

PCB Reduction and Clinical Improvement by Detoxification: an Unexploited Approach?

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1. A detoxification trial was administered to a female worker from a capacitor factory who had been exposed to polychlorinated biphenyls (PCBS) and other lipophilic industrial chemicals.
2. The patient presented with severe abdominal complaints, chloracne, liver abnormalities, and a spontaneous nipple discharge of approximately 50 ml d-1.
3. PCB levels were high in adipose tissue (102 mg kg⁻¹), serum, (512 [tg I⁻¹]), skin lipids (66.3 mg kg⁻¹), and in the nipple discharge (712 [tg I⁻¹]).
4. The patient's history, the medical evaluation and prior unsuccessful symptomatic treatments were indicative of consequences elicited by occupational exposure to chemicals.
5. Detoxification treatment reduced the PCB levels in adipose tissue to 37.4 mg kg⁻¹, and in serum to 261 [tg I⁻¹], a 63% and 49% reduction, respectively.
6. The nipple discharge ceased and the symptoms improved.
7. Excretion of intact PCBs in sebum was appreciable before treatment and was enhanced by up to five-fold during detoxification.
8. This therapeutic approach appears promising for cases involving occupational exposure to lipophilic chemicals.

Introduction

Occupational exposure to industrial chemicals is of increasing relevance to medical evaluation. Among the toxic compounds having had widespread use are PCBS. Though currently banned in most industrial countries, they were commercially used in the electrical industry for more than 40 years and are present in extant electrical equipment throughout the world.^{1,2}

PCBs have a high propensity for accumulation in adipose tissue.³ Although long-term health effects in humans are still being investigated, most reports support an association between the clinical symptoms and the occupational exposure to aromatic hydrocarbons, including PCBs.⁴ In industrial settings, however, this issue remains confounded by the influences of other chemicals used concurrently with PCBs.

A capacitor factory in Semic, a small town in Slovenia, Yugoslavia, used PCBs as the main impregnated substance from 1962 to 1985.

Aroclor 1242 (42% chlorine content) and 1254 (54% chlorine content) were the main PCB mixtures. Their inappropriate handling and disposal resulted in occupational exposure and broad environmental contamination, which were detected in 1983.⁵ Several patients from that region, both occupationally and inadvertently exposed, were referred to the University Medical Centre of Ljubljana, Yugoslavia, for evaluation of their symptoms.⁶ This incited a ban on the use of PCBs in the production lines in 1985.

We present the case of a female patient who was admitted to the University Medical Department of Gastroenterology. The patient was occupationally exposed to PCBs and had elevated levels of these chemicals in serum, adipose tissue and in her spontaneous nipple discharge. She had gradually developed a clinical picture with symptoms of abdominal pains and bloating, general fatigue and muscle pains,

chloracne eruptions and sun sensitivity, joint pains and swelling of her limbs, menstrual irregularities, and a nipple discharge of 50 ml d⁻¹.

The clinical assessment and the results of medical evaluations corroborated the conclusion that complaints followed exposure to chemicals. Since previous treatment with analgesics, skin lotions, and steroids had been ineffective, as was an appendectomy, we explored an alternative therapeutic approach designed to remove chemicals from the body. The assumption underlying this approach was that the observed toxic manifestations may have been related to the continuous presence of certain lipophilic chemicals in the tissues. A recently reported detoxification treatment seemed promising as it had reduced levels of lipophilic chemicals, including PCBS, in adipose tissue.⁷ We present the favourable outcome of this treatment.

Methods

Case presentation

The female patient, 33, was admitted because of frequent attacks of abdominal cramps with visible bloating and nausea. Vomiting, diarrhea, and meteorism were not present. Serum transaminases were periodically increased: aspartate aminotransferase (AST) 20 U I⁻¹; alanine aminotransferase (ALT) 29 U I⁻¹; and g-glutamyl transferase (gGT) 52 U I⁻¹ (Table 1).

History. The patient had an unremarkable childhood. She was a healthy, non-alcoholic, nonsmoking mother of two children and had been capable of full-time employment and the care of her home until 1969. At that time she first noticed eruptions of chloracne, associated in the following years with skin thickening, eye watering, sun sensitivity, muscle pains and a progressive loss of endurance.

From 1970 on, she reported the onset of headaches, non-productive cough and recurrent sinusitis with common-cold like symptoms. Two successive bronchopneumonias required admission to the hospital.

