REDUCTION OF HUMAN ORGANOHALIDE BODY BURDENS FINAL RESEARCH REPORT

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by

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ABSTRACT

Reduction of Human *Organohalide Body Burdens*

With human exposure to ubiquitous environmental contaminants inevitable despite the best application of environmental laws and protection technologies, interest has grown in the potential to reduce the levels of contamination carried in the human host. As the predominant storage compartment within the human body is the fat. techniques have been developed to mobilize fat stored contaminants and enhance their excretion through metabolic and non-metabolic pathways. The study reported herein presents data on the effectiveness of the Hubbard technique in reducing body burdens of polychlorinated and polybrominated biphenyls (PCB's and PBB'S) as well as chlorinated pesticides.

Adipose tissue concentrations were determined for seven subjects at three times: pre-treatment, post-treatment and four months post-treatment. Of sixteen identifiable organohalides, thirteen were present in lower concentrations at the time of post-treatment sampling. Seven of the thirteen reductions were statistically significant. Reductions ranged from 3.5 to 47.2 percent, with a mean reduction among the sixteen chemicals of 21.3 (sd 17.0) precent. To determine if reductions reflected movement to other body compartments or actual burden reduction, a four month post-treatment follow-up sample was taken. Follow-up analysis showed a reduction in all sixteen chemicals averaging 42.4 (sd 17.1) percent and ranging from 1 0. I to 65.9 percent. Ten of the sixteen reductions were statistically significant.

A comparison of post-treatment concentrations and follow-up concentrations suggests the possibility of continued reductions post-treatment. Four of the sixteen chemicals were reduced at follow-up at levels which were statistically significant.

Reduction of Human *Organohalide Body Burdens*

INTRODUCTION

The uptake, concentration and tissue storage of chemicals foreign to the human body has received increasing attention as the list of chemicals found in human tissue grows. By 1980 over 400 chemicals had been identified in human tissue, with some 48 found in adipose tissue, 40 in milk, 73 in liver tissue and over 250 in blood (U.S. EPA, 1980). Evidence on the persistence of these chemicals in humans has accumulated, especially with respect to the organohalides (Kraul and Karlog, 1976; Metcalf et. al., 1975; Morgan et. al., 1972). Of special interest are polychlorinated biphenyls (PCB's), chlorinated pesticides and herbicides, and polybrominated biphenyls (PBB's). The chlorinated chemicals have been found to be ubiquitous in nature and therefore pose a broad exposure threat. PBB's reflect the growing number of unfortunate chemical incidents which result in large public exposure to persistent and potentially hazardous materials.

This report describes the reduction in xenobiotic burdens of seven Michigan residents who underwent treatment intended to reduce their burdens resulting from exposure to PBB's in the early 1970s. In 1973, a fire-retardant was substituted for a cattle feed supplement. Milk and meat were consequently contaminated with a variety of the component compounds in the fire-retardant, primarily PBB'S. In 1978, 97% of individuals tested in Michigan had detectable PBB's in their adipose tissue (Wolff et al., 1982a). PBB's persist in humans, and contaminated Michigan residents may bear this xenobiotic burden throughout their lives (Wolf et al., 1979; Kimbrough et al., 1977; Matthews et al., 1977). In addition, as PBB's have been found in breast milk, the initial PBB exposure incident may ultimately result in a second generation of contaminated individuals.

Because the specific health effects of contamination by PBB's and other persistent compounds are yet to be fully established, it is appropriate to apply a traditional public health approach of prevention in the face of potential health effects. A prudent approach would be to reduce the xenobiotic burden from the body, as long as the reduction process does not result in risks greater than those posed by the existing body burden.

Various attempts have been made to reduce organohalide body burdens (Rozman et al., 1981, 1983; Liska and Stadehnan, 1969; Street, 1969; Meester, 1980). Significant reductions require mobilization of the fat-stored compounds. Once the xenobiotics move into the blood they are available for metabolism and excretion, enhanced binary excretion or preferential ingested materials such as paraffin, activated carbon or saturated and unsaturated oils (Richter et al., 1979; Lambert and Brodeur, 1976; Rozman, 1982a, 1982b).

We present below a trial study intended to evaluate the efficacy of a regimen for reducing several fat-stored persistent environmental contaminants, including PBB'S, PCB's and chlorinated pesticides.

