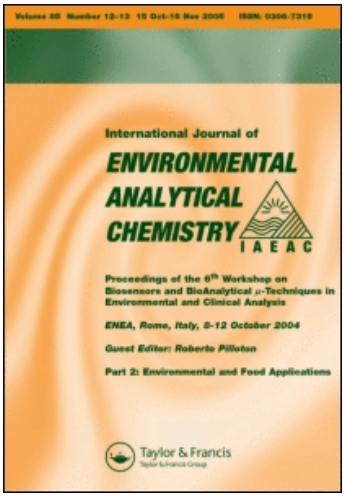

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ORGANOCHLORINE PESTICIDES AND PCBs IN TISSUES FROM DUTCH CITIZENS (1968–1986)

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Adipose tissue, milk and blood from Dutch citizens have been investigated for the occurrence of organochlorine compounds since 1968. In this paper, median values for HCB, α-HCH, β-HCH, γ-HCH, β-Hepo (heptachlorepoxide), dieldrin, p.p'-DDE, o.p'-DDT, TDE and PCBs (first determined by the perchlorination method, later by a selection of individual congeners) are given. Time trends, influence of age and sex of the donors, changes in concentrations of milk during lactation, the possible effect of life-style, and statistical evaluation of the data collected over the past twenty years will be discussed.

PCBs and p.p'-DDE occur in the highest concentrations in all tissues investigated, followed by HCB and β-HCH. Especially the p.p'-DDT levels decreased dramatically over the years of the investigation. Blood/fat accumulation factors were derived; they decrease in the order PCBs ≅ p.p'-DDE > β-HCH ≅ HCB > β-Hepo ≅ dieldrin > α-HCH ≅ γ-HCH.

KEY WORDS: Organochlorine pesticides, PCBs, milk, adipose tissue, blood.

INTRODUCTION

Persistent organochlorine chemicals have been used intensively in both agriculture and industry for a relatively long period of time. The occurrence of organochlorine compounds in the environment and subsequently in parts of the food chain, resulting in the intake of these compounds by man and animal, has already been noted since the early sixties.

The occurrence of chemical contaminants in human milk has been reviewed extensively by Jensen.[1] The comparison of results from these types of monitoring studies in different countries and at different time, however, is troublesome, because donors, sampling and analytical methods may often be different.[2] In a few countries the human milk contamination has been investigated by the same research group for several years and a downward trend in levels has been established for most chemicals in Scandinavia, although in line with the results presented in this study, the decrease with respect to PCBs is not significant yet. In Poland the DDT-levels are declining, but PCB-levels are still increasing.[1]

The levels of organochlorine compounds in human tissues is of special interest because these chemicals can easily be absorbed through skin, lungs and the gastro-intestinal tract of the body. The metabolism and/or elimination of these compounds is slow, and sometimes even apparently absent. Consequently an accumulation of organochlorine compounds in human (fatty) tissues is to be expected.

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In order to estimate the effect of certain government measures to ban the use of persistent toxic chemicals, our institute carries out monitoring programmes in the Netherlands with respect to the occurrence of organochlorine pesticides and polychlorinated biphenyls (PCBs) in human tissues. The tissues investigated are adipose tissue, milk and blood.

In this paper the results of these studies from 1968 up till now are reported. In the discussion, possible correlations between the levels of organochlorine compounds found and some external parameters such as time trends, age and sex are given. Also blood/fat accumulation factors were calculated in order to study the feasibility of monitoring blood, which is easier to obtain in comparison to other tissues. The blood/fat accumulation factor can also give an indication of the behaviour of a certain chemical in different compartments of the human body.

EXPERIMENTAL

Materials

The tissues were obtained as follows:

Adipose tissue

Except for one year (1979), all adipose tissues investigated originated from autopsies carried out in hospitals in Utrecht, Amsterdam, Nijmegen and Groningen. In 1979, a special investigation was carried out in biopsy tissues obtained from gynecological surgery.

The adipose tissues taken were abdominal or perireneal depot fat. No samples were taken from strongly emaciated or heavily medicated subjects. At sampling, desinfectants which could interfere with the analysis were avoided. The samples, which had to contain at least 250 mg of extractable fat, were kept in glass containers at – 18 °C prior to analyses.

