Table IV. Insecticide in Tissues of Cows Fed Hay Treated with 4 Ounces of Dieldrin or Heptachlor per Acre

Insecticide	Cow No.	Insecticide Content, P.P.M. Liver	Muscle	Kidney	Fat
Dieldrin	Hu251	0	0	0.2	2.9
Heptachlor	W256	0	0	0	0.12[a]

[a] Heptachlor epoxide. No heptachlor found in tissues.

Table V. Insecticide in Butter Churned from Milk of Cows Fed Dieldrin or Heptachlor

Insecticide	Oz./Acre Applied	Cow No.	Insecticide Content, P.P.M.
Dieldrin	0	Hu253-W255	0
	1	E240-W258	9.5
	4	W257-Hu251	39.3
Heptachlor	0	Hu253-W255	0
	1	Hu224-E231	0
	4	Hu228-W256	0.2[a]

[a] No heptachlor found in butter. This value is heptachlor epoxide.

The liver, muscle, kidney, and fat tissues of the two slaughtered animals were examined histologically and no abnormalities were observed.

Acknowledgment

Shell Chemical Corp., Denver, Colo., supplied the dieldrin, checked some of the hay and butter analyses, and aided with the analytical methods for dieldrin. In the case of heptachlor, similar services were performed by the Velsicol Corp., Chicago, Ill., which also furnished a sample of heptachlor epoxide. Interpretations of the histological sections of muscle, fat, liver, and kidney tissues were confirmed by A. A. Nelson, U. S. Food and Drug Administration, and Frank P. Cleveland, Kettering Laboratory, University of Cincinnati.

Literature Cited

(1) Bateman, G. Q., Biddulph, Clyde, Harris, J. R., Greenwood, D. A., Harris, L. E., J. AGR. FOOD CHEM. **1,** 322 (1953).
(2) Claborn, H. V., Wells, R. W., *Agr. Chemicals* **7,** No. 10, 28 (1952).
(3) Davidow, Bernard, *J. Assoc. Offic. Agr. Chemists* **33,** 886 (1950).
(4) Davidow, Bernard, Radomski, J. L., *J. Pharmacol. Exptl. Therap.* **107,** 259 (1953).
(5) Davidow, Bernard, Radomski, J. L., Ely, Ray, *Science* **118,** 383 (1953).
(6) Ely, R. E., Moore, L. A., Carter, R. H., Hubanks, P. E., Poos, F. W., *J. Dairy Sci.* **37,** 1461 (1954).
(7) Feinstein, L., U. S. Department of Agriculture, Beltsville, Md., private communication, Nov. 9, 1953.
(8) O'Donnell, A. E., Johnson, H. W., Jr., Weiss, F. T., J. AGR. FOOD CHEM. **3,** 757 (1955).
(9) O'Donnell, A. E., Neal, M. M., Weiss, F. T., Bann, J. M., DeCino, T. J., Lau, S. C., *Ibid.*, **2,** 573 (1954).
(10) Polen, Percy B., Silverman, Paul, *Anal. Chem.* **24,** 733 (1952).
(11) Radomski, J. L., Davidow, Bernard, *J. Pharmacol. Exptl. Therap.* **107,** 266 (1953).
(12) Schechter, M. S., Pogorelskin, M. A., Haller, H. L., *Anal. Chem.* **19,** 51 (1947).

Received for review April 1, 1955. Accepted March 13, 1956. Research supported in part by a research grant from the Division of Research Grants and Fellowships, National Institutes of Health, U. S. Public Health Service. Report on Experiment Station Project 362.

PESTICIDE TOXICITY

Serum Alkaline Phosphatase Levels, Weight Changes, and Mortality Rates of Rats Fed Endrin

S. C. NELSON[1], T. L. BAHLER, W. V. HARTWELL, D. A. GREENWOOD, and L. E. HARRIS

Utah Agricultural Experiment Station, Utah State Agricultural College, Logan, Utah

This work is a part of a larger research project on the toxicity of newer insecticides to animals and the accumulation of such insecticides in products consumed by man. When various levels of endrin (0, 1, 5, 25, 50, and 100 p.p.m.) were added to a basal diet, the serum alkaline phosphatase values were higher among rats consuming endrin than in the control group. All rats receiving 100 p.p.m. of endrin died within the first 2-week period. Mortality rates indicated that male rats were significantly more susceptible to the toxic effects of endrin at the lower levels (1 and 5 p.p.m.) than were females. There was a loss of weight in all rats ingesting endrin. The greatest weight loss occurred in rats consuming the two highest levels of endrin. The total average feed consumption of endrin-fed rats was less than that of the control group. All rats consuming endrin demonstrated hypersensitivity to various stimuli.