In 1975, she observed a spontaneous, bluishgreen coloured, nipple discharge appearing daily, unrelated to the then regular menstrual cycle. Its quantity increased from a few drops, barely staining her clothes, to approximately 50 ml d⁻¹ in 1984. When expressed for diagnostic procedures, 200 ml could be collected in one day.

Since 1979, the patient reported morning joint pains, swelling of the fingers, and sharp bursts of pains in her extremities leading to a momentary loss of strength. Sudden attacks of dull abdominal pains, accompanied by visible abdominal bloating, began in that year. In time the attacks increased, from an initially mild discomfort, to episodes with symptoms of intolerable level. The attacks occurred up to three times per month and could be exacerbated by heavy physical work. Her menstrual cycle became irregular in 1982.

An increasing requirement for sleep beyond her usual 8 h, with general fatigue present even after 16 h of uninterrupted sleep, was apparent in late 1986.

Symptomatic treatments relieved some of the symptoms for brief intervals. They included application of skin lotions and topical steroids for the rashes and chloracne eruptions, dental repairs for chronic sinusitis and headaches, and oral contraceptive agents and dilatation and curettage for the irregular menstrual cycle. The acute nature and the pronounced clinical signs of an abdominal attack prompted an urgent exploratory laparotomy in 1984. Regional mesenteric lymphadenitis was found, while the removed appendix was histologically unremarkable.

Occupational history. The patient was first employed at the Semic factory in 1967. Direct contact with PCBs could be confirmed for 9 months in 1979, when she tested approximately 20,000 small capacitors per day for leakage of PCBS. The work was done by hand, using little or no protection. Though she otherwise did not work directly with PCBS, her working places were close to the uninsulated

impregnating hall. The production process made handling of trichloroethylene (TCE), epoxides, neoprene and similar chemicals unavoidable. Although the patient reported common exposure to these chemicals, the precise timings of the exposures are not available.

Initial examination. Clinical findings upon admission revealed a normally developed, well nourished young white female, body temperature 36.7°C, respirations 12/min, pulse 68/min and blood pressure 112/79 mmHg. The skin of the face and extremities appeared thickened. Scars from healed chloracne and fresh eruptions were present on the face, trunk and extremities. The lower eyelids appeared hyperpigmented. No peripheral oedema or lymphadenopathy were found. Her height was 154.9 cm, weight 57.6 kg, and the lean/fat ratio was 28.8%.

The head was normocephalic. The eyes and ears were unremarkable. Her nasal mucosa was oedematous without excessive secretion, the tongue surface was rough with uneven borders, and the teeth showed extensive dental repair. The thyroid gland was moderately diffusely enlarged. The breasts were normally developed, without chloracne or palpable masses. Dribbling nipple discharge could be provoked by pressing the breasts. Heart sounds were regular and no gallop or murmurs were heard. Respiratory sounds were clear and without rales. Upper abdominal tenderness was present, peristaltic activity was normal, and there were no signs of ascites. The liver span was 14 cm below the right costal margin, the spleen was not palpated. The right leg was slightly shorter, an anomaly noted in her childhood. The entire right side of the body had a discernible loss of sense of touch, the proprioceptive reflexes were normal.

Diagnostic work-up. The patient had normal values in the standard chemical panel, urine analyses and cultures. Coprocultures and stool specimen screen for fat, parasites and occult blood were negative. Pregnancy was excluded, and gynaecologic, oculistic, and orthopaedic examinations were unremarkable. Tests for gonorrhoea and syphilis, the usual sexually transmitted diseases of that region, were negative. The thyroid scintiscan revealed diffuse, grade I struma, classified as euthyreotic. The results of other analyses performed are listed in Table 1.

