DATA EVALUATION RECORD

(1) CHEMICAL: Trichlorfon

(2) TYPE OF FORMULATION: Unspecified

(3) CITATION: Staszyc, J., and Kifer, E. 1974. [Studies on the effect of the phosphororganic preparation on the organism of pregnant rats, fetuses, and the cells in tissue culture.] Ann. Univ. Mariae Curie Sklodowska [Med.] 29:249-254 (Translated from Polish)

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(6) TOPIC: This study has information pertinent to discipline toxicology, topic biochemistry. It relates to none of the Proposed Guidelines data requirements.

(7) CONCLUSION: The effects of daily administration of trichlorfon to pregnant female rats were examined in fibroblast-type tissue cultures derived from the rats and their fetuses. Little, if any, effects of the compound were observed in growth rate of the cultures from the rats, and there were no consistent effects on the activity of acid phosphatase, succinate dehydrogenase, and lactate dehydrogenase.

Several effects were observed in cultures derived from fetuses, however, and include a decrease in culture growth rate, a decrease in acid phosphatase and succinate dehydrogenase activities, and an increase in lactate dehydrogenase. These observations suggest that trichlorfon can traverse the placental barrier and cause cytotoxic effects in the fetus.

These results, however, cannot be adequately evaluated because of the absence of detailed information in the manuscript.

CORE CLASSIFICATION: Not applicable

(8) MATERIALS AND METHODS:

Inbred white adult female rats weighing 120-180 g were used (strain and number unspecified). The females were mated with males (conditions unspecified) and resulting

pregnancies were determined by the presence of vaginal plugs. After the 2nd day of pregnancy, animals received via a sonda a daily aqueous 50 mg/kg dose of "pure" trichlorfon (Azota Co., Jaworzno). A similar number of undosed pregnant females served as the control group. Maintenance conditions for all animals were unspecified.

At 14 and 21 days of pregnancy, subcutaneous tissue cuttings were taken from the females and placed in Parker's culture medium 199 (supplemented with 10% calf's serum) in Legroux cylinders. At the same time, fetuses were removed, decapitated, and the skin was cultured following trypsinization. After two passages of the cells (3 days), the cultures were washed with Hank's solution and fixed to the slides in Baker's solution at 4°C. The slides were then stained histochemically for (1) acid phosphatase by the Gomori method, (2) succinate dehydrogenase by the Nachles method, and (3) lactate dehydrogenase by an unspecified method.

(9) REPORTED RESULTS:

(a) Culture growth. The cell morphology and growth rate of the subcutaneous tissue cultures derived from pregnant female rats were monitored. No differences were observed between the control and dosed groups after 14 days or 21 days of pregnancy. Subcutaneous tissue cultures derived from 14-day fetuses in the dosed group, however,

grew more slowly than those from the control group. Monolayers were achieved within 10-15 days. Cultures derived from 21-day fetuses in the dosed group grew even more slowly (monolayers after 15-18 days). The morphology of 14-day and 21-day "dosed" fibroblasts fetus were similar.

(b) Enzymatic activity. Enzymatic activities were measured histochemically in cultures derived from pregnant female and fetal rats after 14 and 21 days of pregnancy. The activities summarized in the table below indicate the changes in the dosed group relative to the control group.

	Culture Origin			
	Females		Fetuses	
Enzyme	14 day	21 day	14 day	21 day
Acid phosphatase				
Succinate dehydrogenase	-			
Lactate dehydrogenase	-	-	-,	

The activity of acid phosphatase in cultures from 21-day pregnant females (dosed) increased after the second passage. The activity of lactate dehydrogenase in cultures from 14-day and 21-day pregnant females (dosed) decreased after the second passage. Cultures prepared by trypsinization of 14-day fetuses had higher lactate dehydrogenase

activity, whereas cultures prepared by cutting had no change.

(10) DISCUSSION: This manuscript offers no quantitative data for evaluation. The results of the experiments are stated in textual form and provide few numbers. The growth rates of the cultures are expressed as time to reach concluence; however, the times for "control" cultures were not indicated. The histochemical experiments were evaluated by the authors on the basis of stain intensity, and the results are expressed according to their interpretation. Taking the results as presented, however, it is apparent that trichlorfon has a deleterious effect on the growth rate of cells derived from fetuses whose mother had received the drug. The modulation of enzymatic activities, although not quantitative, lends credence to the evidence that trichlorfon crosses the placental barrier and causes cytotoxic effects in the fetus.

(11) TECHNICAL REVIEW TIME: 5.0 hours