Milk

The milk samples were collected through Maternity Home Help Centres from towns of various sizes all over the Netherlands.

The participants were asked to collect 50–100 ml of milk in glass containers. In the containers a small amount (approximately 100 mg) of potassium bichromate was present for preservation of the sample; from experiments, carried out in advance, it was known that potassium bichromate did not influence the concentration levels of the compounds of interest. Two investigations in human milk have been carried out: in the first (1972/73), the participants had been asked to collect samples, if possible, 1, 2, 3, 5 and 7 weeks post-partus. In the second investigation (1983), the samples were collected only once (approximately 10 days post-partus). The participants had a free choice for the moment of collection, but always after feeding the infant. Together with the sample the participants returned, anonymously, a form with data on age, parity, eating habits, possible medication etc. For the determination of organochlorine pesticides and PCBs, a minimum quantity of 50 ml of milk is needed; when less than 50 ml of milk was available, the sample had to be discarded.

Blood

Blood samples were obtained in 1978 and 1980 from 19 year old men undergoing medical examination for military service, and in 1983 from 19–23 year old students at Utrecht University. When the amount of blood available was less than the 10 ml required, individual samples were pooled.

In 1982, the blood samples originated from autopsies. From the same deceased persons, adipose tissues were taken in order to obtain information on the partition of the compounds investigated over the compartments of the body.

In all cases, whole blood was sampled and analysed as such.

Analytical Methods

Over a period of more than twenty years it is to be expected that analytical procedures change in the course of time. Basically, the same analytical methodology (gas/liquid chromatography with electron-capture detection) was followed over the years. When new elements in the analytical procedure were introduced, it was ensured by parallel runs that the results of the "old" method were compatible with those of the "new" method. Recovery experiments were performed on a regular basis in order to check the performance of both method and workers. As a result of the above, it can be stated that the values presented in the present paper are comparable with each other.

Extraction and clean-up of the samples were performed as follows:

Adipose tissues

The tissue was extracted with approximately 100 ml of light petroleum (b.r. 40–60 °C) in a small sized Soxhlet apparatus. The extract was evaporated to dryness and the residue defined as "the fat" was redissolved in light petroleum so that a solution of 45 mg of fat per ml was obtained.

Five ml of the extract (225 mg of fat) was subjected to a chromatographic clean-up and fractionation with alumia (10 g, W200, basic, activity super I, Woelm, deactivated with 9.5% of water) followed by silicagel fractionation (5 g, Kieselgel 60, reinst, 70–130 mesh, Merck 7754, activated for 15 h at 200 °C immediately before use). Presently we are developing an HPLC method for both clean-up and fractionation of organochlorine compounds in fatty substrates.

Until 1983 PCBs were determined as decachlorobiphenyl; the PCB fraction was treated with 0.3 to 1.4 ml of antimony pentachloride and heated at 190 °C for 3 h. After cooling, 2 ml of 20% hydrochloric acid and 5 ml of light petroleum was added. This mixture was shaken for 2 minutes and 1 ml of the upper layer was led over a 2 g alumina column.

The determination of PCBs as decachlorobiphenyl has been used in our laboratory on a routine basis since about 1974.[3] The yield of the perchlorination is higher for the higher-chlorinated PCBs than for the lower chlorinated ones,[4] so that the results obtained by the perchlorination procedure primarily reflect the occurrence of the more persistent higher chlorinated PCBs. The recovery of Clophen A60 over the whole procedure is 80–85%; the recovery of the organo-

chlorine pesticides is >95%. From 1984 onwards, a selection of individual PCB-congeners was determined by capillary gas chromatography. For comparison purposes, the perchlorination period has been carried out as well for 1–2 years.

Milk

The samples were extracted with a mixture of 100 ml of light petroleum and 100 ml of acetone.

After centrifuging, the upper layer was dried over sodium sulphate and evaporated to dryness on a water bath of 60–65 °C. The residue, again defined as "the fat", was processed the same way as the residues from adipose tissue.