MATERIALS AND METHODS

In May, 19 8 2, seven healthy male volunteers age 20-30 were selected for participation in the study. Each had been part of earlier studies on human PBB contamination and were known to have PBB body burdens of between .5 - 1 0 ppm PBB per lipid weight. They received an in depth briefing on their expected involvement prior to signing informed consent. The study protocol and participant selection process was reviewed by the Foundation's Institutional Review Board, and HHS regulations on human experimentation were followed.

The treatment regimen used was that of Hubbard, initially developed for the purposes of reducing body burdens of psychoactive drugs (Hubbard, 1980). The regimen was found to be safe with no side effects in a previous study of 103 individuals (Schnare et al., 1982). The treatment is an approximately three week regimen of (a) polyunsaturated oil supplement, (b) aerobic exercise, (c) sauna at 60-82'C (140180'F), (d) nutritional supplements (vitamins and minerals) centered around gradually increasing doses of nicotinic acid, (e) calcium and magnesium supplements, (O water and salts taken as needed to avert dehydration or salt depletion due to sweating, and (g) an orderly daily schedule with balanced meals and adequate sleep. No medications, illegal drugs or alcohol are permitted during the period of the regimen, unless especially prescribed by the study physician. The regimen length is participant specific and averaged 20 days in our trial.

Samples of adipose tissue and skin lipids were taken the day prior to initiation of the regimen, one day postregimen and four months post-regimen (follow-up).

Adipose tissue was obtained for chemical analysis by subcutaneous needle aspiration (Daum et al., 1978). To determine concentrations of PCB'S, PBB's and chlorinated insecticides on a lipid weight basis, the tissue was mixed with sodium sulfate and extracted with petroleum ether. Lipid content was determined gravimetrically on a portion of the extract. Pesticides were separated using gel permeation chromatography followed by treatment on a Florisil column. The resulting eluents were concentrated and chlorinated insecticides, PCB's and PBB's were determined using gas chromatography equipped with electron capture detection. Identification of specific chemical congeners was determined by gc-mass spectroscopy. Recoveries determined by spiking synthetic samples ranged from 60-100 percent.

Skin lipids were sampled through adsorption onto pre-extracted adsorbant paper using the method developed by Wolff (1982a). In addition to pre-, post- and follow-up sampling, samples were taken every fourth day of the trial, up to 24 days. These samples were analyzed for organohalides. The papers were extracted using 1:1 ethyl ether: hexane. Lipid content was determined gravimetrically on a portion of the extract. Extracts were cleaned up and pesticides were separated using two elutions from a micro-Florisil column. The resulting eluents were concentrated and chlorinated insecticides, PCB's and PBB's were determined using gas chromatography with electron capture detection.

AR samples were frozen with liquid nitrogen immediately upon collection and were kept frozen until analyzed. Adipose tissue was stored and shipped in pesticide free hexane extracted teflon vials. Skin lipid samples were shipped in pesticide free hexane extracted glass vials with extracted foil cap liners.

Measurement of percent of body weight as fat was made using submersion techniques and were correlated with caliper measurements taken at the same time.

RESULTS

Sixteen organohalides were identified in the adipose tissue of the participants. Table 1 shows the range of concentrations found in the subjects. (See Table 1, page 6.)

Of the sixteen chemicals, thirteen were present in lower concentrations at the time of post-treatment sampling. Seven of the thirteen reductions were statistically significant. Reductions ranged from 3.5 to 47.2 percent with a mean reduction among the sixteen chemicals of 21.3 percent (sd 17.0%). (See Table 2, page 7.)

In order to determine if changes in adipose concentration after treatment were due to changes in fat mass, lean body mass measurements were made (Table 3). There was no statistically significant difference ($p < .6$) between body fat mass before and after treatment. Reductions in xenobiotic burdens were thus not attributable to an increase in body fat. Table 4 shows that reductions in adipose tissue concentrations were very similar to estimated whole body burdens. (See Tables 3 and 4, page 8.)