Table 1. Results of additional laboratory procedures

<i>Tests^b</i>	<i>Result</i>	<i>Normal range</i>
Haematologic values:		
Haematocrit	0.48	(0.37-0.48)
Haemoglobin	8.9	(7.4-9.9 mmol I)
Leucocyte count	6.9	(4.3-10.8 X 10 ⁹ I)
Differential count	normal	
Erythrocyte count	5.2	(4.2-5.9 X 10 ¹² I)
Platelet count	452	(150-350 x 10 ⁹ I)
ESR	9	(1-20 mm h)
Prothrombin time	10.1	(10-12s)
Partial thromboplastin time (activated)	11.2	(8.2-23.4 s)
Coombs tests (direct and indirect)	negative	Cryoglobulins
negative	Protoporphyrines in erythrocytes	normal
Biochemical panel:		
Calcium	2.3	(2.1-2.6 mmol I)
Magnesium	1.1	(0.8-1.3mmol I)
Serum iron	1.6	(9.0-26.0 [tmol I)
Iron binding capacity	66	(45-74 [imol I)
Proteins, total	80	(60-84 g I)
Proteins, electrophoresis		

Table 1. Continued.

Albumins	0.56	(0.52-0.681)
a.-2-globulins	0.13	(0.068-0.121)
B-globulins	1.91	(0.093-0.15 1)
IgG	11	(5.5-16.6 g I
Igm	1.0	(0.39-2.9 g I
IgA	1.9	(0.66-3.44gI
Triacyloglycerols	0.6	(0.4-1.5 g I')
Cholesterol	3.4	(3.1-5.7 mmol I
Bilirubin	2	(< 7 [tmol I
AST	15	(8-18 U I
ALT	12	(6-16 U I
gGT	46	(18-50 U I
Vitamin A	0.9	(0.5-2.1 [tmol I
Vitamin B 12	170	(60-210pmoll
Folic acid	5.6	(2.3-4.3 mmol I
Lead	< 1.0	(< 2.4 [tmol I

Additional analyses (blood):

Hepatitis A anti-IgM	negative
anti-IgG	negative
Hepatitis B HbsAg	negative
anti-Hbs	negative
anti-Hbc	negative
Epstein-Barr anti-IgM	negative
Epstein-Barr nuclear antigen antibodies	negative

<i>TeStSb</i>	<i>Result</i>	<i>Normal range</i>
Cytomegaly virus isolation	negative	
Lyme disease anti-IgM	negative	
anti-IgG	negative	
Cl ₁ -binding activity	negative	
Lupus erythematosus cell preparation (Hargraves)	negative	
factor		negative
antinuclear antibodies (ANA)	negative	
cephalin flocculation	negative	
Rheumatoid factor	negative	
Cortisol 8 a.m.	0.24	(0.1@.69[tmoll
Prolactin	3.0	(0.08-6.Onmol I
Testosterone	2.5	(0.9-3.2nmoll
unbound	19.8	(3.0-44.0 pmol I
T3 resin uptake	0.28	(0.25-0.35)
T3 total by RIA	1.82	(1.0-2.9nmol I
Free thyroxine index (FT,I)	35.4	(I 2.8-51 pmol I
T,-RIA	162	(52-154nmol I
Thyroxine binding globulin capacity	227	(190-319 nmol I
TSH	1.2	(0. 4-3.4 mU I
Thyroid colloid and microsomal antibodies	negative	

Additional analyses (urine):**Table 1.** Continued.

Proto-; Copro-; Uro-porphyrines	negative	
17-Ketosteroids	37	(14-49[μ mol/d]
17-Hydroxysteroids	9	(8-22 μ mol/d]
Tests		
Bromosulphthalein retention (5 mg i.v.)	0.03	(< 0.05 I)
Oral lactose tolerance (50 g)	negative	
D-Xylose absorption (25 g)	39	(34-54mmol/5h 'inurine)
Oral barbiturate challenge	negative	
Adrenocorticotrophic hormone stimulation	0.94[μ mol/l]	
Dexamethasone overnight suppression	2 [ng/100 ml]	

^a Reference values in parenthesis where applicable; abnormal results in **bold**

^b AST = aspartate aminotransferase; ALT = alanine aminotransferase; gGT = g-glutamyl transferase; ESR = Erythrocyte sedimentation rate; RIA = radioimmunc assay; and TSH thyroid stimulating hormone.