THE AMOUNT AND DISTRIBUTION of chlorinated insecticides in the tissues and organs of the animal body have been studied in an attempt to determine their harmful effects. The majority of these studies have been concerned with histological observations and accumulation rates (*1, 3, 6, 11, 12*). The reports indicate that other ways of studying the effects of the insecticides on animal tissues might supplement histological and accumulation data. Various workers (*8, 10, 12, 16*) have indicated that one of the changes occurring after the ingestion of chlorinated hydrocarbons is hepatic cellular alteration and degeneration, with hypertrophy of the organ. It is generally accepted that the liver plays an important role as a source of alkaline phosphatase (*4, 14, 17*). Elevated serum alkaline phosphatase levels have been associated with func-

[1] Present address, Hanford Atomic Energy Project, Richland, Wash.

tional impairment of the liver (*5*, *15*, *17*, *18*) and also with abnormalities in dephosphorylation mechanisms (*13*). Popper, Koch-Weser, and De la Huerger (*15*), and Talageri and coworkers (*18*) have reported that following acute carbon tetrachloride damage in rats there is an increase in hepatic and serum alkaline phosphatase. Drill and Ivy (*5*) have indicated similar results with carbon tetrachloride damage in dogs. The purpose of the present study was to determine the effect of the chlorinated hydrocarbon endrin on the serum alkaline phosphatase levels of male and female rats and on feed consumption, changes in weight, and mortality.

Materials and Methods

Sixty sexually mature rats of the Sprague-Dawley strain, averaging 384 grams in weight and equally divided as to sex, were randomized and maintained in individual metal cages. The control rats were kept in a separate battery of cages to eliminate any volatile effects which the insecticide might exhibit. Water and ration were offered *ad libitum*. During the course of the experiment the rats were observed for abnormal actions and any symptoms of toxicity. They were divided into six groups with 10 to a group (five males and five females). Group 1 received the basal diet (Table I) only and served as the control group. All remaining groups received the basal diet containing levels of endrin in the following amounts: group 2, 1 p.p.m.; group 3, 5 p.p.m.; group 4, 25 p.p.m.; group 5, 50 p.p.m.; and group 6, 100 p.p.m.

The endrin was introduced into the basal diet by first dissolving the various levels of the insecticide in ether and then adding it to the wheat germ and soybean oils of the basal diet. The experimental diets were packed in Mason-type jars and refrigerated. To reduce contamination, each jar contained its own feeding spatula and was assigned to a specific rat. Feed consumed and weight gained or lost were measured every 2 weeks for each rat.

Table I. Composition of Basal Diet

	%
Casein	18.24
Brewer's yeast	4.00
Whole liver	4.00
Dextrin	59.90
Fat[a]	9.36
Wheat germ oil	0.50
Salts[b]	4.00
Vitamin A and D supplement, gram (4000 U.S.P. units vitamin A per gram) (500 U.S.P. units vitamin D per gram)	0.003
Vitamin D supplement, gram (9000 U.S.P. units per gram)	0.0044

[a] Soybean oil.

[b] Ingredients. NaCl 27.5%; K_2HPO_4 25.85%; $CaCO_3$ 18.5149%; $Ca(H_2PO_4)_2.H_2O$ 21.65%; $MgCO_3$ 4.6%; $CuSO_4.5H_2O$ 0.02%; $MnSO_4$ 0.035%; KI 0.005%; $CoCl_2.6H_2O$ 0.01%; $ZnCO_3$ 0.005%; NaF 0.00015%; $FeC_6H_5O_7.3H_2O$ 1.8%; $K_2Al_2(SO_4)_4.24H_2O$ 0.01%.