Blood

Ten ml of blood were diluted with 15 ml aqua bidest (distilled over potassium permanganate). Fifty ml of light petroleum were added and the mixture was shaken vigorously for 2 minutes. After separation of the phases, which can be promoted by cooling the mixture in acetone-dry ice, the organic layer was pipetted off. The extraction was repeated three times. The combined extracts were dried over sodium sulphate and concentrated to exactly 100 ml. For the determination of the organochlorine pesticides this solution was injected in a gas chromatograph equipped with an electron-capture detector. For the determination of PCBs an additional alumina clean-up was used.

RESULTS

The results of the monitoring studies are summarised in Tables 1 to 3 giving median and 90% values of the concentrations found. The data are given in this format, because, due to the skew distribution of the data, arithmetic mean and standard deviation do not give an appropriate description of the population. The tables also give the number of samples investigated per sampling period and the average age of the donors of the samples.

The median values for the two most interesting compounds with respect to the time-trends are also summarized in Figures 1 and 2. From these figures, the data from 1979 have been omitted, since the average age of the donors was considerably lower in that year. See also discussion section of this paper.

In 1982, adipose tissues and blood from the same deceased persons were investigated. From these data "accumulation factors" (f) can be derived, using the following equation:

$$f = \frac{\text{concentration in adipose tissue (mg/kg)}}{\text{concentration in blood } (\mu g/l)} \times 1000$$

The average f-values found, and their 95% confidence limits, are given in Table 4. Due to the low concentrations (lower than the limits of detection, see Table 1) of these compounds in blood, no f-values can be given from o.p'-DDT, TDE and p.p'-DDT.

In the investigation of human milk from 1972/73, possible changes in concentration of the compounds under study were estimated from samples collected 1, 2,

Table 1 Organochlorine compounds in human tissues from Dutch citizens (median values in mg/kg on a fat basis for the adipose and milk samples, in μg/l on a product basis for the blood samples)

Adipose (autopsy samples)
average number of samples: 51 per year
average age of the donors: 62 year

Sampling period	*HCB*	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*
1968/69	0.7	<0.1	0.4	<0.1	0.1	0.2	2.8	0.6	0.1	1.4
1973/74	1.2	<0.1	0.6	<0.1	0.2	0.2	2.8	0.1	0.1	0.8
1975	1.2	0.01	0.32	0.04	0.12	0.11	2.7	0.08	0.04	0.47
1976	0.86	0.01	0.38	0.02	0.12	0.09	3.4	0.03	0.03	0.56
1977/78	0.98	<0.01	0.40	0.01	0.14	0.11	3.2	0.03	0.02	0.40
1980	0.85	0.01	0.37	<0.01	0.12	0.10	3.7	0.01	0.01	0.32
1981	0.80	<0.01	0.27	<0.01	0.08	0.07	2.9	<0.01	<0.01	0.25
1982	0.58	<0.01	0.35	<0.01	0.09	0.07	3.5	<0.01	<0.01	0.23
1983	0.49	<0.01	0.29	<0.01	0.10	0.06	3.0	<0.02	<0.02	0.22
1985	0.42	<0.01	0.26	<0.01	0.12	0.07	2.8	0.03	0.01	0.17
1986	0.38	<0.01	0.27	<0.01	0.10	0.05	2.3	0.04	<0.01	0.14

Milk
number of samples: 1972/73: 202; 1983: 278; planned for 1988: 300
average age of the donors: 27 year

Sampling period	*HCB*	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*
1972/73	0.86	0.01	0.28	0.02	0.08	0.11	1.6	0.1	0.4	0.73
1983	0.19	<0.01	0.10	<0.01	0.02	0.03	0.82	<0.02	<0.03	0.04

Blood (1978–1981: biopsy samples, 1982: autopsy samples)
number of samples: 1978: 70; 1980: 48; 1981: 127; 1982: 54
average age of the donors: 1978–1981: 20 year; 1982: 65 year

Sampling period	*HCB*	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*
1978	1.2	<0.1	0.6	0.1	<0.3	<0.4	1.9	<1	<1	<1
1980	1.1	<0.1	<0.4	<0.1	<0.3	<0.4	2.5	<1	<1	<1
1981	1.2	<0.1	0.3	0.2	<0.3	<0.4	2.7	<1	<1	<1
1982	2.2	<0.1	1.4	0.1	0.4	<0.5	4.6	<1	<2	<2

3, 5 and 7 weeks after delivery. Complete series of samples were obtained from 21 mothers, which is sufficient for the purpose of investigation. Linear regressions were calculated from the equation:

$$y = a.t + b$$

where y = concentration of organochlorine compound found (mg/kg)
a = slope (mg/kg/week)
t = time (weeks)
b = intercept (mg/kg)

The average a-values found are summarized in Table 5. The a values underlined differ significantly from 0 ($P = 0.05$).