EKG tracing showed a regular sinus rhythm with normal intervals, and a normal electrical axis. X-ray films of the chest and abdomen appeared normal. Pulmonary function tests were normal. Abdominal ultrasound and CAT scans confirmed hepatomegaly but were otherwise unremarkable. Esophago-gastroscopy was normal, endoscopic retrograde cholangiopancreatography (ERCP) disclosed a minor developmental anomaly in the branching of the main pancreatic duct in the pancreatic head. Colonoscopy with retrograde ileoscopy disclosed no abnormality. Barium-meal and barium enema studies were unremarkable. The X-rays of the skull and of the spine appeared normal. Laparoscopy confirmed enlarged liver with a smooth surface and moderately prominent Glisson's areas. Other inspected abdominal organs appeared unremarkable. Gallium scintiscans of the skeleton and hepatobiliary iminodiacetic (HIDA) scintigraphies of the liver were normal. Mammography was unremarkable. The results of the electroencephalogram with evoked somatosensory potentials and the electromyogram appeared normal.

Biopsy specimens from the stomach (forceps) and small intestine (suction) disclosed no distinct histologic abnormalities. Results of the bone marrow sample analysis were unremarkable. However, light microscopy of the liver biopsy specimen did reveal abnormalities (Figure 1).

A chromosome study, performed as described by Hamerton 8 and Grouchy, 9 revealed chromatid and isochromatid breaks, gaps and minutes in 20% of the 200 analysed lymphocytes (reference value -- 3% per 200 analysed lymphocytes).

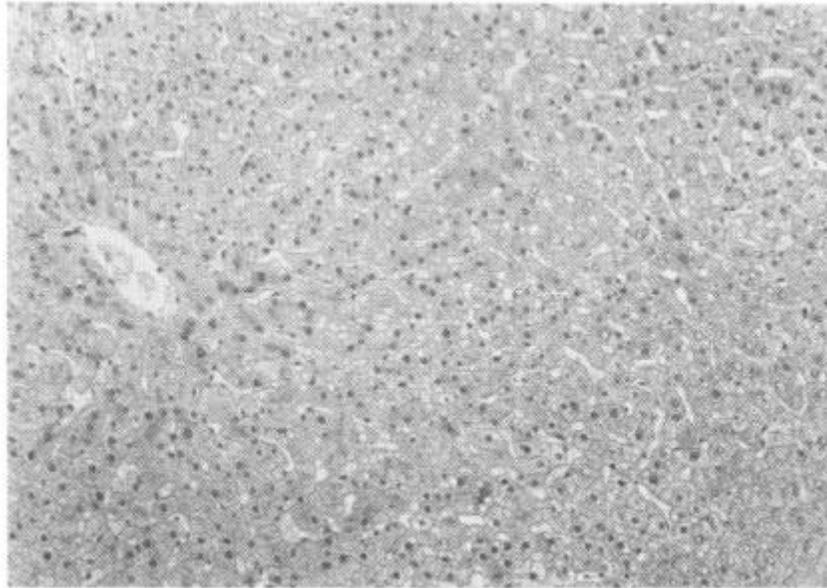


Figure 1 Liver biopsy sample. Note loss of polygonal outline and the swollen appearance of hepatocytes, containing a downy cytoplasm. Nuclei vary in size and appear enlarged or degenerated in some cells. Noninflammatory degeneration of hepatocytes, hyaline inclusions, and a moderate steatosis may be noted. Sinusoidal spaces appear irregularly broadened and inflammatory reaction is not apparent. Trichrome staining and staining for hepatitis B markers were negative. (Haematoxylin and eosin; original magnification **X 10**).

PCBS, determined in Ljubljana by high resolution gas-chromatography with electron capture detector and confirmed with mass-spectrometry,⁵ were 96 mg kg⁻¹ in adipose (reference value 1-2 mg kg⁻¹), and 8 mg kg⁻¹ in the nipple discharge. No attempt was made to assess levels of other chemicals or PCB levels in faeces and urine.

Clinical course. Several abdominal attacks were observed. Each was marked by a concurrent visible symmetrical protrusion of the entire abdominal wall, enduring through the attack. The pain was dull, increased within a day to a barely tolerable level and persisted unchanged for up to 5 d. The attack and the protrusion then subsided within a few hours. During attacks the body temperature was normal and no excessive meteorism was found on plain X-ray films. Sedimentation rate, the standard chemical panel, and the complete blood count were normal, as were levels of ceruloplasmin, copper, porphyrins, and Urinary 17-keto and 17-hydroxy steroids. During some of the attacks serum gGT was elevated to 72 U I l.

Symptomatic treatments of the abdominal discomfort with antacids, spasmolytics, analgesics, infra-red irradiation, acupuncture and nerve blockades alleviated the complaints for short periods. Bromocriptine failed to reduce the nipple discharge.

