COMMUNICATION

Effects of Insecticides on Reproduction in the Laboratory Mouse

IV. Endrin and Dieldrin

Effects of Insecticides on Reproduction in the Laboratory Mouse. IV. Endrin and Dieldrin. GOOD, E. E., and WARE, GEORGE W. (1969). Toxicol. Appl. Pharmacol. 14, 201-203. A single large-scale feeding test was conducted on CFW Swiss mice to measure the influence of sublethal levels of dietary organochlorine insecticides on reproduction. Endrin and dieldrin were fed at 5 ppm for 120 days, beginning 30 days before mating. Endrin produced significant parent mortality, and significantly smaller litters. Dieldrin, a stereoisomer of endrin, produced no parent mortality, but significantly reduced the size of all litters. Neither compound affected fertility, fecundity, or the number of young produced per day.

This is the last in a series of experiments to determine the effects of sublethal dietary concentrations of insecticides on laboratory mice, begun by the authors in 1961. To date eight compounds have been tested. Five of these significantly reduced the reproductive success of the experimental animals under the conditions imposed by the tests. Good et al. (1965) found that a diet containing 5 ppm of Kepone* brought about a reduction in both size and numbers of litters produced by the test animals. Huber (1965) found apparent reduction in luteinizing hormone in the test animals from Kepone*. Ware and Good (1967a) found that Mirex*, an analog of Kepone*, fed at 5 ppm in the diet reduced both litter size and the number of offspring produced per day. In the same experiment DDT at 7 ppm in the diet resulted in slight but consistent reductions in litter numbers. In their third study Ware and Good (1967b) observed no detectable influence on reproductive success in mice when a carbamate insecticide Tranid® and a relative of Kepone® and Mirex®, GC-9160, were fed at 5 ppm for 120 days.

For this final study endrin and its stereoisomer dieldrin, two highly toxic chlorinated hydrocarbons, were selected since there was evidence that both might be expected to produce physiological effects detrimental to reproduction. A number of workers have reported heavy mortality in populations of various vertebrates after field applications of this compound for insect control. Snyder (1963) found that endrin applied to bluegrass meadows at 0.6 to 2.0 pounds per acre resulted in significant reductions in the number of litters produced by meadow voles, Microtus pennsylvanicus, 2 months after application. Both compounds are still commonly used and widely recommended as broad-spectrum insecticides, and were thus selected for this study.

Test compounds1 used in these studies were technical grade dieldrin, 85%, and endrin, 96%. Insecticide-impregnated and control foods were prepared, as described in this journal by Ware and Good (1967a).

1 Entomological Society of America Reference Standards, City Chemical Corporation, 132 West 22nd Street, New York, New York.
Suitable dietary levels were sought through a preliminary range-finding test. Twenty each of virgin male and female mice, held five to a cage, were placed on diets of 0, 25, and 50 ppm endrin. All test animals died; however, several on the 25-ppm diet lived more than 30 days, and one survived to day 41.

The animals used in these tests were the CFW strain of Swiss mice. Purchased simultaneously, they were 6 weeks of age with differences not exceeding a few days.

Test groups of virgin males and females were segregated, and each group was fed one of the repelletized test diets for 30 days. Males and females which had received the same diet were then randomly paired and continued on the same diet for 90 days. Each test group consisted of 101 pairs. Reproduction and mortality data were carefully maintained for each pair.

For statistical convenience, as in previous studies, reproduction was measured by parent mortality, fertility, fecundity, effects on first litters, and effects on all litters. It is apparent from Table 1 that endrin was toxic at 5 ppm in the diet. During 4 months of feeding, adult mortality occurred in one-third of the pairs. Mortality, however, among the dieldrin-fed test animals did not differ significantly from the controls. With the endrin-fed mice, first litters were significantly smaller than those produced by the other groups. Considering all litters, the endrin- and dieldrin-fed animals produced significantly smaller litters than the controls. The time required to produce the first litter was greater for mice receiving the endrin diet, but the difference was not statistically significant.

### Table 1

**Least-Squares Means and Standard Errors** of Reproduction Data from CFW Mice Fed Insecticides (1966)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Dieldrin, 5 ppm</th>
<th>Endrin, 5 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% pairs with mortality</td>
<td>6.93</td>
<td>5.94</td>
<td>32.67*</td>
</tr>
<tr>
<td>Fertility (% surviving pairs producing young)</td>
<td>100.0</td>
<td>99.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Fecundity (young/producing pair)</td>
<td>21.330 ± 0.67</td>
<td>20.968 ± 0.63</td>
<td>21.418 ± 0.88</td>
</tr>
<tr>
<td>Litters per producing pair</td>
<td>2.330 ± 0.06</td>
<td>2.415 ± 0.06</td>
<td>2.463 ± 0.08</td>
</tr>
<tr>
<td>Litters per surviving pair</td>
<td>2.330 ± 0.06</td>
<td>2.389 ± 0.07</td>
<td>2.426 ± 0.09</td>
</tr>
<tr>
<td><strong>First litters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>8.511 ± 0.02</td>
<td>8.543 ± 0.02</td>
<td>7.925 ± 0.02*</td>
</tr>
<tr>
<td>Days to produce</td>
<td>24.745 ± 0.95</td>
<td>23.830 ± 0.67</td>
<td>26.209 ± 1.40</td>
</tr>
<tr>
<td>Young produced per day</td>
<td>0.367 ± 0.01</td>
<td>0.377 ± 0.01</td>
<td>0.334 ± 0.01*</td>
</tr>
<tr>
<td><strong>All litters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>9.2 ± 0.15</td>
<td>8.7 ± 0.14*</td>
<td>8.7 ± 0.17*</td>
</tr>
<tr>
<td>Days to produce</td>
<td>28.7 ± 0.54</td>
<td>28.1 ± 0.48</td>
<td>28.1 ± 0.48</td>
</tr>
<tr>
<td>Young produced per day</td>
<td>0.338 ± 0.007</td>
<td>0.326 ± 0.007</td>
<td>0.331 ± 0.008</td>
</tr>
</tbody>
</table>

* Tested by Duncan's Multiple Range test.
* Significant at 5% level of probability from other diets.
As in previous studies, these results indicate that reproductive effects were observed in a single generation of mice fed sublethal levels of insecticides continuously. Although endrin was the only toxicant producing mortality, both compounds resulted in significantly smaller litters than the controls. There was, however, no influence on the time required to produce these litters, suggesting no effect on the estrous cycle, as observed with Kepone (Good et al., 1965). This suggests that the direct influence of endrin and dieldrin on reproduction in mice is probably due to fetal mortality, inferred by the heavy mortality which occurred in the adults fed endrin continuously at 25 and 5 ppm. Further studies should include placental scar counting at termination to confirm the fetal mortality implication.

ACKNOWLEDGMENTS

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REFERENCES


Department of Zoology and Entomology
The Ohio State University
Columbus, Ohio 43210

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2 Present address: Professor and Head, Department of Entomology, The University of Arizona, Tucson, Arizona 85721.