Table 1
Range of Adipose Tissue Concentrations (ppm)

Chemical	Range	Level of Detection
PCB's		
2,4,5,2',3',6'-hexa'	0.01-0.37	0.005
2,4,5,2',4',5'-hexa	0.09-0.73	0.005
2,4,5,2',3',61-hexa'	0.07-0.67	0.005
2,3,4,5,2',4',5'-hepta'	0.02-0.20	0.005
2,3,4,6,2',3',4'-hepta	0.007-0.23	0.005
2,3,4,5,3',4',5'-hepta'	0.08-0.59	0.01
2,3,5,6,3',4',5'-hepta'	0.05-0.35	0.01
PBB's		
2,4,5,3',4'-penta	nd -0.16	0.009
2,4,5,2',4',5'-hexa	0.01-2.72	0.004
2,3,4,2',4'51-hexa	nd -0.22	0.001
2,4,5,3',4'5'-hexa	nd -0.09	0.002
2,3,5,2',4',5',6'-hepta	nd -0.26	0.002
2,3,4,5,2',4',5'-hepta	nd -0.01	0.002
DDE	0.30-1.58	0.05
Heptachlor Epoxide	0.02-0.82	0.01
Dieldrin	0.04-0.14	0.01

' Chlorine configuration is estimated, based on gas-chromatographic retention times.

Table 2
Reductions in Adipose tissue Concentrations (percent)

	Post-treatment			Four Month Follow-up		
Chemical	**%**	n	sd	%	n	sd
PCB's						
2,4,5,2',3',6'-hexa'	32.83**"	6	17.86	60.58**	6	24.93*'
2,4,5,2',4',5'-hexa	17.24	6	21.74	27.76*	6	27.68
2,4,5,2',3',6'-hexa'	20.36*	5	21.31	45.26**	5	25.08##
2,3,4,5,2',4',5'-hepta'	34.89**	5	16.82	29.16	6	46.19
2,3,4,6,2',3',4'-hepta	26.21*	6	30.82	56.47**	6	32.02
2,3,4,5,3',4',5'-hepta'	11.87	6	21.92	13.34	6	42.54
2,3,5,6,3',4',5'-hepta'	36.96*	6	27.99	58.95**	6	21.59
Total PCB (sum of peaks)	34.17**	6	24.41	38.44*	6	27.68
PBB's						

2,4,5,3',4'-penta	34.0	4	39.7	52.1*	4	34.2
2,4,5,2',4',5'-hexa	25.0*	5	21.4	65.9**	5	37.3
2,3,4,2',4',5'-hexa	47.2*	3	12.4	51.4	3	35.4
2,4,5,3',4',5'-hexa	+ 4.2	4	84.3	30.3	5	50.5
2,3,5,2',4',5',6'-hepta	+ 8.0	2	96.2	61.5**	4	27.1
2,3,4,5,2',4',5'-hepta	36.3	5	34.0	37.5	5	95.4
Total PBB (sum of peaks)	34.5**	6	20.9	58.7*	5	33.0
DDE	3.5	7	26.1	40.2**	6	22.9
Heptachlor Epoxide	31.2	7	49.4	37.8*	6	33.4
Dieldrin + 3.9	7	19.9	10.1	6	21.9	

[a] *Chlorine configuration is estimated, based on gas-chromatographic retention times.*
[b] ** p < .05 and ** p < .01 (Wilcoxon sign rank test)*
[c] *# p < .05 and # # p < .01 (comparing post-treatment with follow-up)*

Table 3
Body Fat Mass Before and After Treatment

Participant		Body Weight (kg)	Percent Fat	Fat Weight (kg)
01	pre-	83.9	15.2	12.8
	post-	85.3	13.7	11.7
02	pre-	74.0	13.6	10.1
	post-	76.2	14.5	11.0
03	pre-	87.4	25.9	22.6
	post-	91.2	26.2	23.9
04	pre-	91.9	34.2	31.4
	post-	92.5	32.5	30.1
05	pre-	51.9	15.3	7.9
	post-	51.9	14.9	7.7
06	pre-	85.0	24.1	20.5
	post-	91.6	24.0	22.0

Table 4
Mean Post-treatment Reductions for Some Chemicals (percent)

Chemical	Adipose Tissue Concentration	Body Burden
2,4,5,2',3',6'-hexa PCB	32.8**[a]	32.3**
2,3,4,5,2',4',5'-hepta PCB	34.9**	34.0**
Total PCB	34.2**	34.0**
2,4,5,2',4',5'-hexa PBB	25.0*	27.2*
Total PBB	34.5**	39.2**
DDE	3.5	10.5

Heptachlor Epoxide	31.2	38.1
Dieldrin	+ 3.9	2.5

[a] - ** p < .05 and ** p < .01*

The relative contributions of the major PBB and PCB congeners were calculated from chromatographic spectra Proportions were the same in pre-, postand follow-up adipose tissue samples.

