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ABSTRACT

Pure and Commercial samples of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) were tested on Swiss-Webster mice for: (1) interruption of the estrus cycle and (2) teratogenic effects. The estrus cycle of mice administered Commercial 2,4,5-T was interrupted in 42.9% of the animals and in 12.5% of the animals given Pure 2,4,5-T.

No fetal abnormalities were found in pregnant animals treated with Commercial or Pure 2,4,5-T. Fetal resorptions were found in both treatment groups. Treatment with Pure 2,4,5-T produced a significant decrease in viable fetal weight and increased fetal deaths.

INTRODUCTION

One of the most widely used herbicides is 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) which has been in use since 1945. Despite the fact that much information is available on its effects on plants and soil (Audus, 1964), toxicological studies in higher vertebrates were limited. The first study indicating 2,4,5-T had undesirable effects on higher animals was by Courtney et al. (1970) who later (1971) failed to confirm their previous results. Subsequent authors (Neubert and Dillmann, 1972; Bage, Cekanova and Larsson, 1973) also failed to produce consistent results in studies with this compound.

The purpose of the present study was to investigate the effect of 2,4,5-T on the estrus cycle of Swiss-Webster mice and the effect of the compound on pregnancy and fetal development.

MATERIALS AND METHODS

Male and female Swiss-Webster mice were used along with two preparations of 2,4,5-T: (1) a Dow sample of pure 2,4,5-T (containing 2,3,7,8-tetrachlorodibenzo-para-dioxin [dioxin] less than 0.004 ppm) and (2) a commercial preparation from Hercules Powder Company (with a dioxin level of 2.7 ppm).

The dosages to be used were determined by evaluating the LD_{50}. These were 16 mg/100 g body weight for Pure and 8 mg/100 g body weight for Commercial 2,4,5-T. All samples were suspended in solution and administered subcutaneously daily. Autopsies were performed on day 18 of pregnancy. Vaginal smears were taken and studied microscopically.

Mean values and standard deviations were calculated using standard methods.

RESULTS AND DISCUSSION

The results from the estrus study are in Table I which shows all animals were cycling prior to treatment and that there was no significant difference in the cycle lengths during treatment. However, 12.5% of the Pure group and 42.9% of the Commercial group had an interruption of the cycle during treatment. These data seem to suggest that high levels of Pure 2,4,5-T interrupts the estrus cycle, but does not stop it as prevalently as Commercial 2,4,5-T.

Since 2,4,5-T interrupted the estrus cycle of treated animals, it was necessary to determine whether the effects were permanent or transitory. The animals were, therefore, injected daily for 14 days and allowed to mate, and the period from the time of mating until impregnation was measured by examining the animals for vaginal plugs. Table I shows pure 2,4,5-T delayed impregnation for a longer period than commercial 2,4,5-T. However, neither compound prevented impregnation. Thus, the effects of the compounds appear to be transitory.

In another study, mice were impregnated and then treated daily from day 6 to day 15 of pregnancy. The data from the litters of these animals are shown in Table II. The treatment produced no difference from controls in the average number of fetuses per litter. However, the average number of viable fetuses per litter was reduced.

Fetuses undergoing resorption, regardless of the extent, were considered as resorption sites (RS). The number of RS produced with the commercial preparation was consistently greater than with the pure compound. Neubert and Dillmann (1972) suggested that dioxin and 2,4,5-T might synergistically increase fetal toxicity. Although there is no evidence either way in the present study, it is possible this is the explanation for the increased number of resorption sites in animals treated with Commercial 2,4,5-T.

The data on the weights of the fetuses compare favorably with previous studies (Courtney et al. 1971; Neubert and Dillmann, 1972; Bage, Cekanova, and Larsson, 1973). There was a decreased fetal and maternal weight in treatment groups with a much greater decrease in those animals administered Pure 2,4,5-T. However, the decrease in fetal weight may only be a reflection of the decreased maternal weight.

In contrast to the observations of Courtney et al. (1970, 1971), there were no indications of cleft palate or gastrointestinal hemorrhaging in the Swiss-Webster mice used in this study. There are, however, data (Highman et al., 1976) indicating there is a difference in response to 2,4,5-T depending upon the strain of mice. It is possible that the Swiss-Webster strain is relatively resistant to the toxic effects of 2,4,5-T.

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Table 1. Effects of 2,4,5-T on Estrus Cycles of Mice

	Control	Pure 2,4,5-T	Commercial 2,4,5-T
No. Animals	15	16	21
% Cycling:			
Before Treatment	100	100	100
During Treatment	100	87.5	52.3
Cycle Before Treatment	3.9 ± 0.2 days	4.1 ± 0.2 days	4.0 ± 0.2 days
Cycle During Treatment	4.2 ± 0.2 days	4.7 ± 0.2 days	4.3 ± 0.4 days
$\bar{X}$ Days of Treatment Until Cycle Interrupted		8.5	7.3 ± 1.0
$\bar{X}$ Days Until Pregnancy Following Completion of Treatment	9.3 ± 3.0	20.7 ± 7.0	11.1 ± 4.4

Data shown as $\bar{X}$ ± Standard Deviation

Table II. Effects of Maternal Treatment on Fetuses

	Control	Pure 2,4,5-T	Commercial 2,4,5-T
No. Animals	15	14	14
$\bar{X}$ Fetuses/Litter	8.2 ± 1.0	8.5 ± 0.8	9.6 ± 1.5
$\bar{X}$ Viable/Litter	6.9 ± 0.9	5.8 ± 0.6	5.6 ± 1.3
$\bar{X}$ RS/Litter	1.2 ± 0.4	2.2 ± 0.5	3.8 ± 1.5
$\bar{X}$ Maternal Wt. Gain (g)	14.1 ± 1.7	8.9 ± 1.6	8.1 ± 2.5
$\bar{X}$ Fetal Wt. (g)	1.25 ± 0.03	0.87 ± 0.03	1.01 ± 0.04
$\bar{X}$ Placenta Wt. (g)	0.13 ± 0.00	0.10 ± 0.00	0.11 ± 0.00

Data shown as $\bar{X}$ ± Standard Deviation