Blood volumes of 0.2 to 0.3 ml. were obtained from the orbital sinus by the method of Halpern (*9*). The procedure as outlined by Bessey, Lowry, and Brock (*2*) was employed in the determination of the serum alkaline phosphatase. All measurements were carried out with the Coleman Junior spectrophotometer. The *p*-nitrophenol phosphate and *p*-nitrophenol were obtained from the Sigma Chemical Co., St. Louis, Mo.

Phosphatase determinations were made once a week on each rat from the beginning of the experiment until its termination 16 weeks later. All rats were conditioned to the basal diet for a 2-week period before the various levels of endrin were added. The phosphatase levels obtained while rats were maintained on the basal diet are referred to as the original values. The alkaline phosphatase values are expressed in "millimole units" with a "unit" defined as "the alkaline phosphatase activity which will liberate 1 millimole of nitrophenol per liter of serum per hour."

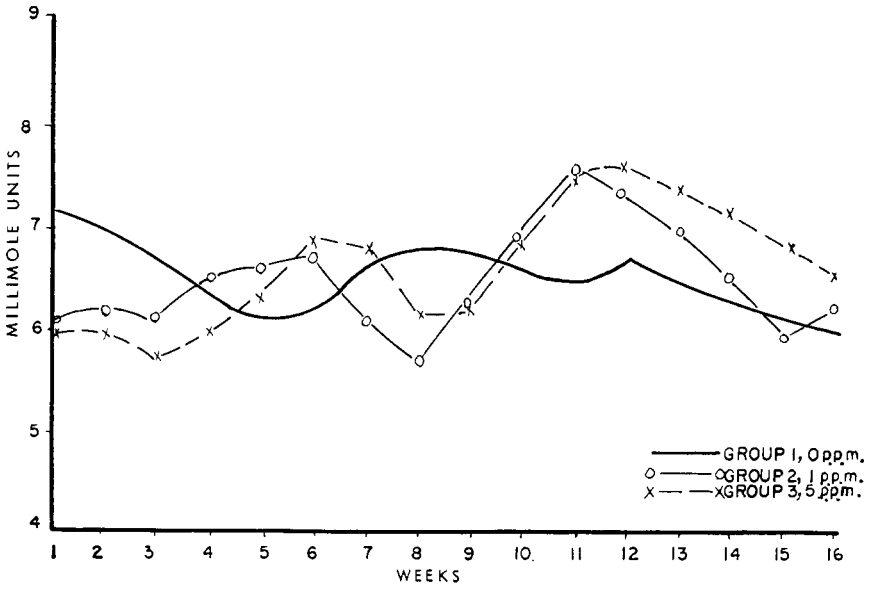

Figure 1. Average values of serum alkaline phosphatase for groups 1, 2, and 3, fed various levels of endrin

Alkaline Phosphatase

The group mean values of both sexes for serum alkaline phosphatase, shown in Figures 1 and 2, represent an average of 3 consecutive weeks. The data in Figures 1 and 2 indicate greater varia-

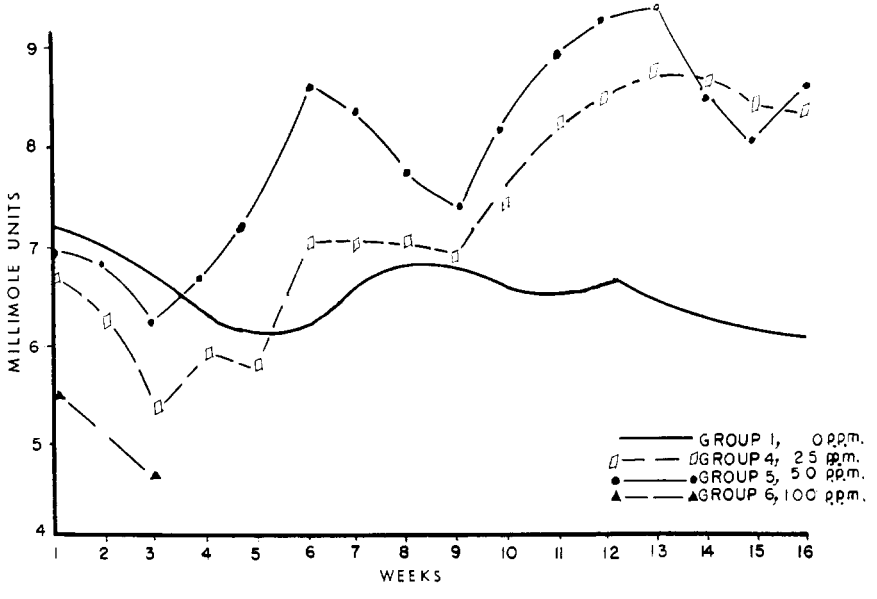

Figure 2. Average values of serum alkaline phosphatase for groups 1, 4, 5, and 6, fed various levels of endrin