Table 2 Polychlorinated biphenyls in human tissues from Dutch citizens (median values in mg/kg on a fat basis for the adipose and milk samples, in μg/l on a product basis for the blood samples)

Adipose (autopsy samples)
average number of samples: 51 per year
average age of the donors: 62 year

Sampling period	*PCBs total*[a]	*PCB-congeners (IUPAC #)*								
		028	*052*	*101*	*118*	*128*	*138*	*153*	*180*	*194*
1973/74	2.2									
1975	1.8									
1976	1.6									
1977/78	1.9									
1980	2.5									
1981	1.8									
1982	2.1									
1983	2.1									
1984		0.008	0.002	0.007	0.068	0.016	0.190	0.260	0.155	0.028
1985		0.004	–	0.005	0.052	0.006	0.178	0.250	0.160	0.023

Milk
number of samples: 278
average age of the donors: 27 year

Sampling period	*PCBs total*[a]	*PCB-congeners (IUPAC #)*								
		028	*052*	*101*	*118*	*128*	*138*	*153*	*180*	*194*
1983	0.72	0.009	–	0.009	0.039	–	0.120	0.110	0.068	0.007

Blood (1978–1981: biopsy samples, 1982: autopsy samples)
number of samples: 1978: 70; 1980: 48; 1981: 127; 1982: 54
average age of the donors: 1978–1981: 20 year; 1982: 65 year

Sampling period	*PCBs total*[a]	*PCB-congeners (IUPAC #)*								
		028	*052*	*101*	*118*	*128*	*138*	*153*	*180*	*194*
1978	3.5									
1980	3.1									
1981	4.4									
1982	4.4									

[a]Determined as decachlorobiphenyl after perchlorination and expressed as Clophen A 60
– = < 0.001 mg/kg on a fat basis.

DISCUSSION

It should be emphasized that the discussion of the results in this type of study is almost always thwarted by the questionable representativity of the samples investigated for the population as a whole: in the case of autopsy samples, the aged are overrepresented, and only persons taken to a hospital before their death were among the donors. In the case of milk, only fertile females can naturally provide samples, and from them only those who visited a Maternity Home Help Centre and were willing and able to provide samples. In the case of blood samples, young males and university students were overrepresented. A truly aselect sampling scheme for human tissues, however, is practically utopic, so that generalisations

Table 3 Organochlorine compounds in human tissues from Dutch citizens (90% values in mg/kg on a fat basis for the adipose and milk samples, in μg/l on a product basis for the blood samples)

Adipose (autopsy samples)
average number of samples: 51 per year
average age of the donors: 62 year

Sampling period	*HCB*	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*	*PCBs*
1968/69	1.3	<0.1	0.7	<0.1	0.2	0.4	8.7	0.4	1.0	2.0	–
1973/74	2.0	<0.1	0.9	<0.1	0.3	0.4	7.7	0.2	0.3	1.1	3.8
1975	1.8	0.01	0.67	0.05	0.20	0.20	6.0	0.08	0.14	1.1	2.8
1976	1.6	0.01	0.72	0.03	0.20	0.14	5.6	0.05	0.05	0.84	2.4
1977/78	1.7	0.01	0.71	0.03	0.26	0.22	6.3	0.04	0.06	0.74	3.0
1979	1.0	0.06	0.44	0.02	0.15	0.13	3.4	0.03	0.05	0.40	2.6
1980	1.7	0.01	0.84	<0.01	0.24	0.25	8.8	0.04	0.04	0.68	4.2
1981	1.6	<0.01	0.66	<0.01	0.18	0.19	5.4	<0.02	<0.02	0.55	3.2
1982	1.2	0.01	0.77	0.01	0.19	0.15	6.1	0.04	0.03	0.63	3.5
1983	1.0	<0.01	0.77	<0.01	0.19	0.14	6.7	0.04	0.02	0.50	3.4
1985	1.0	0.01	0.76	0.05	0.17	0.19	5.5	0.09	0.02	0.56	–
1986	0.7	0.01	0.59	0.01	0.18	0.12	5.4	0.08	0.02	0.30	–

