PCB - effects on mammals.

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Already in 1899 Herxheimer described a condition that he called chloracne, which was caused by chlorinated biphenyls or chlorinated naphtalenes. Chloracne is a type of follicular pyodermatitis, e g pyongenic inflammation in the sebaceous glands of the skin. Clinical experience indicates that the capacity to produce this condition increases with chlorination of the biphenyls. Around 10 cases of fatal intoxication with chlorinated biphenyls or naphtalenes have since been described (ref. 2, 3, 4). They all showed liver atrophy and necroses. Histological examination revealed fatty degeneration, necroses and cirrhosis. All cases involved persons who handled or were exposed to these compounds in their occupations.

Animal experimentation has confirmed that chlorinated biphenyls and naphtalenes can produce liver damage of this kind. Chlorinated biphenyls and naphtalenes can be absorbed by the skin, by inhalation or by ingestion. In tables 1-3 Dr. Ulf Ahlborg (ref. 5) has summarized the published toxicological investigations in mammals involving chlorinated biphenyls and naphtalenes. The results shown on the tables indicate that the toxicity of these compounds is proportional to their degree of chlorination.

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A comparison between the chlorinated naphtalenes and the biphenyls based on existing studies indicates that the biphenyls are more toxic. However, it must be emphasized that all the experiments done have been screening experiments involving technical preparations with an undefined purity, - usually mixtures of compounds having different degrees of chlorination - and that these investigations have generally focused on liver damage. Investigations of the effect on the brain for example seem to be lacking. So, in general, the present material

permits only very limited conclusions.

It has been shown that the chlorinated biphenyls stimulate the liver microsomes as revealed by an increased metabolisation of oestrediols in the pigeon liver (ref. 9). The biphenyls seem to be about 5 times more potent in this respect than either DDT or dieldrin (ref. 9). Drinker (ref. 4) has observed a synergistic effect on the liver of carbon tetra-chloride and chlorinated biphenyls - i.e. animals exposed to chlorinated biphenyls show severe liver injury with considerable lower doses of carbon tetra-chloride.

In this connection it could be mentioned that a fatal case of biphenyl intoxication recently occurred in Finland (ref. 10). A 31-year-old man was working in an industry that used biphenyl - not chlorinated - for impregnation. The exposure level was around 100 mg/m^3, 10 times the MAC. He had been working in this industry for 11 years and suddenly developed liver insufficiency which appeared histologically as necroses, atrophy and cirrhosis. A general atrophy of the brain cortex was also found. Medical examination of the about 120 persons working in this industry revealed 3 additional cases with liver injury (biopsy) and 2 cases with pathological EEg and impaired periferal nerve function.

In order to make a toxicological evaluation of the risks involved in exposure to chlorinated biphenyls, it is necessary to have knowledge about 1) the distribution of these compounds in the body, 2) their metabolism, retention and elimination in different organs and 3) the toxicity of these substances for different cell systems and their metabolites.

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With respect to the distribution, we know that there is a tendency to accumulate in body fat and in the lipid-containing tissues of the brain. That is about all we know. Our knowledge about the metabolism of these compounds is minute. From a theoretical point of view and on the basis of existing experimental data, there is reason to believe that the compounds with a low degree of chlorination should be more easily metabolised and broken down in the body than those with a high degree of chlorination. The turnover of the discrete compounds and their metabolism in different kinds of organs is unknown. The toxicity to different cell systems is also unknown

except for the fact that liver cells can be interfered with at those concentration levels which occur in man due to industrial exposure. Liver injury also occurs early in animal intoxication experiments. However, quantitative data regarding the concentration in the liver cells at which disturbances occur is lacking at present.

Conclusion.

There is a strong suspicion that chlorinated biphenyls can be retained and accumulated in the body with chronic exposure. Present data do not permit evaluation of the risk of organ damage in the body at different doses of defined chlorinated biphenyls. There is a strong need for studies of the metabolism of chlorinated biphenyls in the body, as well as the mechanism of the toxic effect due to these substances.

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TABLE I

DERMAL TOXICITY OF CHLORINATED BIPHENYLS

Chlorine %	Chlorine atoms	Animal	Dose	Effect
42	3	Guinea pig	34.5 mg/daily over 11 days	All animals died within 21 days. Liver damage (Miller 1944)
42	3	Rat	34.5 mg/daily over 25 days	All survived. Minor liver change Skin affected (Miller 1944)
42	3	Rabbit	86 mg/day with 2-day intervals for 7 applications and 172 mg/day with 2-day intervals for 8 applications.	All died betwee 17 and 98 days. Liver damages more pronounced than ir rat or guinea pig (Miller 1944)

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Table 2

ORAL TOXICITY OF CHLORINATED BIPHENYLS

Chlorine		Animal	Dose	Effect
%	atoms			
42	3	Guinea pig	69 mg/animal 2 doses 1 week apart	Death in 11-29 days. Liver damage (Miller 1944)
42	3	Rat	139 mg/animal 25 daily doses	All animals survived Liver damages (Miller 1944)
65	7	Rat	50 mg/animal every second day	50 % dead [redacted] 35 days Severe liver damages (Bennett 1938

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Table 3

VAPOR EXPOSURE TOXICITY OF CHLORINATED BIPHENYLS

Chlorine %	Chlorine atoms	Concentration mg/m^3	Concentration ppm	Daily exposure time hours	Exposure number	Exposure period days	Symptoms
42	3	8.6	830	7	17	24	No effect o[illegible] rabbits, rats & mice. Poor gro[illegible] in guinea pigs (Treon 1956)
42	3	6.83	660	7	84	122	No effect on[illegible] mals as above (Treon 1956)
54.3	5	5.4	410	7	83	121	Liver cell inj[illegible] Increased live[illegible] weight in the [illegible] (Treon 1956
54.3	5	1.5	115	7	150	213	Histological changes in the liver in the [illegible] (Treon 1956)
45	7	0.57 0.93		16 8		37-134 42-143	Advancing liver damage (Bennet 1938)

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