Table II. Total Average Feed Consumption of Male and Female Rats[a]

	Grams
Group 1	193
Group 2	174
Group 3	183
Group 4	161
Group 5	134
Group 6	109

[a] Amount of feed consumed for each rat was measured every 2 weeks.

tions in the serum alkaline phosphatase levels of rats receiving endrin than in the control animals. By an analysis of variance on phosphatase values, using the method of least squares, it was found that there was a statistically significant association between endrin consumed and phosphatase levels at different time intervals. There was a significant increase in the serum alkaline phosphatase levels in rats receiving the various levels of endrin, and this increase was related to the quantity of endrin consumed during a period of time. The serum alkaline phosphatase levels of all rats ingesting endrin, with the exception of rats receiving 1 p.p.m., dropped to a minimum by the third week and then increased. The minimum alkaline phosphatase level of the rats receiving 1 p.p.m. (group 2) occurred at the eighth week. During the experiment the highest phosphatase level of the control group was consistently less than the highest levels in all groups receiving endrin. The highest phosphatase values occurred in groups 5 and 4 followed by groups 3 and 2. All the rats fed on a diet containing 100 p.p.m. (group 6) died within 2 weeks.

Weil and Russell (*20*) studied the relationship between feed consumption and phosphatase levels and found that the alkaline phosphatase levels in rats decreased after 8 hours' fasting. The data presented in Table II indicate that the control group consumed more feed than any of the groups receiving endrin. Yet after the fourth week, the phosphatase levels of the endrin-fed groups were, in general, greater than that of the controls. To study further this relation between feed consumption and phosphatase values, all rats living beyond the sixteenth week were subjected to starvation for 72 hours. Phosphatase levels measured at 24-, 48-, and 72-hour intervals as shown in Table III are in agreement with the data obtained by Weil and Russell (*20*). However, after the first 24 hours of starvation phosphatase levels decreased little. Rats receiving the higher dietary levels of endrin, particularly those of groups 4 and 5, maintained a much higher phosphatase level throughout the starvation period than did the control group.

Because of the relatively small number of rats surviving on the higher levels of endrin, the data obtained were not statistically significant as determined by an analysis of variance. However, the phosphatase values obtained from the fasting rats help to substantiate the evidence that endrin causes an increased serum alkaline phosphatase. This might logically indicate some degree of enzymatic abnormality and functional liver damage.

Table III. Phosphatase Levels of All Rats Living 16 Weeks after Being Starved for 72 Hours

Rat No.	Sex	Endrin in Diet, P.P.M.	Phosphatase Mmols/Liter/Hour: Prior to fasting	After 24 hr.	After 48 hr.	After 72 hr.
1	M	0	6.60	2.80	4.40	2.00
3	M	0	5.60	2.80	3.00	2.70
4	M	0	6.00	2.50	2.50	2.90
5	M	0	4.70	3.00	2.80	2.40
6	F	0	6.20	2.40	2.80	2.80
7	F	0	5.50	3.00	2.70	2.40
8	F	0	7.80	2.70	2.80	2.80
9	F	0	5.10	2.70	3.00	2.70
10	F	0	4.50	3.20	2.90	1.90
Group mean			5.79	2.79	2.99	2.51
1	M	1	5.10	2.70	3.00	3.00
4	M	1	8.20	3.00	3.20	3.60
6	F	1	9.40	4.70	3.90	3.40
7	F	1	6.50	4.20	3.50	3.00
8	F	1	8.70	2.40	2.50	1.90
9	F	1	6.00	2.50	2.80	2.20
10	F	1	7.50	2.70	3.00	2.40
Group mean			7.34	3.17	3.13	2.70
1	M	5	6.90	3.60	3.00	2.80
4	M	5	5.50	4.50	3.90	4.20
6	F	5	4.70	2.00	2.70	2.40
7	F	5	6.20	3.60	3.40	3.40
8	F	5	7.80	3.70	3.90	3.00
9	F	5	7.00	3.30	3.00	3.00
10	F	5	8.70	3.00	2.40	3.40
Group mean			6.67	3.40	3.19	3.17
2	M	25	11.00	4.60	6.00	6.20
3	M	25	8.50	3.80	4.40	3.60
9	F	25	9.50	4.80	4.00	3.70
Group mean			9.66	4.40	4.80	4.50
7	F	50	10.30	4.60	5.00	4.30