The patient's history of exposure to chemicals was substantiated by the elevated levels of PCBs in the samples and the microscopic appearance of the liver structure. The clinical picture, with the unremarkable results of the medical evaluation and the failure of several treatments, supported the tentative diagnosis of occupational chemical exposure, specifically to PCBS.

We decided to attempt a detoxification treatment reported to reduce body burdens of accumulated lipophilic chemicals.^{7,13}

Detoxification treatment

This treatment has been shown to mobilize and enhance the elimination from the body of stored lipophilic xenobiotics, including PCBs.^{7,13} It is a medically supervised regimen, pursued individually until a stable clinical improvement is achieved. It consists of several components: Daily aerobic exercise is followed by frequent periods of low-heat (60-80 °C) sauna. Niacin and polyunsaturated oil are administered to sustain the mobilization and elimination. Vitamins and minerals are supplemented and the daily liquid losses are substituted. Body weight is kept constant throughout the programme. A more detailed description is provided elsewhere.¹⁴

The patient was informed both verbally and in writing of the potential adverse effects from mobilization of chemicals. Her questions were answered regarding the detoxification procedure before obtaining an informed consent.

PCB analyses

Adipose tissue was obtained by aspiration biopsy from the gluteal region as described by Daum *et al.*¹⁵ five days before treatment, on day 19 of treatment, and 10 d after the conclusion of the programme.

Blood (20 cm³) was drawn after overnight fast and centrifuged. Serum was decanted for PCB determination at pretreatment, on days 2, 5, 10, 14, 19, and 23 of the treatment, and at 5 and 10 d after the conclusion of the programme.

Skin lipids were blotted by cigarette paper on the forehead. The procedure followed the protocol by Strauss and Pochi.¹⁶ All papers were from the same batch. Samples were taken from 5 to 8 p.m. on the days of blood sampling.

Nipple discharge was collected without expression into a precleaned vial at pretreatment and on day 5 of treatment.

All precleaned vials, cigarette papers, and the analyses of the samples for PCBs were provided by Pacific Toxicology Laboratories, California, USA. For analysis, PCBs were extracted from the tissue samples, deproteinized with hexane/ethyl ether, and separated from co-extracted biogenic material and organochlorine pesticides. Samples were analysed by the Varian 3500 high-resolution gas-chromatographer with electron capture detector and a 30 m non-polar bonded phase DB-1 capillary column. Confirmation of qualitative results was done by gas-chromatography/mass-spectrography. ¹⁷ Aroclor 1242, 1254, and 1260 in iso-octane served as external standards.^{18,19}

PCBs were reported as the sum total of up to 17 congeners. Peak assignments were made from Balischnitter and Zell.^{8,19} Their numbering follows that proposed by International Union for Pure and Applied Chemistry (IUPAC). No attempt was made to determine the levels of other industrial chemicals.

Statistical evaluation

The pre- and post-treatment levels of PCB congeners in tissue samples were evaluated with a linear regression technique. A probability level of $P < 0.05$ was considered to be statistically

significant. 20 The evaluations were performed by 'Statgraphics V 2.6' statistical graphics program from STSC Inc., Rockville, MD.

Results

Clinical manifestations

The treatment lasted for 23 consecutive days, until the complaints reported by the patient were judged to convey a clinically stable remission. The symptoms reported in the medical history (above) manifested exacerbations of fluctuating severity during the treatment programme. The flare-ups subsided within 1-2 d, some remittently, others permanently. A persistent sense of general well-being was attained during the last week of the programme. No new or previously unreported symptoms occurred during the treatment.

The nipple discharge cleared from a bluish green colour to become translucent, progressively decreased in quantity and ceased on day 15 of treatment. Muscular pains and weakness subsided at mid-treatment. During the last week of the programme, headaches, sinusitis, bursts of limb pains, the joint aches and the swellings stopped. Abdominal complaints subdued to a mild discomfort, tenderness was not evoked on pressure, and the liver span was 12 cm below the right costal margin. The skin appeared softer, without new chloracne eruptions, and exposure to sun did not elicit signs of sensitivity. The hyperpigmentation of the eyelids remained unchanged as was the loss of sense of touch. The sleeping pattern was reduced from 16 to 12 h d⁻¹ without lassitude upon arousal.

