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Project Summary

Effects of Post-Implantation Exposure to Selected Pesticides on Reproductivity in Rats

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The post-implantational effects of dinoseb, PCB's (Aroclor 1254), rotenone and zineb on reproductive systems were examined using decidualized pseudopregnant rat as a model. Uterine protein, uterine glycogen, uterine water, and ovarian protein were studied in day-10 decidualized pseudopregnant rats fed the toxicants from days 6 through 9 of pseudopregnancy. Dinoseb reduced uterine protein and uterine glycogen in rats fed 25 ppm and higher concentrations. Uterine water and uterine weight were reduced at the highest dosage of 750 ppm. Ovarian protein was diminished at 150 ppm and higher concentrations. PCB's lowered uterine glycogen, but uterine protein content was not reduced in a dose-related manner. Ovarian protein content was diminished at 50 ppm and higher concentrations. Uterine weight and uterine water were not changed in rats fed up to 1000 ppm of the PCB's. Rotenone reduced uterine protein in rats fed 200 ppm and higher concentrations. Uterine glycogen was diminished at 10 ppm and higher concentrations. In day-16 pregnant rats fed rotenone (100, 200, 400, and 600 ppms) from days 6-16 of pregnancy, placental protein, placental glycogen, ovarian protein, and maternal body weight were reduced. Additionally, these dosing regimens reduced fetal survival rate. Fetal weight of fetus delivered from rotenone-fed dams was not affected. The decidualized pseudopregnant uterine, and placental functions and fetal survival rate of rats were not affected by zineb up to 2500 ppm.

This Project Summary was developed by EPA's Health Effects Research Laboratory, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

The talidomide episode caused great public concern and left no doubt on the necessity of testing possible teratogenic and fetotoxic effects of compounds that may be encountered by pregnant women.

Since the presence of many classes of pesticides in the environment offers numerous opportunities for these toxicants to enter the physiological systems of various species of animals including man, there has been an increased interest in studying the teratogenic effects of certain pesticides on mammalian reproduction.

Pesticides such as DDT have been shown to reduce estradiol titer in blood of ringdoves, *Streptopelia risoria*. On

the basis of experiments, the eggshell thinning action of chlorinated hydrocarbons has been attributed to direct estrogenic action of DDT and its analogs (PCB's).

Because pseudopregnant and pregnant rats have identical mechanisms for controlling the onset and loss of uterine sensitivity, the deciduomal response in decidualized pseudopregnant rats was used to study possible reproductive disruption as caused by various pesticides in pregnant uteri.

Results and Discussion

Uterine weight and uterine water content of decidualized pseudopregnant rats exposed to dinoseb were only reduced at the highest dosage of 750 ppm. In comparison with the control, uterine protein and uterine glycogen contents were reduced at 25 ppm and higher concentrations. Ovarian protein content of the rats exposed to dinoseb for 4 days was not affected up to 500 ppm. The difference in susceptibility to dinoseb, between uterine protein content and ovarian protein content might be attributed to a differential distribution of dinoseb within the reproductive system. In pregnant rats, exposed to dinoseb for 10 days, ovarian protein content was reduced at 200 ppm and higher concentrations.

Ovarian protein of the decidualized pseudopregnant (DCR PSPG) rats exposed to the PCB, Aroclor 1254, was reduced to 50 ppm and higher concentrations. Uterine protein content was reduced at 25 ppm and higher concentrations. This reduction was not dose-dependent, and the difference was attributed to abnormal control value. Uterine glycogen content of the rats was reduced at 150 ppm and higher concentrations. Uterine weight and uterine water content, regardless of the dose of the PCB's being tested, were not affected.

In DCR PSPG rats exposed to rotenone, uterine weight was reduced at 100 ppm and higher concentrations, but uterine water content was not affected. Ovarian protein content was not reduced up to 750 ppm. Uterine protein content was reduced at 200 ppm, in comparison with the control. Uterine glycogen content was decreased at 10 ppm and higher concentrations. Placental protein content and placental glycogen content of pregnant rats exposed to rotenone were reduced. Ovarian protein content of rats was diminished. Rotenone did not affect the developing embryos. Fetal survivial rate of the fetuses was decreased at 100 ppm and higher concentrations. Fetuses delivered from dams exposed to rotenone during the post-implantational stage of pregnancy did not exhibit any reduction in body weight. The levels of zineb tested in the intrauterine environment, i.e. uterine protein, uterine glycogen and uterine water contents of the rats, were not affected. Ovarian protein in both the pseudopregnant and pregnant rats exposed to zineb for 4 days and 10 days, respectively, was not affected. Placental protein was not affected by zineb. In comparison with the control, placental glycogen content was increased. This increase was not dose-dependent. Development of implantation sites in pregnant rats after 7 days of exposure to zineb was not affected. The fetal survival rate was not affected. Fetal weight was reduced but this decrease was not regarded to be compound-related since it was not dose-dependent.

Conclusions

Dinoseb, PCB's (Aroclor 1254), and rotenone are uterotoxic, causing disruption on the integrity of decidualized pseudopregnant uterus. Since the intrauterine environment is maintained by sex hormones, namely, estrogen and progesterone, anti-estrogenic, and anti-progrestogenic properties of these toxicants could be inferred.

Rotenone interferes with fetal development. Because development of the placenta corresponds with that of the fetus, any interference imposed on the placenta by rotenone may be viewed as essentially disruptive to the fetal development process. In addition, rotenone is fetotoxic. The fetotoxic potential of rotenone is designated by a decrease in fetal survival rate.

This study shows that zineb has low toxic effects on the maternal reproductive system and the fetus. This could be attributed to the fact that zineb does not accumulate to a large extent in mammalian tissues and could be metabolized readily.

Recommendation

Further studies on the toxicological effects of pesticides upon the reproductive system should be correlated with the adrenal functions.

Consideration should be given to dietary intake of the animal during any toxicological studies in reproduction.

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***August Curley** is the EPA Project Officer (see below).*
The complete report, entitled "Effects of Post-Implantation Exposure to Selected Pesticides on Reproductivity in Rats," (Order No. PB 81-213 209; Cost: $6.50, subject to change) will be available only from:
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