To determine if post-treatment reductions reflected movement to other body compartments (eg. liver) or actual burden reduction, a four month posttreatment follow-up sample was taken. Follow-up analysis showed a reduction in all sixteen chemicals averaging 42.4 percent (sd 17.1%) and ranging from 10. I to 6 5.9 percent. Ten of the sixteen reductions were statistically significant.

Due to the heat stress component of the treatment, we examined the potential significance of the skin oil excretion pathway. Skin oil was sampled to determine the levels of xenobiotics in the oils. No significant correlation was noted between days on the program and levels of chemicals in the skin oil. However, all of the organohalides identified in the adipose tissue were also found in the skin oil.

Figure I shows the concentration of total PBB's and PCB's over the period of the trial. Concentrations of PBB's and PCB's in skin lipids did not vary, but amounts of skin hpids excreted increased, presumably due to the sauna exposure. (See Figure 1, page 10.)

DISCUSSION

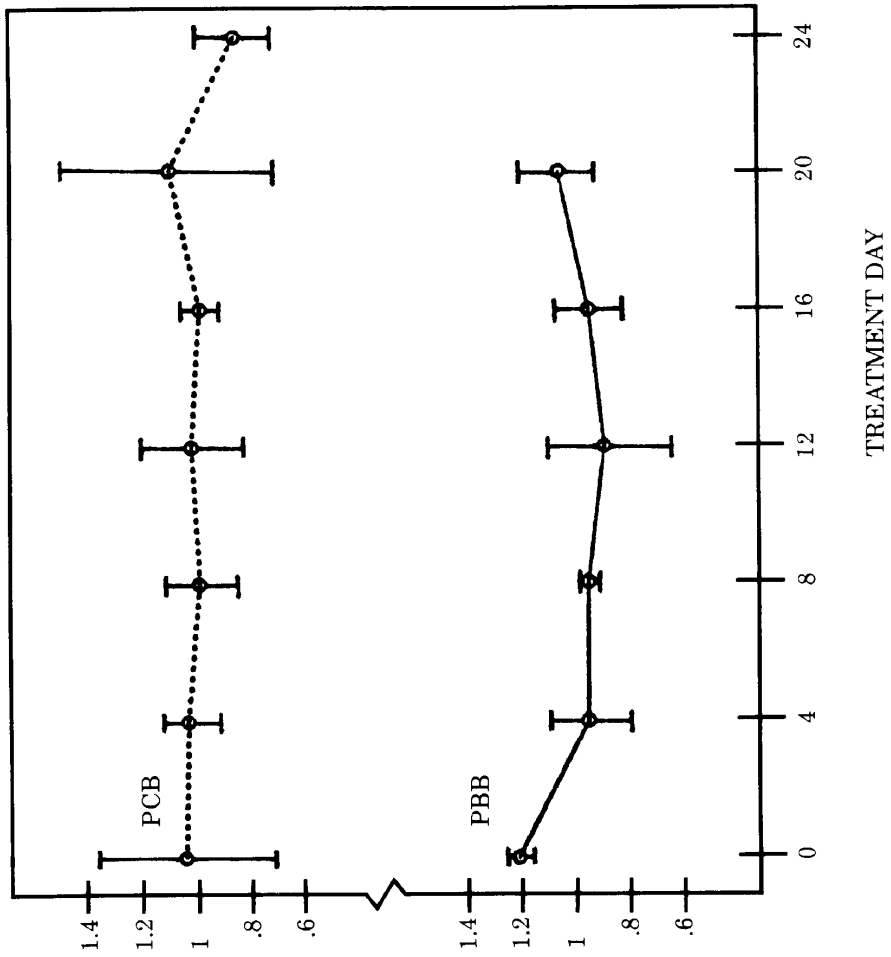
Reducing body burdens of persistent chemicals need not be limited by the rate of their metabolism, and techniques which tend to be blind to the potential for metabolism of these compounds remain an active topic (Guzehm and Wolff, 1979; Maugh, 1982). Burden reduction of lipophilic xenobiotics is governed by the rate of excretion and the rate of mobilization from fat stores.

Mobilization of lipids within the body occurs several times each day, can be caused by several means, and may involve both the active and inactive fraction of the adipose tissue. Oschry and Shapiro indicate the active fraction constitutes only five percent of the adipose tissue and does not appear to contain many xenobiotics found in the inactive fraction (1981). Starvation (fasting) has been recognized as an effective method for lipid mobilization. Both DDE and PCB's can be mobilized with lipid under these conditions (Clark and Prouty, 1977). Exercise has also been shown to mobilize lipids, with some indication that the rate of mobilization is dependent upon the rate of blood flow through the adipose tissue (Wirth et aL, 1979; Esser4 1977; DiMauro et al., 1980).

