Effects of 3,4,5,3',4',5'-hexachlorobiphenyl alone and in combination with 3,4,3',4'-tetrachlorobiphenyl on the reproduction capacity of rats

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In 1989 a research project was started in the Netherlands on the long-term effects of perinatal exposure to PCB's and/or dioxins. The research project included both human and animal studies. The present abstract concerns the animal study.

Pregnant female rats were treated with single PCB congener after which the effects on behavior and reproduction capacity of the offspring were studied. The following PCB's were selected: PCB 169: 3,4,5,3',4',5' hexachlorobiphenyl (HCB) and PCB 77: 3,4,3',4'-tetrachlorobiphenyl (TCB). HCB was administered at 3 different dose levels, TCB at 1 dose level in combination with the middle dose level HCB. Both PCB's are highly toxic, but whereas HCB is very persistent, TCB has a relatively short half-life.

The study was carried out with adult Wistar W.U. derived SPF-bred albino rats, obtained from Charles River Wiga GmbH, Sulzfeld, Germany. Two females were placed with each male, and successful copulation was detected by examination of vaginal smears. Females with a sperm-positive smear (gestation day 0) were given test substance or control vehicle (corn-oil) by gavage on day 1, or day 2 through 18 of gestation. Thirty-five mated female rats were allotted to each of 5 dose groups.

Dose group	test substance	dose level (mg/kg bw)
A	(corn oil)[1]	
B	HCB[1]	0.2
C	HCB[1]	0.6
D	HCB[1]	1.8
E	HCB[1] +	0.6 +
	TCB[2]	17.0

[1]: one single dose on day 1 of gestation
[2]: 1 mg/kg TCB was administered daily between gestation day 2 and 18.

During gestation, body weight and food consumption of the females were recorded weekly. After parturition, body weights and food consumption of both parents and offspring were recorded weekly. Among the other parameters recorded were the moment of testes descent and vaginal opening.

F0-generation reproduction experiment

Body weights and food consumption during gestation of the F0-females were lower in the D and E group than in the control and low dose groups. During week 1 of lactation only the body weights of the females in group E were lower, otherwise they were similar.

Mean duration of gestation was about half a day to nearly 1 day longer in F0- females of the D and E group, whereas they delivered per litter about 2 pups less than in the control group. Pup mortality just after birth was rather high in the dose groups. Control group: 0%, B: 0.3%, C: 7.7%, D: 1.1% and E: 3.7%.

Body weights of the F0-offspring in group D and E was low when compared to the controls both during lactation and after weaning. Food consumption was similar in all groups.

General health of the F0-offspring in the D and E group was not very good, in many cases emaciation and/or a crouched posture was observed.

The physical landmarks showed that the pups in all groups developed at the same rate. Vaginal opening occurred at the normal moment, even in the higher dose groups, but due to vaginal constriction and/or abscesses, copulation was not always possible.

F1-generation reproduction experiments

In the group of pups selected for the F1-reproduction studies, sibling relations were avoided.

For the first F1-reproduction experiment 25 young adult males and 25 young adult females (age: 13-20 w) were selected per group. Males and females were mated within the same dose group. Mating success of the F1-animals was relatively low for reasons unknown (mating index control group: 60%, B and C: 68%), but extremely low in the D and E group (24% and 28%, respectively). The number of pregnant F1-females was normal in the control and lower dose groups (fecundity index control group: 73%, B: 88%, C: 65%), but once again low in the D and E group (33% and 14%, respectively), resulting in 2 pregnant females in the D group, and 1 pregnant female in the E group. As in the F0-generation, duration of gestation was longer in the D and E group, but the difference with the control group did not reach the level of statistical significance.

The second F1-reproduction experiment was conducted with other F1-animals of the control, D and E group when they were about 1 year old. In this experiment, PCB- treated males were paired with untreated females of the same strain, and PCB-treated females were paired with untreated males of proven fertility of the same strain. Immediately after being placed together, male and female behavior was recorded on video during half an hour.
The animals were sacrificed at least six days after detection of a positive vaginal smear and the number of implantation sites in the uterus was counted.

Preliminary analysis of behavioral data suggests that sexual behavior might be disturbed, especially in males. Pregnancy rate was again very low in the D and E group: in the

experiment in which PCB-treated males were used, 75% of the control animals was pregnant, in the D group not one female, and in the E group 45%. In the experiment in which PCB-treated females were used 80% of the controls was pregnant, against not one female in either D and E group.

From the results described above it can be concluded that the PCB's used in this study, HCB and the combination HCB-TCB, if applied at a sufficiently high level, affect several aspects of sexual behavior and reproductive performance, resulting in a profound effect on the reproduction capacity of rats. It is interesting that the effects of a relatively non-toxic dose of HCB are enhanced to the extent for the highest dose of HCB by concommitant administration of TCB. An explanation for these additive or synergetic effects will have to await further studies.

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