Table IV. Summary of Mortality at Various Periods throughout Experiment

Endrin in Diet, P.P.M.	Sex	Mortality End 4th Week: Number died/fed	Mortality, %	P[a]	Mortality End 10th and 16th Weeks: Number died/fed	Mortality, %	P[a]
100	M	5/5	100	0.0039	5/5	100	0.0079
50	M	4/5	80	0.023	5/5	100	0.0079
25	M	2/5	40	0.222	3/5	60	0.119
5	M	2/5	40	0.222	3/5	60	0.119
1	M	0/5	0	...	3/5	60	0.119
0	M	0/5	0	...	0/4[b]	0	...
100	F	5/5	100	0.0039	5/5	100	0.0039
50	F	2/5	40	0.222	3/5	60	0.083
25	F	3/5	60	0.083	4/5	80	0.023
5	F	0/5	0	...	0/5	0	...
1	F	0/5	0	...	0/5	0	...
0	F	0/5	0	...	0/5	0	...

[a] Value of P less than 0.05 is considered significant.
[b] One rat eliminated from control group because of severe eye infection.

Mortality

The mortality of the various groups at the 4th, 10th, and 16th weeks as presented in Table IV was subjected to statistical analysis using the method of exact treatment of 2 × 2 tables (*7*). A value of P of less than 0.05 is considered significant. At the end of the fourth week the mortality in group 6 was significant in both sexes, while group 5 was significant only in the males. At the end of the 10th week, mortality was significant in two male groups (5 and 6). Mortality was significant in two female groups (4 and 6) at the end of the 10th week, but no mortality was ob-

served in groups 2 and 3. At the termination of the experiment (16th week) the mortality within the groups remained the same as at the end of the 10th week.

When the mortality data at the termination of the experiment were subjected to a chi-square test of independence to show the relation of sex to tolerance to endrin, it indicated that the males were more susceptible to endrin than were the females. This difference between sexes was significant at a P value of 0.049. Nineteen males died among the five male groups receiving endrin, compared to 12 in the corresponding female groups. This largely resulted from the fact that male rats were more susceptible at the lower levels of endrin (groups 2 and 3) than were females. There was no significant difference between sexes at the highest level (group 6). However, the males had significantly greater mortality than females in group 5, and females had significantly greater mortality than males in group 4.

Treon, Cleveland, and Cappel (*19*) reported a sex difference in mortality, but their work indicated a greater incidence of mortality among females than among males fed 50 and 25 p.p.m. of endrin. However, the present study showed a significant mortality rate only for males receiving 50 p.p.m. At 25 p.p.m. the mortality rate in females only was significant, which was in agreement with the data of Treon, Cleveland, and Cappel (*19*). Male rats in the present study receiving 1 and 5 p.p.m. of endrin (groups 2 and 3) showed a significantly greater susceptibility to endrin than did the females in the corresponding groups (P value, 0.005).

Treon, Cleveland, and Cappel (*19*) have reported that 3 of 40 and 4 of 40 rats, respectively, ingesting 100 and 50 p.p.m. of endrin survived a 2-year experiment. In this investigation there was no instance wherein an animal receiving 100 p.p.m. of endrin survived beyond the second week. Of the 10 rats which consumed 50 p.p.m. of endrin, only two females survived the experiment.

Weight Change

A significant relation between endrin consumed and weight change at various time intervals was found by statistical analysis of the data using the method of least squares. A significant sex difference was also indicated by the analysis. Rats on 100 p.p.m. lost the greatest weight, followed by those on 50 and 25 p.p.m. There was no significant difference in weight loss between those ingesting 1 and 5 p.p.m., although the weight gains were less than those shown by the control group. These results are shown in Figure 3. A greater weight loss was found in male rats than in females; however, in the control group the males gained more than the females. This sex difference is shown in Figure 4, when group 2 is used as a typical example.