Stress has been found to cause lipid mobilization, apparently through sympathetic nerve stimulation which increases lipolysis as a result of diffusion of norepinephrine from nerve

terminals on blood vessels to nearby adipose cells (Cleghorn, 1970). Continued stress has been known to mobilize deep lipid stores, and the hallucinogenic 'flashback' may be an example of such an event.

Figure 1
SKIN OIL CONCENTRATIONS



Skin oil (sebum) concentration of PCB and PBB in seven adult males undergoing sauna and polyunsaturated oil based detoxification treatment. Individual mean skin oil concentrations varied from 0.94 - 4.92 ppm and.85 - 1.67 ppm for total PCB's and PBB's respectively. Concentrations were assessed on a per lipid weight basis.

In addition to these physiologic factors, therapeutic doses of various drugs, vitamins and oil will also mobilize lipids. Polyunsaturated oils have been found to replace existing adipose tissue stores, thereby mobilizing some lipids through that exchange (Shepherd et al., 1980; Rozman, 1981). Administration of phenobarbital for the purposes of mobilization of stored residues has been suggested in order to enhance fecal excretion of metabolizable organohalides (Carlson, 1980). A component of vitamin B which similarly could be used to these ends is nicotinic acid (niacin).

Nicotinic acid has long been used to lower blood lipid levels, but its use has not been uniformly successful in that it requires frequent and large doses to maintain a lowered hpid level (Carlson, 1978). It is useful as a mobilizing agent in that within one to five hours after

administration, depending upon dose, there is a pronounced overshoot in arterial free fatty acids (FFA) levels, well above basal levels (Carlson, 1979; Schlierf and Dorow, 1973). Norris has shown that the period of suppressed mobilization does not prohibit exercise as required by the treatment we studied (1978).

DeFreitas and Norstrom observed that during lipid mobilization, the fractional turnover of all PCB's is approximately equivalent to the fractional turnover of the lipid pool under fully fed conditions as well as during periods of induced depletion of lipid reserves (1974). Such a turnover would not be expected to favor one PCB over another, and the potential for excretion of each in the same proportion they are found in adipose tissue would be possible. However, the exact mechanism of xenobiotic transfer from adipose tissue to other sites within the body is not definitively known. While it has been shown that PCB's mobilize at the same rate as the lipid, DDT has not shown that characteristic (Findlay and DeFreitas, 1971). Our findings tend to support a lack of preferential mobilization and excretion of PCB'S.

Mobilization of persistent xenobiotics into the blood permits their excretion through the biliary and/or fecal pathway. Richter has shown that increased blood levels of PCB's cause increased PCB concentration in the liver (1979). These increased levels in the liver exit the body through the feces (Allen et al., 1974). Rozman et al. have shown that fecal excretion of PBB's is due to both biliary and intestinal elimination (1982a). However Kirnbrough et al. demonstrated that these xenobiotics will re-enter the body due to enterohepatic recirculation (1980).

Various methods have been suggested to overcome enterohepatic recirculation. Cholestyramine, high fiber diets, vegetable diets, sucrose polyester, and paraffin have all been used

(Meester, 1980; Richter et al., 1979; Kimbrough et al., 1980; Stoewsand, 1978; Cohn et al., 1978). Each has a side effect which tends to stress the liver due to fat deposition. A less stressing approach to overcoming enterohepatic circulation is the use of dietary polyunsaturated oil. Total fecal steroid excretion has been increased by 45 percent through use of corn oil versus cocoa butter as the source of dietary fats (Connor et al., 1969). This type of supplement has been found to produce a decrease in plasma cholesterol which appears to be indicative of increased fecal excretion (Wood et al., 1966; Helman, et al., 1957).

Associated with overcoming enterohepatic recirculation is the potential for a lowering of absorption of important nutrients and thus increasing the toxicity of persistent chemicals such as PBB's (Kirnbrough et al., 1980). This can be especially important for the lipophilic vitamins. Vitamin A, for example, undergoes extensive enterohepatic recirculation and must be supplemented at higher than normal intakes if increased fecal excretion is likely (Smith, 1973). This is particularly important for PCB poisonings where animal studies show a significant decrease of vitamin A in the liver and serum during P CB administration, thus leading to an increased A requirement (Innami et al., 1977; Kato et al., 1978).

