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Equilibrium of Polybrominatd Biphenyl (PBB) Residues In Serum and Fat of Michigan Residents

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Study of accumulation and long-term tissue storage in humans of chemicals present in the environment has been of increasing interest, including investigations of tissue burdens of such compounds as PCBs (polychlorinated biphenyls), DDE/DDT, BHC (lindane and its isomers) and HCB (hexachlorobenzene). Most reports have been limited to analysis of levels observed at one point in time, generally without information concerning time of intake, and consequently unable to consider half-life or other pharmacokinetic patterns. An exception is the work of MORGAN AND ROAN (1974) which reviewed accumulation and storage of DDE/DDT following ingestion of DDT, considered variations with dose, and found what was termed essentially a lifetime adipose tissue burden of DDE. With PCBs and PCTs (polychlorinated terphenyls), studies of Japanese subjects demonstrated little change in blood levels from 1973 to 1975 (DOGUCHI 1977).

The recent episode of food contamination with polybrominated biphenyls (PBB) in Michigan, starting in 1973, has resulted in populations of uniquely, though non-uniformly, exposed persons who were exposed to PBB over a short period of time (KAY 1976). In a group of 993 dairy farm residents and 55 chemical workers in Michigan, examined during November, 1976, we found less than 1% with no detectable PBB in serum and 2% with levels at the limit of detection of the method used (0.2 ppb) (Table 1). Among 163 Wisconsin dairy farm residents examined in March, 1977, not known to have been exposed to PBB, 95% were at or below the limit of detection; and 6 of the 8 with detectable PBB in their sera were members of a family which recently had moved from Michigan to Wisconsin (Table 1).

In November, 1977 and April, 1978 we re-examined 92 dairy farm residents (31 of whom also had had subcutaneous fat biopsies in 1976) and fourteen PBB-exposed chemical workers. Measurements of serum and adipose tissue concentrations of PBB, which we report herein, suggest that these persons have apparently achieved equilibrium of their PBB body burdens.

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TABLE 1

Serum analyses for polybrominated biphenyls among Michigan and Wisconsin dairy farm residents

Serum PBB	Wisconsin	Michigan
Nondetectable[a]	127 (78%)	7 (<1%)
Limit of detection (<0.2 ppb)	28 (17%)	29 (3%)
Detectable (>0.3 ppb)	8[b] (5%)	902 (96%)
n	163	938

[a]Nondetectable values showed no PBB peak on gc analysis
[b]Six of these individuals were members of family recently moved from Michigan; serum PBB concentrations were below 1.3 ppb.

MATERIALS AND METHODS

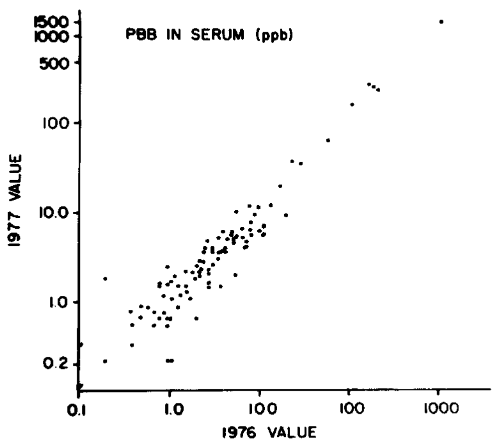
In November, 1977, 92 individuals were selected for reexamination. All had been previously examined in November 1976. Review of dietary and residence histories in 1976 had indicated the ingestion of PBB contaminated food could have begun in the summer or fall of 1973 or the spring of 1974 (ANDERSON et al. 1978a).

Selection was based upon residence within 50 miles of Reed City, Michigan, where our Laboratory had established a temporary field station for extended study of PBB health effects. According to the study design, which had a specific aim irrelevant to this report, 76 males ages 25-40 were invited to attend a special clinic. Of those invited, 70 volunteered to participate, and 52 actually attended. Forty wives of these men also attended. Of these men nine were re-examined in April 1978. In November, 1976, 55 workers in a chemical plant which produced PBB were examined (ANDERSON et al. 1978b). Of these, 24 were invited to the April, 1978 clinic; fourteen responded.

The method for serum PBB analysis used in our laboratory has been reported (WOLFF et al. 1978). Adipose tissue, obtained by subcutaneous needle aspiration (DAUM et al.1978), was extracted with ethyl acetate: toluene (3:1) and lipid separation performed by automatic gel-permeation chromatography (gpc; JOHNSON et al. 1976). Optimum operating conditions for our equipment required a "dump" cycle of 125 mL, "collect" 90 mL. A portion of the initial extract was evaporated for lipid weight, and the final concentration expressed as ng per mg lipid (ppm). Approximate wet and lipid weights were 0.2 g (total) and 0.05 g (for the gpc fraction), respectively. Recoveries of fortified chicken fat prepared in the same way were in the range of 90-110%, with an occasional recovery as low as 80%. Gas chromatographic analysis was identical to that for serum (WOLFF et al. 1978).