Milk
number of samples: 1972/73: 202; 1983: 278; planned for 1988: 300
average age of the donors: 27 year

Sampling period	*HCB*	*α-HCH*	*β-CH HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*	*PCBs*
1972/73	1.4	0.05	0.50	0.05	0.14	0.31	2.9	0.83	0.24	1.3	–
1983	0.34	<0.01	0.16	0.02	0.03	0.05	1.6	<0.03	<0.02	0.13	1.1

Blood (1978–1981: biopsy samples, 1982: autopsy samples)
number of samples: 1978: 70; 1980: 48; 1981: 127; 1982:54
average age of the donors: 1978–1981: 20 year; 1982: 65 year

Sampling period	*HCB*	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*	*PCBs*
1978	1.9	<0.1	0.7	0.2	<0.4	<0.5	3.9	<2	<1	<2	11
1980	1.8	0.2	1.3	0.4	0.3	<0.4	5.0	<1	<1	<1	19
1981	2.0	0.1	0.9	0.4	0.3	<0.4	4.6	<1	<1	<1	11
1982	5.6	<0.1	2.1	0.5	1.4	0.8	22	<1	<2	<2	9.1

must be made on the basis of the material available, bearing in mind the shortcomings of the sampling procedure. With due precaution, the following remarks can be made.

Time Trends

One of the most important objectives of this study was the establishment of possible time trends for the compounds investigated, since in this way the effectiveness of measures taken to diminish the exposure of the population to these compounds can be estimated.

In Figure 1, illustrating the trend for the adipose tissues and human milk, a

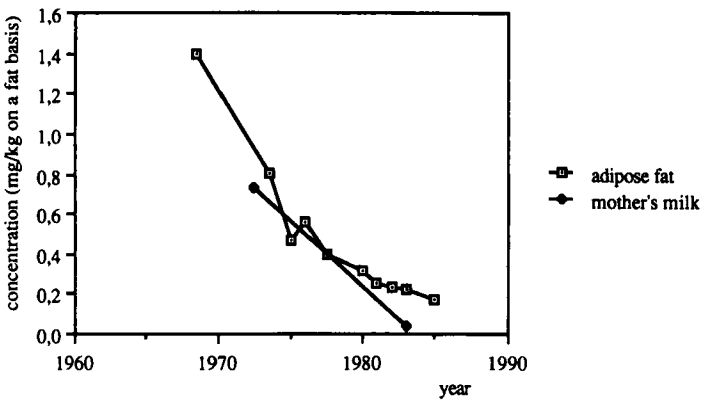

Figure 1 Median concentrations of p.p'-DDT in adipose tissue and human milk from Dutch citizens as a function of time (cf. also table).

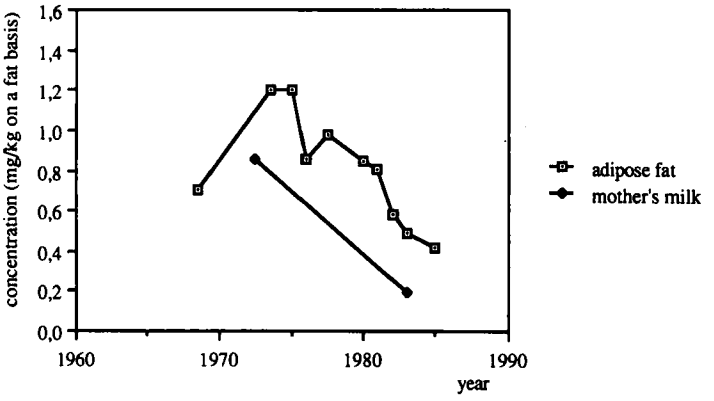

Figure 2 Median concentrations HCB in adipose tissue and human milk as a function of time.