Another vitamin supplement potentially required during PCB mobilization is ascorbic acid. It has been found that PCB contamination brings about a depression in the activities of the

enzymes L-gluonolactone oxidase and dehydroascorbatase along with an increased urinary excretion of L-ascorbic acid. PCB toxicity disturbs the normal histological pattern of the liver cells and also significantly changes the hepatic lipid composition. L-ascorbic acid supplementation can afford protection against the enzyme activity alterations and histological changes resulting from PCB toxicity (Chakraborty et al., 1978). We feel that any work in humans which involves mobilization of fat stored xenobiotics should reflect the need for vitamin supplementation.

Measurement of skin lipids provided an opportunity to estimate the rate of excretion of hpophilic compounds through a dermal pathway. Calculation of the increase in skin oil discharged results in ai@ approximate 175 gram increase over the 20 day program, based on a 10 percent increase in excretion per degree centigrade and an increase in skin temperature of approximately 40C, the temperature increase we measured in a sauna at 63'C (Williams et al., 1973). This presumes a 3.0 gram per day whole body skin oil excretion rate over and above the excretion while in the sauna (Bhattacharyya et aL, 1972). This is approximately what was calculated when extrapolating the forehead excretion we measured during the study to the rest of the body, based on the relative excretion rates of the other skin areas, and assuming skin areas represented by the ICRP reference man (Bhattacharyya et al., 1972; International Commission on Radiological Protection, 1975). The 175 gram increase would decrease the body burden by only 1.6 percent, based on skin oil concentrations we found on day 16 of the program.

Continued reduction of body burdens after conclusion of the treatment regimen may occur for some chemicals, as we found that 15 of the 16 chemicals analyzed were present in lower concentrations, and four had a statistically significant reduction at follow-up when compared with post-treatment levels (Table 2). This confirms a report by Roehm of a similar finding when using the same treatment regimen (1983). These chemicals are considered persistent in humans. Rozman indicates that in primates PCB's have a half-life of 4 years (1982). The reductions we observed suggest that it is possible to increase the rate of excretion as much as 12 times over normal rates in primates. Further investigation on these techniques is vital due to the absence of other burden reduction treatments, especially for highly exposed or high risk groups.

CONCLUSION

A pilot trial was conducted to evaluate a treatment intended to enhance excretion of fat stored drugs and persistent environmental contaminants. The average body burden reduction of

stored persistent organohahdes in adipose tissue was 21.3 percent immediately post-tiial, and 42.4 percent upon 4 month follow-up. The probable mech@m for the reduction in body burdens is sauna induced mobilization of stored xenobiotics, followed by increased fecal, and to a much lesser extent dermal excretion.

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REFERENCES

Allen J, Norback, D., and Hst4 I:'nssue modifications in monkeys as related to absorption, distribution and excretion of polychlorinated biphenyls. ArcIL Envir-on. ContanL Toxicol. 2:86-95, 1974.

Bhattacharyya, A., Connor, *W.,* and *Spector,* A.: Excretion of sterols from the skin of normal and hypercholesterolemic humans. J. Clin. Invest. 51:2060-2070, 1972.

Carlson, L.: Nicotinic acid and inhibition of fat mobilizing lipolysis. Adv. Exp. Med. BioL 109:225-238, 1978.

Carlson, L.: Nicotinic acid; its metabolism and its effects on plasma free fatty acids. Stockholm. King Gustav Vth Research Institute, 1979.

Carlson, Q.: Effects of halogenated aromatic compounds on the metabolism of foreign organic compounds. U.S. Environmental Protection Agency, project report to EPA Grant R805070, 1980.

Chakraborty, D., Bhattacharyya, A., Chatterjee, J, Chatteriee, K, Sen, A., Chatterjee, S., Majumdar, K, *and Chatterjee, G..@* Biochemical studies on polychlorinated biphenyl toxicity in rats: manipulation by vitamin C. Int. J. Vitam. Nutr. Res. 48:22-31, 1978.

Clark, D., and Prouty, R: Experimental feeding of DDE and PCB to female big brown bats. J. Toxicol. EnvirorL HealtIL 2:917-928, 1977.

Cleghorn, J: Psychosocial influences on a metabolic process: The psychophysiology of lipid mobilization. Canad. Psychiat. Ass. J. 15:539-546, 1970.