No adverse side-effects were noted due to the treatment. The patient fared well at a follow-up examination 6 months after treatment completion. She declined a liver biopsy and did not report for subsequent medical evaluations.

Laboratory values

The values of the repeated biochemical analyses were in normal ranges. The post-treatment chromosome study revealed a reduction of the number of isochromatid and chromatid breaks and gaps to 10% in 200 examined lymphocytes.

PCB levels

Prior to treatment, PCB levels were 102 mg kg in adipose tissue, 512 [tg l-1 in serum and 712 [tg l-1 in the nipple discharge (Figures 2a-c). The initial amount of skin lipids was 3.9 Mg 10 CM⁻² 3 h⁻¹ with a PCB content of 66.3 mg kg⁻¹ (Figure 2d).

The PCB content of the nipple discharge on day 5 of treatment was 289.1 [µg l-1 (Figure 2c). The fluctuations of PCBs in serum observed during the treatment (Figure 2b), were not found to parallel the changes in symptom severity. The quantity of skin lipids and their PCB contents also varied considerably during the programme. Compared to the initial levels, both the quantity of skin lipids and their PCB content collected at day 14 of treatment were doubled (Figure 2d).

Ten days after the conclusion of the programme, PCB levels in adipose tissue were 37.4 mg kg a reduction of 63.3% (Figure 2a). At this time, the PCB content was 261 µg l⁻¹ in serum and 44.3 mg kg⁻¹ in skin lipids, a 49 and 33.2% reduction, respectively (Figures 2b,d).

PCB congener analysis

Seventeen congeners were monitored in the samples. They are listed in Table 2, ordered according to their respective retention times. Relative amounts of these congeners were comparable in the various samples. The highest amounts were derived from congeners # 31/28, 74, 66 and 60. Three congeners, # 4, 16, and 49, were not detected in all samples (Figure 3). Major contributors to the total PCB concentration were congeners nominally substituted at 4; 2,4; 2,5; or 2,4,5 positions. Congener # 153,

with a 2,4,5 substitution pattern, seems exceptional as it is not a substantial proportion of Aroclor 1242 or Aroclor 1254 but was relatively high in adipose tissue.

Linear regression analysis of the post-treatment PCB congener levels on the pretreatment values revealed a linear correlation, statistically significant ($P < 0.05$), for all samples. The correlation coefficients were ($r = 0.95$) for adipose tissue, ($r = 0.99$) for serum, and ($r = 0.99$) for skin lipids.

Figure 2 Total PCB levels. Arrows mark first and last days of treatment. \wedge = PCB concentration in (a) adipose tissue, (b) serum, (c) nipple discharge, and (d) skin lipids. \diamond = Quantity of skin lipids.

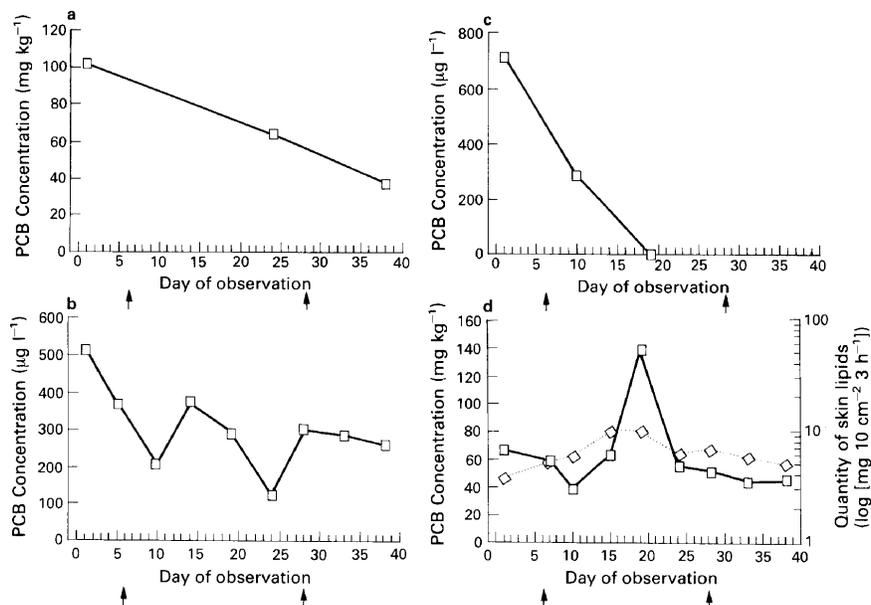


Table 2. Chemical structure of monitored PCB congeners.