downward trend for p.p'-DDT is clearly visible, reflecting the ban of this compound in many countries. The main metabolite p.p'-DDE, however, does not yet show any tendency to decrease in concentration. Apparently this compound is more resistent to degradation and/or excretion than p.p'-DDT itself. For HCB, as illustrated in Figure 2, an increase was found in the early seventies, which can be connected to an increase of the HCB concentration in products of animal origin on the market in the Netherlands. The increase was caused by the occurrence of high HCB residues in, among others, pollard pellets imported from South America.[5] Effective measures have now been taken to avoid the contamination of such products by HCB, eventually resulting in a gradual decrease of the HCB concentration in human adipose tissues. A slight downward trend for dieldrin can possibly be noted, but the values found for this compound are so low that time trends are difficult to ascertain. The use of dieldrin and its precursor aldrin were strongly reduced during the past 15 years throughout the world, so that a decrease of the levels in human adipose tissue in due time must be expected. Although the values per se are low, dieldrin is still a residue of considerable concern, since its

Table 4 Accumulation factors fat/blood: average (f) and 95% confidence limits (c.l.) given concentration in blood (μg/l)

	HCB	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*	*PCBs* [a]
f	320	60	340	70	180	170	610	–[b]	–[b]	–[b]	660
c.l.	280–360	30–90	280–400	20–120	140–220	70–270	430–790	–	–	–	550–770

[a]Determined after perchlorination as Clophen A60
[b]Insufficient data available due to low levels in blood

Table 5 Changes of the concentration in human milk during lactation: average slopes (a.mg/kg/week) (the values *underlined* differ significantly from 0 (P = 0.05, N = 21)

	HCB	*α-HCH*	*β-HCH*	*γ-HCH*	*HEPO*	*Dieldrin*	*p.p'-DDE*	*TDE*	*o.p'-DDT*	*p.p'-DDT*	*PCBs* [a]
a	*0.022*	0.001	*0.012*	0.003	0.005	0.006	*−0.027*	0.011	0.001	0.001	*0.038*

[a]Determined after perchlorination and expressed as Clophen A60.

daily intake, as calculated from total diet studies, is from all organochlorine pesticides the nearest to the Allowed Daily Intake (ADI).[6] Little, if any, downward trend is visible for β-HCH, which seems somewhat surprising, since the use of β-HCH containing BHC-mixtures has been prohibited for a long time in large parts of the world for use on edible crops or on animals. Apparently, the persistence of β-HCH in fatty tissues is high. The same remark applies for PCBs, for which group no significant downward trend can be found yet. The use of PCBs has also been considerably reduced in the course of this investigation, but the effect of prohibiting measures remains yet invisible from our data. The levels of the other organochlorine compounds investigated in this study, α-HCH, γ-HCH, β-HEPO, o.p'-DDT and TDE are low; since 1981, only for β-HEPO have median values above the limit of determination been found (see Table 1). It is to be expected that eventually also the level of β-HEPO will diminish, as the use of heptachlor, from which insecticide β-HEPO is the main metabolite, is gradually decreasing.

Regarding the levels found in milk samples, the downward trends are more profound. Less data are available for human milk compared to adipose tissue, as the latter are more easily obtainable. The levels in human milk are generally lower than those in adipose tissues, due to the lower age of the donors in the case of milk. The general policy to follow the levels in human tissues primarily from post-mortem adipose samples thus gives a conservative, and in any case not a flattered, picture of the situation in human milk, both with regard to levels as with regard to the time trends.

Influence of the Age of the Donors

In Figure 3, again the six most important compounds, with regard to level as well as persistence, are chosen here to illustrate the interrelation between the age of the donors and the levels found. In order to simplify the presentation, the levels found