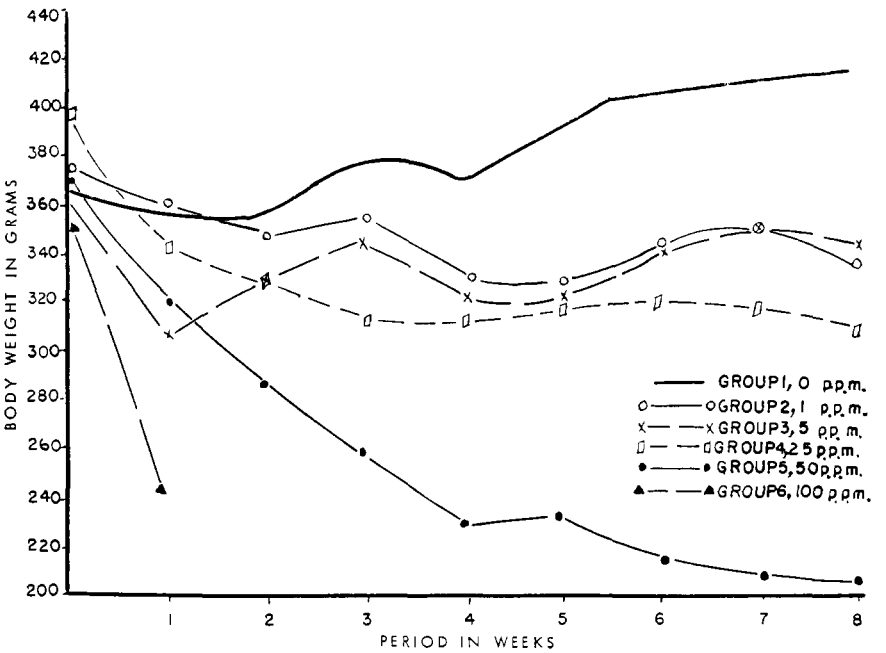

Figure 3. Weight changes of experimental animals fed various levels of endrin

It was first believed that the greater weight loss among rats fed the higher levels of endrin was attributable in part to a reduced feed intake. Table II indicates that the total average feed consumption of rats receiving various levels of endrin was less than that of the control group. However, paired feeding experiments in which feed consumption of control and endrin-fed rats was maintained at a similar level suggests that a reduced feed intake is not entirely responsible for the greater weight loss in the endrin-fed rats. This experiment was designed so that control and experimental animals consumed the same amount of feed. However, the rats used in the paired feeding experiment were young, and death occurred too soon to balance feed intake. Thus the total diet consumed by paired mates varied by a few grams. Even so, the difference in feed intake between the control and its paired mate was probably not great enough to account for the difference in weight change expressed as a percentage of the initial weight. A summary of the results of the paired feeding experiments is shown in Table V. In all cases the endrin-fed animal lost considerably more weight than did its control. It is apparent that endrin has some effect on the weight change of the animal.

Laug and coworkers (*12*), in their work on dietary levels of 800 and 1200 p.p.m. of DDT in rats, found that in paired feeding the experimental animal