RESULTS

Serum PBB levels measured in November 1976 and November 1977 were highly correlated ($r^2=0.998$; fig. 1*). Replicate samples were usually within 5%. The regression coefficient (1.19) suggested an increase in serum levels in 1977 ($p<0.001$). However, recognizing that the largest experimental variation would be expected in samples with the highest concentrations, the data were reanalyzed without the 7 highest values (those greater than 35 ppb). The regression coefficient was 0.98, insignificantly different from 1.0. For serum DDE (also determined; WOLFF et al. 1978), the regression coefficient was 0.92, $r^2=0.63$ (fig. 2).



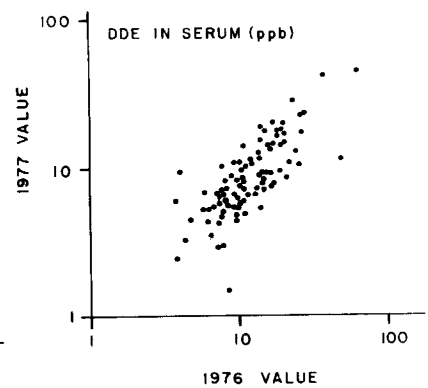


Fig. 1. Serum PBB values of Michigan dairy farm residents determined in November, 1976 and November, 1977.

Fig. 2. Serum DDE among Michigan dairy farm residents in 1976 and 1977.

For those persons in this group with adipose tissue PBB determinations, serum PBB levels were highly correlated with PBB concentrations in fat (Fig. 3). The linear regression coefficient (least squares) indicated a fat-to-serum partition of about 500:1. The slope, however, was again influenced by the highest PBB value

*Graphical data hereinafter are presented logarithmically; statistical analysis is based on linear regression by the least squares method, except where indicated.

(serum 182 ppb, fat 89.0 ppm), without which the partition was 370 (r^2=0.94). The 1977 serum value for this subject was 275 ppb, suggesting a possible analytical error in the 1976 determination. Serum 1977 vs. fat 1976 PBB concentrations for this same group gave a line with a slope of 320 (r^2=0.999, n=31). For either set of data (serum 1976 or 1977 vs. fat 1976), the partition coefficient calculated from a linear regression of logarithmic values was near 300 (fig. 3).

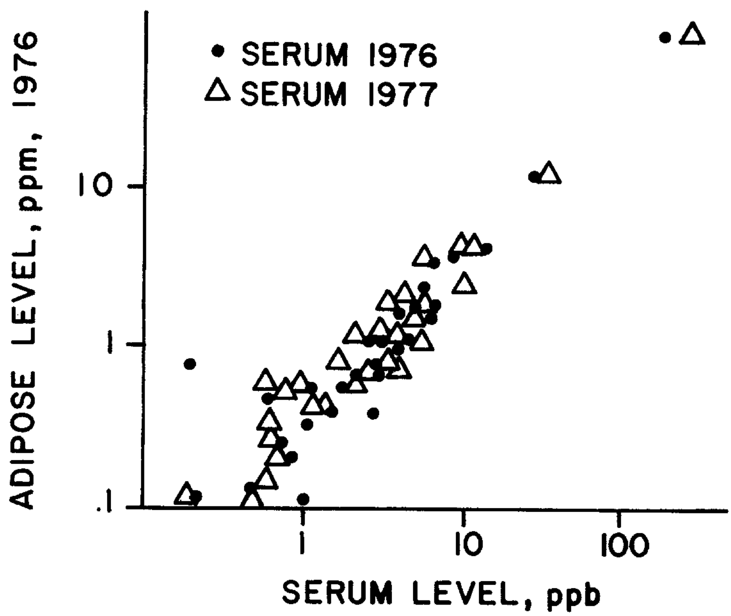


Fig. 3. Adipose (1976) vs. serum (1976-1977) concentrations of PBB and DDE (1976) among 31 Michigan dairy farm residents.

The partition value, 320, is also closer to that which we have observed in a larger number of persons (WOLFF, work in progress), and is close to the values reported by MORGAN AND ROAN (1974) for p,p'-DDT (314), o,p'-DDT (247), and DDE (284). Their calculations suggested that these partition values represented the theoretical value for equilibrium between adipose and serum lipids. The analagous serum:fat correlations for DDE in our study had a slope of 210 (r^2=0.62, n=29). The actual correlation is apparently quite similar to that for PBB, although it encompasses a smaller range of values, since the points are superimposable on the PBB serum:fat correlation (Fig. 4).

