Increased liver enzyme values in workers exposed to polychlorinated naphthalenes

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Object of the study:
Polychlorinated naphthalenes (PCNs), biphenyls (PCBs), dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) are classes of compounds causing very similar clinical and toxicological symptoms[1]. In a plant 16 workers had been exposed to fumes of waxes (Beranit^{R}) that contained polychlorinated naphthalenes. The waxes were used for checking casting molds. The exposure lasted from 1958 to 1989 in most cases and it was the main exposure to hazardous materials for the 16 workers. Over 90 % of the wax consisted of polychlorinated naphthalenes (Nibren^{R} wax) with varying composition. In some cases the polychlorinated naphthalenes contained only 5 % pentachlorinated naphthalenes, in other cases they consisted of 40 % pentachlorinated and 35 % hexachlorinated naphthalenes. The wax (1 to 10 kg) was heated in a small pot at the workplace (to about 130-150°C) and afterwards casted into the molds; there was no protection for the workers at the workplace.
The factory physician detected elevated liver enzyme values in some of these workers and informed the accident insurance company. Our institute had to provide expertises for 8 cases in order to decide whether the insurance company has to give compensation. One of the 8 patients had developed tumors of the bladder and kidney. Two other workers out of the group (of 16 workers) developed tumors (larynx; stomach or colon).

Approach and methods used:
6 of the 8 workers could be examined clinically. The examination included electrocardiography, X-ray image of the chest and laboratory investigations (blood: liver enzymes, hematological and renal values, electrolytes, protein electrophoresis, lipids, lymphocyte subpopulations - CD4, CD8, CD3, CD19, CD3-/CD16+/CD56+, CD3+/CD56-, DR3+/HLA-DR+ - , hepatitis markers; porphyrins in urine). One worker could not be examined medically because of severe diseases

(diabetes mellitus with blindness and apoplectic insult); the other worker died of tumors of the bladder and kidney.
We tried to get additional information about the other members of the group by contacting them and their doctors.
At the time of the study the original workplace no longer existed.
Therefore a laboratory investigation was initiated in order to investigate possible emissions of halogenated compounds in case the wax was heated to temperatures slightly above its melting point (i.e. to 130°C). Used wax material was melted in a small quarz vessel positioned in a quartz tube that was gently fluxed with synthetic air (test procedure based on DIN method 53 436 01/02). The test parameters were: temperature of 130°C for 8 hours, mean air flow velocity of 23.5 cm/min, mean air exchange rate in the tube of 10.8/h, surface of the melted wax of 24.1 cm^2. The emission phase was analyzed for PCNs, PCBs, PCDDs and PCDFs (GC/MS analytical method).

Results:
The workers were all male and born between 1911 and 1949. The gamma-glutamyl transpeptidase (GGT) values were increased (maximum 190 U/l) in 6 cases of the 16 workers and in 4 of the 8 about whom we had to prepare expertises. In one patient the bilirubin (1,5 mg/dl) and glutamic-oxaloacetic transaminase (GOT) and in two cases the glutamic-pyruvic transaminase (GPT) values were increased. In two cases histologically fatty livers could be found. The markers for hepatitis B were examined in 6 cases and were found negative. There were no pathologic values for lymphocyte subpopulations beside a slight decrease in the relative number of CD3-lymphocytes in two patients (58 % and 54 %; normal values 61-85 %). No dermal disease could be detected.
The melting point of the wax was between the melting points of the chloronaphthalenes Halowax 1009 (102°C) and 1014 (137°C)[2]. The emission rates derived from the detected amounts of emitted halogenated compounds under the experimental conditions mentioned above were:

Class of compound	*homologues*	*emission rate*
PCNs	Mono- to HexaCNs	4.6 mg/h x cm^2
PCBs	Tri- to HexaCBs	7.8 µg/h x cm^2
PCDFs	Tetra- to OctaCDFs	27.3 pg/h x cm^2
PCDDs	Tetra- to OctaCDDs	1.3 pg/h x cm^2
PCDF/Ds	Tetra- to OctaCDF/Ds	0.7 pg ITE^{17}/h x cm^2

Discussion and conclusions:
Irritations of the eyes, fatigue, headaches, abdominal pain, weight loss, insomnia, alopecia, disturbances of taste, dizziness, anemia, hematuria and impotentia have been detected in persons exposed to polychlorinated naphthalenes at their workplace[1,3-5]. The main symptom is chloracne[1,6-8]; in many cases disturbances of liver function and acute yellow liver distrophies have been described[1,3-5,9-14]. Liver diseases may occur even if no chloracne can be detected[4,5]. The toxicity is especially high for pentachlorinated and higher chlorinated naphthalenes. In animal

experiences the metabolism of these is limited. Most of the cases of chloracne and liver disease seem to be caused by penta- and hexachlorinated naphthalenes[1,4,5,15,16].

In the group of 16 workers exposed to chlorinated naphthalenes at their workplace over a period of about 30 years no chloracne occured. 6 of the 16 workers showed increased liver enzyme values, especially increased gamma-glutamyl transpeptidase (GGT) values. Fatty livers could be detected histologically in two patients. Other than occupational reasons for the liver diseases could not be evaluated (e.g. chronic hepatitis B, alcohol abuse). Therefore, we think that the disturbed liver functions in these 6 patients may be a result of the exposure to polychlorinated naphthalenes at the workplace.

This conclusion is supported by an estimation of the potential exposure to polychlorinated naphthalenes, biphenyls, dibenzodioxins and dibenzofurans: for the estimation a working room volume of 100 m^3, a melting temperature of 130°C, a melting pot surface of 314 cm^2 (diameter 20 cm) and no ventilation were taken as a basis. Using the emission rated derived from the laboratory investigation the following mean air concentrations after different emission times were calculated:

Time of emission (h)	*0.5*	*1.0*
Concentration of PCNs (mg/m^3)	7.25	14.5
Concentration of TriCNs (mg/m^3)	2.42	4.9
Concentration of PentaCNs (mg/m^3)	0.48	1.0
Concentration of PCBs (mg/m^3)	0.012	0.025
Concentration of PCDF/Ds (pg ITE^{17}/m^3)	1.1	2.2

The MAK values (maximum concentration at the workplace) are 5.0 mg/m^3 for TriCNs, 0.5 mg/m^3 for PentaCNs, 1.0 mg/m^3 for PCBs (42 % chloro content) and 0.5 mg/m^3 for PCBs (54 % chloro content)[18]. Typical concentrations of PCDF/Ds in the outdoor air are in the range of 0.01 to 0.1 pg ITE^{17}/m^3. Thus for our model case the calculated exposure values for polychlorinated biphenyls are below the MAK values, whereas the calculated air concentrations of some polychlorinated naphthalenes are in the range of the MAK values or higher even after short exposures which may have been exceeded under real working conditions. The calculated exposures to polychlorinated dibenzodioxins and dibenzofurans are above outdoor air concentrations, but below the NOELs in animal experiments[19]. Therefore the polychlorinated naphthalenes are supposed to be the most relevant emissions and the exposure to this class of compounds the main reason for the liver dysfunctions discovered in the workers exposed.

In conclusion, our study supports reports that polychlorinated naphthalenes can produce liver diseases, especially liver dysfunction and fatty livers. The development of liver diseases is not necessarily associated with the occurence of chloracne. Whether the exposure to polychlorinated naphthalenes may have a causative role in the development of the cancers reported in our group of workers needs further investigation.

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