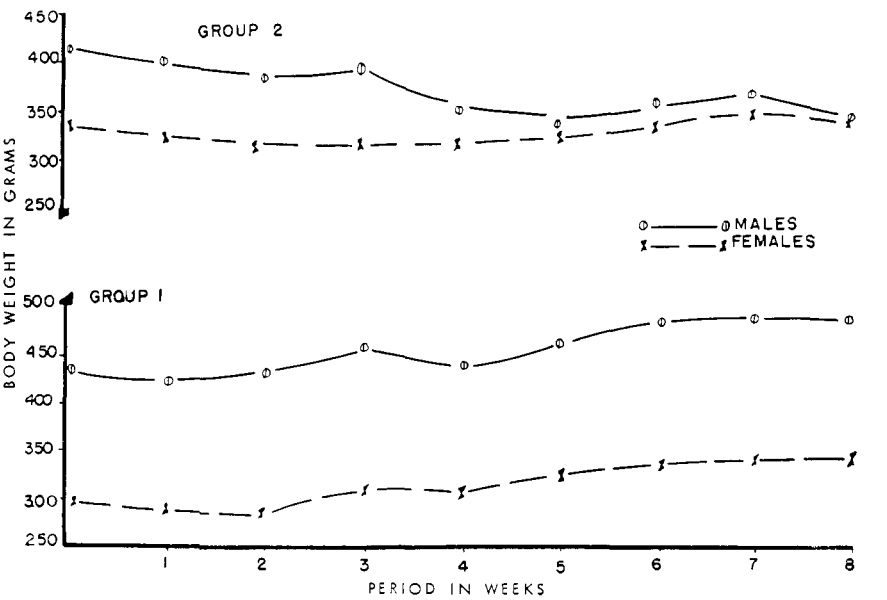

Figure 4. Weight changes associated with sex in groups 1 and 2

Table V. Weight Changes in Paired Feeding Experiments

Rat No.	Sex	Endrin in Diet, P.P.M.	Survival for Endrin-Fed Rats, Days	Total Diet Consd., G.	Weight, Grams			Change in Weight, % of Initial Wt.
					Initial	Final	Change	
1-A	M	0	[a]	25.5	322	273	−49	−15
2-A	M	100	10	24.0	355	268	−87	−25
1-B	F	0	[a]	12.0	204	191	−13	−6
2-B	F	100	5	10.0	190	163	−27	−15
1-C	M	0	[a]	18.0	275	270	−5	−2
2-C	M	100	4	15.0	290	266	−24	−8
1-D	F	0	[a]	14.0	170	167	−3	−2
2-D	F	100	3	8.0	160	133	−27	−17

[a] In all cases control rats were in good health.

ate more than its litter control mate. It is evident in the present investigation that endrin in dietary levels of 100 p.p.m. definitely curtailed the feed intake of rats ingesting the compound, for in no instance did the endrin-fed rat eat more than its control mate.

At the time the experiments were set up, no information on effects of various levels of endrin was available. The 100 p.p.m. level was arbitrarily selected as the best, but 50 p.p.m. would have been more satisfactory.

Symptoms of Toxicity

Hypersensitivity to sound, touch, and pressure stimuli was observed in all rats ingesting endrin. Rats receiving 100 and 50 p.p.m. of endrin were most sensitive. This extreme sensitivity was followed by convulsions, which occurred only among the three groups receiving the highest levels of endrin.

Convulsions were spasmodic, occurred once every 1 to 3 hours, and lasted from 5 to 20 minutes. Once these convulsive patterns were established, rats rarely lived more than 1 week.

Common characteristics of these convulsive spasms were self-inflicted wounds in the posterior areas of the body, particularly in the anal region. In extreme instances two rats chewed away portions of the hind legs. It was a common occurrence to find tail extremities completely lacerated and sometimes severed.

Rats in groups 4, 5, and 6, that consumed the higher levels of endrin, demonstrated additional characteristics, which included dysenteric symptoms, intermittent blindness, and slight bleeding through the nares. Clotting also appeared to be delayed when blood specimens were obtained from the orbital sinus. The latter characteristic could perhaps indicate a decreased prothrombin level, although no tests for prothrombin levels were conducted.

The only apparent abnormalities occurring in groups 2 and 3 were hypersensitivity to stimuli and slight bleeding through the nares.

Fitzhugh and Nelson (*8*) relate that characteristic tremors were observed within 24 hours after the withdrawal of feed from rats receiving 400 to 800 p.p.m. of DDT. In a similar fasting experiment conducted in this investigation no tremors were observed in any of the rats which had been starved for 72 hours. However, rats of groups 3, 4, and 5 were more irritable than those of the other groups.

At no time during the experiment did the control rats show any of the foregoing symptoms of toxicity.

Summary

Serum alkaline phosphatase levels were measured weekly, and the amount of feed consumed and weight gained or lost was measured every 2 weeks on 60 mature rats of the Sprague-Dawley strain for 16 weeks. The rats were equally divided as to sex and segregated into 6 groups with 10 to a group. Group 1 served as the control group. The remaining five groups received a basal diet containing endrin in the following amounts: group 2, 1 p.p.m.; group 3, 5 p.p.m.; group 4, 25 p.p.m.; group 5, 50 p.p.m.; and group 6, 100 p.p.m.

