantage and for comparison. However, meticulous attention to quality assurance and comparability of measurements over time is required for study of PCB decrements. The 1973 and 1980 studies of Michigan sportfishers (Table 2) cannot be compared because the Aroclor standards used in analytical procedures were not comparable. Optimally, quality assurance standards, including pooled serum, should be available for the duration of a longitudinal study.

Some questions regarding subclinical biochemical associations with PCB concentrations require further understanding of serum–adipose partition. In this regard, the finding by Chase et al. (8) that plasma PCB level, but not adipose concentration, correlated with plasma triglycerides suggests that the association may be unrelated to body burden. Rather, persons with higher fat content in the blood may simply partition their body burden of PCBs to favor higher PCB concentrations in blood. One simple way of examining this hypothesis would be to compare fasting and nonfasting serum PCB and lipid levels. Indeed, no one has shown that serum samples taken from fasting individuals are comparable to samples drawn at random in relation to meals, another potential difficulty in comparing results from different investigators or sequential cross-sectional evaluations of the same population. Further work on serum–adipose ratios may also reveal age-dependent or gender-dependent partition of such compounds. Were such differences by age or gender to exist, conclusions about body burdens and health effects, presently based on serum concentrations, would need modification. Clarification of the nature of the serum lipid–PCB correlation is best done before cohort mortality studies for heart disease are considered.

More sensitive and specific tests of hepatic effects of chlorinated hydrocarbons need trial in populations with unusual exposure. Urinary porphyrin measurement is a leading candidate for a new generation of screening tests.

The acceleration of fecal excretion of Kepone with

cholestyramine is a paradigm for needed work with other persistent halogenated compounds. Nonabsorbable fats such as sucrose polyester have been proposed as possible means of decreasing body burdens of persistent fat-soluble compounds, as well as decreasing dietary absorption. Before documentation of such a possible effect, fecal metabolites of these congeners must be characterized in persons with extremely large body burdens. For example, the Triana citizen with a serum total DDT level of 2820 ng/mL and an adipose DDT concentration of 638.5 mg/kg provides a unique opportunity for investigation of DDE metabolites in feces. Although information available at present would not appear to warrant the possible long-term risks of treatment with nonabsorbable fats in persons with subclinical effects from chlorinated hydrocarbons, information gained concerning metabolism and excretion of DDT congeners or PCBs may be critical in our handling of more toxic body burdens of more toxic fat-soluble chemicals.

Finally, the possibility that chlorinated hydrocarbons may affect blood pressure has such public health importance that it must be evaluated by investigators in a variety of settings. Hypertension is largely responsible for stroke, the third leading cause of death in the United States. As a risk factor for cardiovascular disease, hypertension contributes to a portion of the leading cause of death as well. Since the vast majority of hypertension is of unknown etiology, any contribution by environmental exposures is of particular interest. Alternatively, the poorly understood physiology of essential hypertension may affect metabolism or excretion of these persistent compounds. Further evaluation of exposed populations for any relation between chlorinated hydrocarbon level and blood pressure measurement should incorporate methods such as the random zero manometer and control of confounding variables.

The Triana population, industrial populations, and PBB cohort in Michigan have been specifically mentioned as populations offering unique opportunities to increase our knowledge of accumulation, excretion, and subclinical and clinical effects of this diverse family of man-made chemicals. The newly defined cohort of Michigan sportfishers and controls and the cohort of persons ingesting meat and dairy products from farms with PCB-lined silos (4) are two other groups which should be studied with good blood pressure measurements and biochemical laboratory indices such as urinary porphyrins. Since all of these cohorts have been identified and characterized, at least in part, contributions to our understanding of chlorinated hydrocarbons are potentially available at comparatively little cost in epidemiologic effort.

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