Effect of human PCB exposure on lymphocyte function

U. Rohr, N. Rothe, W. König & F. Selenka

Institut für Hygiene und Institut für Medizinische Mikrobiologie, Ruhr-Universität Bochum, Universitäts-str. 150, 4630 Bochum, Federal Republic of Germany

Abstract

Blood samples of occupationally PCB exposed persons (n=16) and controls (n=23) were tested for PCB content and for phytohemagglutinin induced lymphocyte transformation. A blood burden with lower chlorinated PCB's (28 and 31) was found in the exposed population. PCB 28 and 31 blood concentrations of the controls (mean 50.9 ng/l) and exposed (mean 2383 ng/l) were significantly different. Lymphocyte mitogenic response showed a marked depression in the PCB exposed group. Stimulation indices ranged from 1.7 to 30.6 (mean 15.3) in the PCB exposed group, while the controls showed 1.6 to 101 (mean 33.9). Statistically the difference was not significant (p=0.0617), but there is further strong evidence of PCB induced depression of lymphocyte function. This is strengthened by the fact that correlation between PCB blood levels and lymphocyte proliferative response calculated for all samples reveals a negative trend (r=0.293).

Introduction

An important aspect of PCB toxicity is the immune suppressive effect which has been demonstrated in numerous experimental animal studies (e. g. KOLLER, 1979, SILKWORTH & LOOSE, 1981, EXON et al., 1987). The evidence concerning human immunotoxicity is still equivocal (CHANG et al., 1981, LAWTON et al., 1985, STEHR-GREEN et al., 1986). The approach of the present pilot project was to study a possible correlation between blood burden PCB levels and alterations in the lymphocyte function. In this pilot project we studied people with a high occupational exposure to PCB's, which were compared to a normal unexposed population. This is because for the investigation of the immune toxic effects of PCB's in the small dose ranges relevant to unexposed people, larger collections of samples would be necessary.

Methods

Subject population
In 1988 two groups of subjects resident in Northrhine-Westfalia, Germany were examined: 1) 16 persons with long-term occupational exposure to machine and hydraulic oils, 2) 23 persons without occupational exposure to PCB. All study subjects were interviewed to obtain data on their state of health, past medical history, sociodemographic characteristics, alkohol consumption, cigarette consumption and drug treatment. Analysis of anamnese data revealed no statistically significant differences between the exposed and nonexposed population.

Blood PCB determinations
PCB extraction from 10 ml heparinized blood was carried out by Extrelut column elution with 100 ml hexane followed by a silicagel cleanup with 12 ml hexane. PCB components were quantitated as lower chlorinated biphenyls (Ballschmiter-No. 28 and

31) and higher chlorinated biphenyls (Ballschmiter-No. 52, 101, 138, 153, 180) using an electron capture gas chromatographic procedure.

Lymphocyte transformation
Mononuclear cells were obtained from heparinized blood through a Ficoll-isopaque gradient and resuspended in RPMI at $2x10^6$ cells/ml. 100 µl of the suspension was activated with 10 µg/ml phytohemagglutinin (PHA). After incubation for 72 h, cells were pulse-labelled for 4 h with ^3H-thymidine (0.2 µCi/well). The amount of ^3H-thymidine incorporation (cpm) was determined in a liquid scintillation spectrometer. Lymphocyte responses were expressed as stimulation index (=SI=cpm of PHA activated cells/cpm of cells without activation).

Results

In the investigations shown here, it can be seen that in the exposed group a highly significant contamination by the low chlorinated PCB 28 an 31 had taken place. However, the highly chlorinated PCB 101, 138 and 153 show only a slight increase, where PCB 52 and 180 show no difference between the two groups. The range of the PCB 28 and 31 concentrations were between 10 and 130 ng/l for the control group and 300-6800 for the exposed group (table 1). The difference in the averages 50.9 ng/l (median 40.0) and 2383 ng/l (median 1650) of the two groups is highly significant (p=0.000).

To test the PCB effect on the immunosystem the measurement of the polyclonal lymphocyte proliferation was chosen for this study. In contrast to the measurement of the phenotype characteristics, the measurement of the degree of possible lymphocyte stimulation yields information on the reactivity of immuno-competent cells and therefore also on possible loss of function of the immune system. The individual results of the lymphocyte proliferation tests are reproduced in figure 1. The control group has an mean SI of 33.9 (median 19.5) whereas the exposed group desplays a clearly lower mean SI of 15.3 (median 14.0). Figure 1 shows a mirror plot in increasing order SI value of the PCB 28 and 31 blood concentrations. There is an obvious reduction in the ability to stimulate lymphocytes in the PCB exposed group compared to the control. The mean lies, with p=0.0617, on the margin of significance (computed with logarithmic data from the 2-sample student t-test). The correlation between the stimulation index and PCB 28 and 31 blood concentration over the complete population is r=-0.293, a negative correlation tendency.

Conclusion

The job of a pilot study is to reveal obvious points and possile correlations. The results of the present study provides clear evidence that a low chlorinated biphenyl burden suppresses human lymphocyte function. This should motivate a thorough immunotoxicological investigation of a large sample population.

	CONTROLS		EXPOSED	
peak*	mean	range	mean	range
28+31	50.9	<10- 130	2383.1	300-6800
52	55.3	<10- 200	65.0	<10- 140
101	17.6	<3- 40	73.1	20- 200
138	829.6	350-1800	1188.1	460-2700
153	629.6	290-1700	1155.0	430-2800
180	416.5	190- 980	480.0	230-1100

Table 1. **Blood PCB levels (ng/l) of occupationally PCB exposed (n=16) and nonexposed (n=23) persons.**
*** Ballschmiter nomenclature**

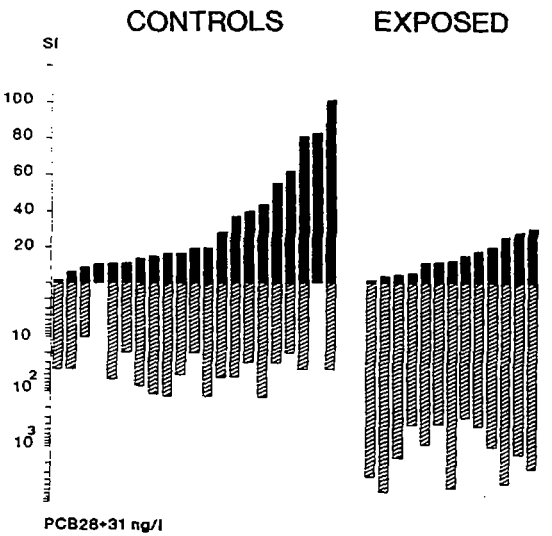

Figure 1. **Single PCB 28 and 31 blood analyses (ng/l) as well as the lymphocyte proliferation tests (SI) of exposed and control populations.**

Literature

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