Serum alkaline phosphatase values were significantly higher among rats consuming endrin than in rats of the control group. The phosphatase level of endrin-fed rats remained higher than those of the control group, even in a period of fasting. The total average feed consumption of rats receiving various levels of endrin was less than that of the control group.

Mortality at the termination of the experiment was significant in two male groups (5 and 6) and two female groups (4 and 6). Males were significantly more susceptible to endrin than females. This was particularly true of groups 2 and 3.

There was a significant loss of weight in all rats ingesting endrin. The greatest weight loss occurred in rats consuming the two highest levels of endrin. In conjunction with the weight changes of 60 mature rats, a paired feeding experiment involving eight rats (four males and four females) indicated that reduced feed intake of rats receiving 100 p.p.m. of endrin was not great enough to account for their weight loss. A greater weight loss was found in male rats ingesting endrin than in females.

Hypersensitivity to various stimuli was observed in all rats consuming endrin. Convulsive spasms were noted only among rats receiving the three highest levels of endrin.

Literature Cited

(1) Allen, N. N., Lardy, H. A., Wilson, H. F., *J. Dairy Sci.* **29,** 530 (1946).
(2) Bessey, O. A., Lowry, O. H., Brock, M. J., *J. Biol. Chem.* **164,** 321 (1946).
(3) Biddulph, C., Bateman, G. Q., Bryson, M. J., Harris, J. R., Greenwood, D. A., Binns, W., Miner, M. L., Harris, L. E., Madsen, L. L., *Advances in Chem. Ser.*, No. **1,** 237 (1950).
(4) Burke, J. O., *Gastroenterology* **16,** 660 (1950).
(5) Drill, V. A., Ivy, A. C., *J. Clin. Invest.* **23,** 209 (1944).
(6) Finnegan, J. K., Haag, H. B., Larson, P. S., *Proc. Soc. Exptl. Biol. Med.* **72,** 357 (1949).
(7) Fisher, R. A., "Statistical Methods for Research Workers," 6th ed., Oliver & Boyd, London, 1936.
(8) Fitzhugh, O. G., Nelson, A. A., *J. Pharmacol. Exptl. Therap.* **89,** 18 (1947).
(9) Halpern, B. N., *Science* **119,** 100 (1954).
(10) Konst, H., Plummer, P. J. G., *Can. J. Comp. Med. Vet. Sci.* **10,** 128 (1946).
(11) Laug, E. P., Fitzhugh, O. G., *J. Pharmacol. Exptl. Therap.* **87,** 18 (1946).
(12) Laug, E. P., Nelson, A. A., Fitzhugh, O. G., Kunz, F. M., *Ibid.*, **98,** 268 (1950).
(13) Madsen, N. B., Tuba, J., *J. Biol. Chem.* **195,** 741 (1952).
(14) Oppenheimer, M. J., Flock, E. V., *Am. J. Physiol.* **149,** 418 (1947).
(15) Popper, Hans, Koch-Weser, D., De la Huerger, Jesus, *J. Mt. Sinai Hosp. N. Y.* **19,** 256 (1952).
(16) Sarett, H. P., Jandorf, B. J., *J. Pharmacol. Exptl. Therap.* **91,** 340 (1947).
(17) Sulkin, N. M., Gardner, J. H., *Anat. Record* **100,** 143 (1948).
(18) Talageri, V. R., Samarth, K. D., Bodi, A. J., Venkataraman, P. R., *Brit. J. Exptl. Pathol.* **32,** 118 (1951).
(19) Treon, J. F., Cleveland, F. P., Cappel, J., J. Ag. Food Chem. **3,** 842 (1955).
(20) Weil, L., Russell, M. A., *J. Biol. Chem.* **136,** 9 (1940).

Received for review September 14, 1955. Accepted March 23, 1956. Division of Agricultural and Food Chemistry, Symposium on Metabolism of Pesticides in Plants, Mammals, and Insects, 128th Meeting, ACS, Minneapolis, Minn., September 1955. Submitted as partial requirement for M.S. degree in physiology at Utah State Agricultural College, 1955. Work supported in part by a grant from the Division of Research Grants and Fellowships, National Institutes of Health, Bethesda, Md.