Chemical structure	IUPAC ¹ No.	Remarks
2,2'	4	Initially in nipple discharge
2,3,2'	16	Small amounts in nipple discharge; appeared in skin lipids after treatment day 14
2,5,4'/2,4,4'	31/28	
2,5,2',5'	52	
2,4,2',5'	49	Not present in nipple discharge
2,4,2',4'	47	
2,3,2',5'	44	
2,3,4,2'/2,3,6,4'	41/64	
2,4,5,4'	74	
2,4,3'4'	66	
2,3,4,4'	60	
2,4,5,2',5'	101	
2,4,5,2',4'	99	
2,4,5,3',4'	118	
2,4,5,2',4',5'	153	Higher levels in adipose tissue; insignificant constituent of Aroclor 1242, 1254
2,3,4,2',4',5'	138	
2,3,4,5,2'4'5'	180	

¹ IUPAC - International Union for Pure and Applied Chemistry.

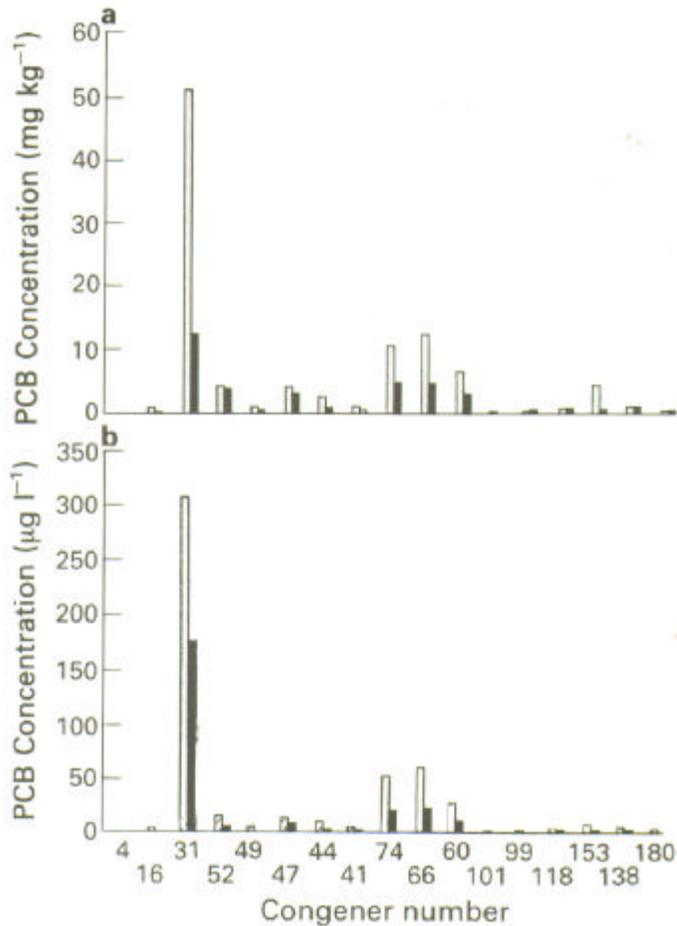


Figure 3 PCB congener profiles. Congeners listed in order of elution (TUPAC numbering as in Table 2. 31 = 31/28 and 41 = 41/64.) Concentration of congeners at pre- (1-1) and post-treatment (0) for (a) adipose and (b) serum.

Discussion

We present the case of a female patient occupationally exposed to several chemicals, where a clinical improvement and a reduction of accumulated PCBs was attained with a detoxification treatment.

High PCB levels in the samples of this patient aligned with her occupational exposure. However, polychlorinated biphenyls probably were not the only elements evoking the clinical picture. Exposure to various chemicals was known to have occurred and the complaints presented most likely indicate a combined influence of several chemicals. In this setting, PCBs and TCE may be assumed to be the major sources of exposure.