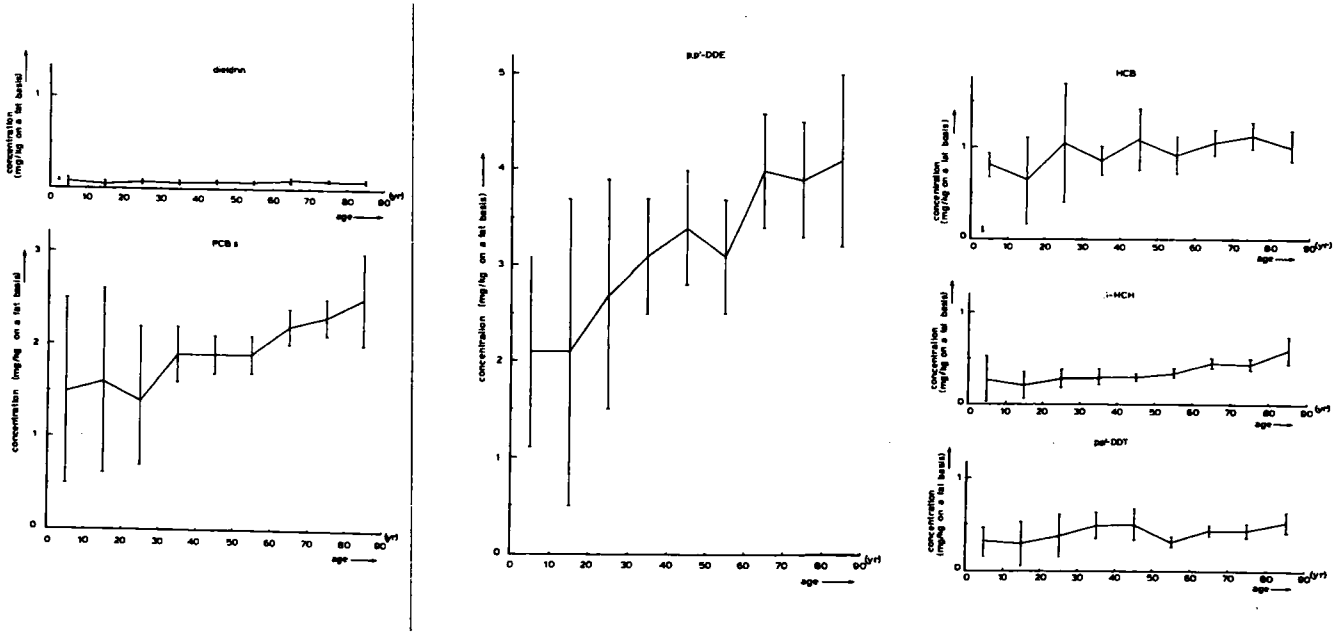

Figure 3 Average concentrations and 95%-confidence limits for p.p'-DDE, PCBs, HCB, β-HCH, p.p'-DDT and dieldrin in adipose tissue as a function of age. Numbers of observation per group are:

0- 9: 5	30-39: 32	60-69: 90	>90: 2 (not incorporated
10-19: 6	40-49: 45	70-79: 87	in the figure)
20-29: 16	50-59: 67	80-89: 38	

Table 6 Influence of sex of donors on the concentrations of six organochlorine compounds in adipose tissue: average values and 95% confidence limits given in mg/kg on a fat basis

Sex	*Number of observations*	*HCB*	*β-HCH*	*Dieldrin*	*p.p'-DDE*	*p.p'-DDT*	*PCBs* [a]
men	190	0.95±0.12	0.40±0.05	0.12±0.03	4.0±0.48	0.38±0.05	2.5±0.28
women	177	0.92±0.11	0.40±0.04	0.11±0.02	3.3±0.10	0.50±0.10	1.8±0.13

[a]Determined after perchlorination and expressed as Clophen A60.

have been taken together in age groups of 0–9, 10–19 etc. years, and the average, together with the 95%-confidence limits are given for each group. Not surprisingly, consistent with the *f*-values given in Table 4, the highest influence of age has been found for p.p'-DDE and PCBs, followed by the less accumulating compounds HCB and β-HCH. The p.p'-DDT and dieldrin levels are influenced by the age of the donors to a limited extent only.

The influence of age is also clearly visible from the data from 1979 when the average age of the donors was only 39 years, rather than the usual 57–68 years for the other sampling periods. The values found in 1979, especially those for p.p'-DDE, PCBs, β-HCH and HCB, are clearly lower than those found in the immediately preceding and following years, thus disturbing the overall trend. For this reason, the values for 1979 have been omitted from the time-trend evaluations.

The levels of blood, although low (see Tables 1 to 3), follow the same trend with age as the levels in adipose tissue and milk: in 1982, when post-mortem samples were investigated from donors with an average age of 65 years, the levels were generally higher than in the years before when the average age of the donors was 19 to 21 years.