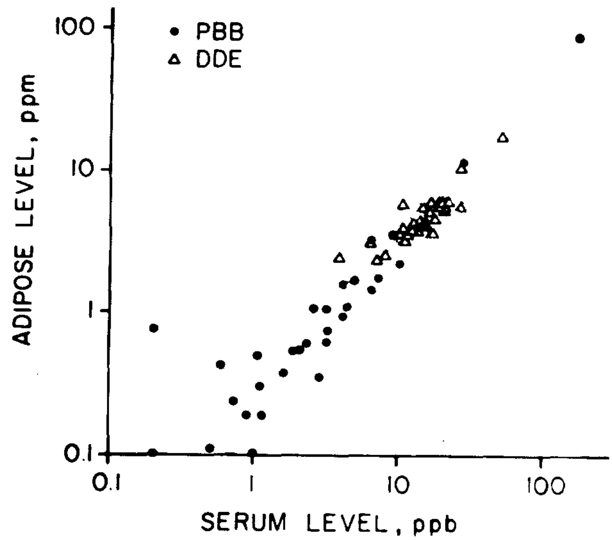


Fig. 4. Adipose vs. serum concentrations of PBB and DDE (1976) among 31 Michigan dairy farm residents.

Nine of these re-examined dairy farm residents and, in addition, 14 employees of the chemical company which manufactured the PBB (who were also examined in 1976 and whose exposures could have begun at work in 1970-1971) were re-studied in April, 1978. The farm dwellers in the 3 time periods showed no significant variation in serum PBB levels (Table 2). The chemical workers,

TABLE 2
Serum PBB concentrations in nine dairy farm residents during 18 months' observation

Subject	PBB serum concentration (ppb) 11/76	11/77	4/78
1	9.2	9.9	11.5
2	21.0	9.1	11.6
3	1.9	2.0	1.9
4	2.1	2.4	1.9
5	8.1	7.6	7.9
6	1.0	1.5	1.5
7	4.0	3.5	3.8
8	1.1	1.0	1.6
9	2.8	4.5	4.5

re-examined after 18 months, also showed similar serum PBB levels (Table 3). It was of some interest, nevertheless, that several of these chemical worker values appeared to have increased significantly; there may possibly have been continuing exposure in the plant, known to have been contaminated during the production of the chemical from 1970-1975.

TABLE 3
Serum PBB concentrations in 14 chemical company workers in November, 1976 and April 1978

Subject	1976 serum PBB, ppb	1978 serum PBB, ppb
1	1530	1363
2	1326	1286
3	216	264
4	48	87
5	38	69
6	18	53
7	16	27
8	8	7
9	8	10
10	4	8
11	4	9
12	4	4
13	2	1
14	1	1

Subjects 1,2,3, & 6 were former PBB production workers. Subjects 4, 5, & 7 were maintenance workers in all areas of the plant. Subject 13 ceased work at the plant in 1976; the remainder were currently employed, and all had worked at the plant since at least 1973.

DISCUSSION

The observation that PBB serum values in 104 persons, with a wide range of concentrations, did not change significantly during 12-18 months strongly supports the proposal that equilibrium had been achieved in body distribution of PBB. In some of our cases, however, serum PBB values were higher in 1977-1978 than in 1976, which may be due to inherent analytical error (ca. 10%), but may also be attributed to continuing exposure (especially apparent with the chemical workers) or to mobilization from fat stores. Thus, an alternative interpretation of our observations could be that while serum levels are not strictly at equilibrium, the concentrations have not significantly decreased in this time period. HUMPHREY AND HAYNER (1975) observed that June and fall, 1974, serum PBB values were correlated, but at that time there were no clear correlations between fat and serum PBB levels. MEESTER AND MCCOY (1976) observed a marked decline over 3 years in serum levels of PBB, while fat concentrations remained fairly constant.

Studies in animals have shown that during redistribution of PCB's, PBB and DDT residues, blood and fat concentrations gradually achieve steady-state concentrations. MORGAN AND ROAN (1974) showed in humans that DDT residues reached equilibrium 1-3 years after dosing.

The strong correlation of serum and adipose tissue PBB concentrations is also consistent with equilibrium, since during dynamic redistribution, a wide variety of serum:fat ratios would be expected, especially over such a wide range of concentrations. Such variations may explain previous observations (MEESTER AND MCCOY 1976, HUMPHREY AND HAYNER 1975), although continuing ingestion of PBB in food could also have then been a factor. In 1977, however, since the major source of exposure to PBB in Michigan (contaminated food) had been controlled, and since ingestion of additionally significant amounts of PBB is unlikely to have occurred, maintenance of PBB levels along with correlation of serum:fat PBB levels bespeak equilibrium. It may be expected that these persons now have a more or less permanent body burden of PBB.

MATHEWS et al. (1977) studying rodents, observed that "PBB concentration of adipose tissue would not be expected to show an appreciable decline during the lifetime of the animal." MORGAN AND ROAN (1974) predicted that "elimination of DDE would require the better part of a man's natural life-span"; our findings suggest that the same may be predicted for PBB.

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