Occupational exposure to TCE has been related to chronic neurological damage, liver

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dysfunction and dermatitis. 2

PCBs and their impurities have been implicated in producing a peculiar toxicity syndrome which includes hepatotoxicity with histopathologic alterations, abdominal pains, chloracne, hyperkeratosis, intermittent joint pains, lassitude and oedema. 4,24-26 Aromatic chlorinated hydrocarbons have been associated with galactorrhoea, possibly due to local effects or to a metabolic

pathway common to prolactin and steroids.²⁷ Changes in thyroid function could be anticipated in humans as animal studies have shown that polyhalogenated hydrocarbons compete with thyroxine (T₄) for a common carrier.^{28,29} Finally,

several forms of DNA damage have been described in patients exposed to polychlorinated aromatic hydrocarbons.^{30,31}

All of the symptoms presented by the patient followed occupational exposure and deteriorated with the duration of employment. Their relation to chemical exposure appeared strengthened by the elevated PCB levels, which are among the highest so far reported⁴ and by being comparable to some of the symptoms in similarly exposed workers.^{27,29,32} Unremarkable results of the diagnostic procedures and the unresponsiveness to symptomatic and surgical treatments sustained the clinical conclusions. High levels of PCBs in the samples prior to treatment suggest, further, an ongoing source of exposure.³³

A search of the literature disclosed few attempts to eliminate accumulated PCBs in humans. One employed starvation which apparently reduced the clinical complaints, but PCB serum levels at post- were higher than at pre-treatment. PCB content of adipose tissue was not monitored in that study.³⁴ Cholestyramine, an anion exchange resin, was reported successful in pesticide poisoning,³⁵ while activated charcoal³⁶ and ingestion of non-absorbable compounds such as paraffin oil³⁷ or cauliflower³⁸ did not appear to reduce the body burdens of polyhalogenated aromatic hydrocarbons in animals. We chose the detoxification treatment developed by Hubbard because the reports of reduction of PCBs and other lipophilic organo-chloride compounds seemed applicable to our case.^{7, 10-13}

Our patient had frequent chloracne eruptions. Chloracne is a very persistent skin disease. It may be sustained by the chloracne-producing chemicals (mainly chlorodiphenyls, chlorodiphenyloxides, and chlorinated naphthalenes) which have been absorbed and stored in the body, particularly the adipose tissue. In patients with chloracne, offending polycyclic polychlorinated compounds may be detected in adipose tissue and also in sebum of the skin.³⁹ We decided to follow PCB levels in skin lipids in order to evaluate this alternative route of elimination.

Skin lipids on the forehead consist predominantly of sebum.⁴⁰ Our patient's sebum quantity at pretreatment was higher than usual for her sex and age group; in agreement with seborrhoea with acne.⁴¹ Sebum quantity increases with a rise of body temperature.⁴² This aligns with the initial increments observed in our case. A late peak of almost three times the initial volume of skin lipids occurred the second week of the programme. This may be, in part, related to the rate of sebum production by sebaceous glands as it is known that the rate of sebaceous gland turnover is on the order of several days.^{43, 44}

Under basal steady-state conditions, the skin surface has been found to contain only traces of PCBs.^{45,46} The elevated levels of PCBs found in the skin lipids of our patient contrast those findings (Figure 2d). That the PCBs found in skin lipids represent endogenous compounds is supported by the presence of the same PCB congeners in both serum and skin lipids. Thus the PCBs in skin lipids appear to exemplify excretion of endogenous chemicals representative of the body burden.⁴⁷

The nipple discharge of this patient may, of course, be regarded as an unusual elimination route. Insufficient data, however, preclude conclusions regarding this symptom. This discharge ceased early in the programme - a goal not achieved with the usual medical treatment.

Clinical problems of the patient were attenuated or alleviated during treatment. The persisting neurological symptoms may indicate irreversible damage, though neurological signs were difficult to quantify. Given the excessive body burdens in our patient, the remaining amounts may produce further clinical consequences requiring a repetitive treatment. Overall, however, the attained reduction of PCBs in adipose tissue, serum and in the nipple discharge appear to validate the effectiveness of the method. The quiescence of the disabling and discomforting symptoms, most notably the nipple discharge and the attacks of abdominal pains, corroborate the clinical value of this procedure.

Prior studies have described this method of detoxification as safe and effective, with results acquired within an acceptable time frame. Our results extend these findings to a case involving very high PCB

levels and a history of exposure to other lipophilic xenobiotics. Although further studies on mechanisms of elimination of particular chemicals are warranted, we believe this method may be considered as a treatment option for management of patients with recurring symptoms following exposure to persistent lipophilic chemicals.

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