Changes in the Levels in Milk During Lactation

From Table 5 it can be seen that significant *in*creases of the levels in milk can be observed during lactation for HCB, β-HCH and PCBs; a significant *de*crease was observed for p.p'-DDE. However, the changes are rather small, in the order of a few hundredths mg/kg on a fat basis per week and so of virtually no practical interest. From these data we conclude that there is no absolute necessity to standardise the sampling time to a fixed number of weeks post-partus. For future programs we choose to sample at 3 days to 2 weeks after delivery, because in this period the donors are still under surveillance of the Maternity Home Help Centres, and so a maximum response can be anticipated.

Influence of the Sex of Donors

The average levels for the previously mentioned 6 main compounds in adipose tissue, together with their 95% confidence limits, are given in Table 6. A significant difference is found for the PCBs only, mainly caused by some exceptionally high values for individual male donors: 2 out of 190 observations were >10 mg/kg (fat basis), 8 >5 mg/kg (fat basis); for the female donors only one of the observations

was >5 mg/kg (fat basis) and none >10 mg/kg (fat basis). Professional exposure might be the cause of the high values, but this could not be retraced from the obduction protocols.

A second factor must also be mentioned here, viz. the "excretion" of PCBs in the case of women feeding a baby: In the 1983 human milk study it was established that a significant decrease (8% per parity) occurs for the PCB concentration in human milk. It can be anticipated that similar effects can be found in the body fat of the mother. However, no information was available with respect to the parity of the female donors of the adipose tissues, so that this effect cannot be quantified for the adipose tissues yet.

Other Effects

No influences were detected in any of the investigations up till now of origin (rural vs. urban), eating habits (vegetarian vs. omnivorous, fish vs. meat as a main protein source) or medication of the donors on the levels found in any tissue. This is not too surprising, as the difference between urban and so-called rural surroundings is small in a densely populated country like the Netherlands, as is the difference in food quality between cities and villages. The influence of a vegetarian life style can only be significant if also dairy products and fish are banned from the diet (which is rarely the case) and if this strict diet is followed for a long period (eg. from childhood onwards). Influences of medication and/or diseases were not liable to be found either, as clearly ill or heavily medicated persons were not chosen as donors for the investigation.

Usefulness of Sampling Blood

As can be seen from Tables 1 to 3, only a limited number of organochlorine compounds can be monitored satisfactorily in blood, due to the low concentrations present in blood. Nevertheless, investigations in blood can be useful in case of suspected professional exposure or calamities. The values found up till now can be used as reference or "normal" values. As a matter of fact, blood samples can be taken from a living person more easily than fat samples. By using the *f*-values given, a first estimate of the levels in fat can be derived from those in blood, if desired. It should be emphasized, however, that variations in blood levels are higher than those in adipose tissues, as blood interacts more closely with the diet than depot fat.

CONCLUSIONS AND FUTURE RESEARCH

The results of this study are presently being evaluated by toxicologists and epidemologists of our institute in order to formulate our monitoring program for the occurrence of organochlorine compounds in human material for the years to

come. Presently we are performing a 330 samples monitoring program for human milk from all over the country in order to investigate in more detail the effect, if any, of urbanisation on the levels of organochlorine compounds in this matrix. In the near future human milk will be monitored on a 5 year basis and adipose tissue on a 2 year basis in order to follow the time-trends found in this study.

The time-trends investigated in this study appear to be a good instrument for monitoring the effect of certain measures against the use of certain persistent fat-soluble chemicals. For example, during the course of the investigation described in this paper we observe a dramatic decrease of the levels of p.p'-DDT, due to a greatly diminished use of this compound and a slow decrease of its main metabolite p.p'-DDE. The other metabolites, TDE and o.p'-DDT also a decrease parallel to that of p.p'-DDT is observed, but it is less profound because of the lower levels of these metabolites. For β-HCH a similar decrease is found due to measures taken to promote the use of pure lindane. For α- and γ-HCH no trends are visible due to the low levels, caused by the biodegradability of these compounds. For dieldrin a small decrease can be observed due to its diminished use. For PCBs up till now no downward trend can be found, probably due to a combination of the ubiquity and the persistence of these compounds. For HCB an even more interesting phenomenon can be observed: after an initial increase from 1968 up till the mid-70's, now a decrease can be observed. This trend can be connected to contamination of animal products in the first period, while in the second period effective measures have been taken to prevent contamination of animal feed with HCB.

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