Co@ W, Boylan, J, Blanke, R, *Fariss, M, Howel4* J, and *Guzelian, P:* TYeatinent of cliordecone (Kepone) toxicity with cholestyramine: Results of a controlled clinical trial. N. Eng. J. MecL 298:243-248,1978. Connor, W, *Witiak, D., Stone,* D., and Armstrong, M: Cholesterol balance and fecal neutral steroid and bile acid excretion in normal men fed dietary fats of different fatty acid composition. J. Clin. Invest. 48:1363-1375, 1969.

Daum, *S., Knittle,* J, Rosenman, K, Ron4 W, and *Holstei4 E.:* A simple technique for fat biopsy of PBB-exposed individuals. Environ. HealthPerspect23:183-185,1978. *DeFreitas,* A., and *Norstrom, R:* Turnover and metabolism of polychlorinated biphenyls in relation to their chemical structure and the movement of lipids in the pigeon. Canad. J. Physiol. 52:1080-1094, 1974.

DiMauro, S., Revisan, C., and Hays, A.: Disorders of lipid metabolism in muscle. Muscle Nerv. 3:369-388, 1980.

Essen, B.: Intramuscular substrate utilization during prolonged exercise. Ann. N.Y. Acad. Sci. 301:30-44, 1977.

Findlay, G., and DeFreitas, A.: DDT movement from adipocyte to muscle cell during Epid utilization Nature 229:63-65, 1971.

Guzelian, P, and *Wolff, M:* Body clearance of halogenated hydrocarbons: Workshop summary. Ann. N.Y. Acad. Sci. 303:271-272, 1979. Helman, *L., Rosenfeld, R., Insull,* W, *and Ahrens, E.:* Intestinal excretion of cholesterol: a mechanism for regulation of plasma levels. J. Clin. Invest. 36:898, 1957.

Hubbard, L. Ron.: The Technical Bulletins - Volume 12. Los Angeles. Bridge Publications, Inc. 1980. pp. 163-181.

Innam@ *S., Nakamura, A., Miyazaki, M, Nagayama, S., and Nishide,* E.: Further studies on the reduction of vitamin A content in the livers of rats given polychlorinated biphenyls. J. Nutr. ScL Vitaminol. 22:409-418, 1977.

Inte@nal Commission on *Radiological* Protection: Report on the Task Group on Reference Man. New York, Pergamon Press. 1975.

Kato, N, Kato, M, Kimura, T, and *Yoshida,* A: Effect of dietary addition of PCB, DDT or HGT and dietary protein on vitamin A and cholesterol metabolism. Nutr. Rep. Int. 18:437-445,1978.

Kimbrough, R, Burse, V, andliddle, J: Toxicity of polybrominated biphenyl. Lancet Sept. 17:602-3, 1977.

Kimbrough, R., Korver, M, Burse, V, and *Groce, D.:* The effect of different diets or mineral oil on liver pathology and polybrominated biphenyl concentration in tissues.
Toxicol. Applied Pharmocol.
52:442-453, 1980.

Kraul, L, and Karlong, P: Persistent organochlorinated compounds in human organs collected in Denmark 1972-1973. Acta PharmacoL Toxicol. (Kbh.) 38:38-48, 1976. Lamber4 *G., and Brodeur, J:* Influence of starvation and hepatic microsomal enzyme induction of DDT residues in rats. Toxicol. App. Pharmacol. 36:111-120, 1976.

Liska, B., and Stadelman, W: Accelerated removal of pesticides from domestic animals. Residue Rev. 29:51-60, 1969.

Matthews, H., Kato, S., Morales, N, and 71zey, D.: Distribution and excretion of 2,4,5,2', 4', 5'-hexabromobiphenyl, the major component of Firemaster BP-6. J. Toxicol. Environ. Health. 3:599605, 1977.

Maug/4 T: Clearing pesticides from the body. Science. 218:336,1982.

Meester, W: A progress report on the effect of polybrominated biphenyls (PBB) in Mchigan residents. Vet Human ToxicoL 22:2, 1980.

Metcalf, RL., Sanbo@ J., Lu, P, and *Nye, D.:* Laboratory model ecosystem studies of the degradation and fate of radiolabeled tri-, tetra-, and pentachlorobiphenyl compared with DDE. Arch. Environ. Contam. 3:151-163, 1975.

Morgan, D., Roan, C., and Paschal, E.: Transport of DDT, DDE and Dieldrin, in human blood. Bull. Environ. Contam. Toxicol. 8:321326, 1972.

Norris, R, Schade, D., and Eaton, R: Effects of altered free fatty acid mobilization on the metabolic response to exercise. J. Clin. Endocrin. Metabol. 46:254-259, 1978.

Oschry, Y, and *Shapiro, B.:* Fat associated with adipose hpase the newly synthesized fraction that is the preferred substrate for lipolysis. Biochim. Biophys. Acta. 664:201206, 1981.

Richter, E., Lay, J., Kleir4 W, *and Korte,*
F:Paraffin stimulated excretionof carbon-14 labeled 2,4,6,2',4'-
pentacluorobiphenyl by rats. Toxicol. Appl. Phartnacol. 50:17-24, 1979.

Roehm, D.C.: Effects of a program of sauna baths and mega-vitamins on adipose DDE and PCB's and on clearing of symptoms of Agent Orange (Dioxin) toxicity. Clin. Res. 31:243(a), 1983.

Rozman, K, Rozman, T, and *Grein4 H:* Enhanced fecal elimination of stored hexachlorobenzene from rats and rhesus monkeys by hexadecane or mineral oil. Toxicol. 22:33-44, 1981.

Rozman, K, Rozman, *T, Williams,* J, and *Grein, H:* Effect of mineral oil and/or cholestyramine in the diet of biliary and intestinal elimination of 2,4,5,2',4',5'-hexabromobiphenyl in the rhesus monkey. J. Tox. Environ. Health. 9:611618, 1982a.

Rozman, K., Rozman, T, *Greim, H., Nieman, L, and Smith, G.:* Use of aliphatic hydrocarbons in feed to decrease body burdens of lipophilic toxicants in livestock. J. Agricul. Food Chem. 30:98-100, 1982b.

Rozman, K., Rozman, T, and *Greim, H.:* Enhanced intestinal excretion of hexachlorobenzene in rats by intraluminal injection of hexadecane. J. Appl. Toxicol. 3:48-50, 1983.

Schlierf F., and Dorow, W: Diurnal patterns of triglycerides, free fatty acids, blood sugar, and insulin during carbohydrate-induction in man and their modification by nocturnal suppression of lipolysis. J. Clin. Invest. 52:732-740, 1973. *Schnare, D. W., Denk, G., Shields, M,* and Brunton, S.: Evaluation of a detoxification regimen for fat stored xenobiotics. Med. Hypoth. 9:265-282, 1982.

Shepherd, J, Stewart, J, Clark, J., and *Carr, K:* Sequential changes in plasma lipoproteins and body fat composition during polyunsaturated fat feeding in man. Br. J. Nutr. 44:265-271, 1980.

Smitk R.: Implications of biliary excretion. In the excretory function of bile. London. Chapman and Hall. 1973. ch. 8.

Stoewsand, G: Inhibition of hepatic toxicities from polybrominated biphenyls and aflatoxin B in rats fed cauliflower. J. Environ. PathoL Toxicol. 2:399-406, 1978. *Street, J.:* Methods of removal of pesticide residues. Canad. Med. Ass. J. 100-16-22, 1969.

U.S. Environmental Protection Agency, Washington, D. C.: Chemicals identified in human biological media. EPA560/13-80-036B, PB81-161176. 1980.

Williams, M, Cunliff W, Williamson, *B., Forster, R., Cotterill,* J, and *Edwards,* J: The effect of local temperature changes on sebum excretion rate and forehead surface lipid composition. Brit. J. Dermatol. 88:257-262, 1973.

Wirth, A., Schlierf, E, and Schettler, F: Physical activity and lipid metabohsm. YJirL Wochenschr. 57:11951201, 1979.

Wolff M, Anderson, H, Rosenman, K, *and Selikoff, L:* Equilibrium of polybroniinated biphenyl (PBB) residues in serum and fat of Michigan residents. Bull. Environ. ContanL ToxicoL 21:775-781, 1979. *Wolff,* M, Andersor4 H, *and Selikoff, I.:* Human tissue burdens of halogenated aromatic chemicals in Michigan. J. Am. Med. Assoc. 247:2112-2116, 1982a.

Wolff, M, Taffe, B., Roesch, R., and *Selikoff, L:* Detection of polycyclic aromatic hydrocarbons in skin oil obtained f rom roofing workers. Chemosphere. 11:595599,1982b.

Wood, P, Shioda, R., and Kinsell, L.: Dietary regulation of cholesterol metabolism. Lancet. 2:604,1966.

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