interbureau By-Lines

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE Food And Drug Administration

VOLUME 6 No. 6, Consecutive No. 36 MAY 1970

Helen L. Reynolds, Editor
Nancy J. Palmer, Laura A. Kovach, and Alberta E. Blair, Assistants
Dorothy H. Mahoney and Joanne Aitken, Page Makeup

IN THIS ISSUE

Collaborative Study of the Determination of Ammonia as an Index of Decomposition in Crabmeat by Kurt Steinbrecher. 281

Spectrofluorometric Determination of Rauwolfia Serpentina Tablets and Whole Root by Charles C. Clark 288

Application of Neutron Activation Analysis to Food Products: A Bibliography by James T. Tanner and Melvin Friedman. 294

Polarographic Determination of Nitrates in Aqueous Media Containing Nitrites by Albert L. Woodson 299

Correlation of Organoleptic Evidence with pH, Volatile Bases, and Indole as Indices of Decomposition in Raw, Frozen Shrimp by Billy G. Miles. 304

Differential Effects of DDT and Polychlorinated Biphenyls on the Central Nervous System by Thomas J. Sobotka. 313

Microbiological Contamination Bibliography (Continued) by Harriet M. Oxley 320

Publications List. 325

Cumulative Index to Interbureau By-Lines, Vols. 1-6... 328

MONS 029498

Interbureau By-Lines No. 6
May 1970

DIFFERENTIAL EFFECTS OF DDT AND POLYCHLORINATED BIPHENYLS ON THE CENTRAL NERVOUS SYSTEM

By Thomas J. Sobotka, Division of Pesticide Chemistry and Toxicology

Refined chemical procedures have only recently been developed which enable DDT to be differentiated from polychlorinated biphenyls (PCB) in single samples (personal communication from Judith Armour, DPCT, to be published in JAOAC, July 1970). Because these two classes of compounds are difficult to separate and because they are both found in wildlife species, it is possible that effects previously attributed to DDT may in fact be due to PCB residues. The present work was undertaken to determine whether central behavioral and physiological systems are similarly or differentially affected by DDT and polychlorinated biphenyls. Two representative samples of the PCB class were investigated, namely, Aroclor 1260 and Aroclor 1254.

Methods

Adult male mice (Flander's Research Farm) were used throughout the study. Animals were housed in groups of 15-20 with constant lighting and temperature. Food and water were provided ad libitum.

All compounds were dissolved in corn oil and administered orally at volumes equivalent to 0.01 ml/g body weight.

Open-Field Activity (Exploratory Activity). - The apparatus to measure exploration of the DDT and Aroclor 1260 groups was different from that used to gauge exploratory activity of the Aroclor 1254 groups. Therefore, only the DDT and Aroclor 1260 groups can be validly compared. However, the data from the Aroclor 1254 groups will be presented for completeness.

Exploratory behavior for the DDT and Aroclor 1260 groups was measured by the use of a large rectangular box (10 x 18 x 6") with marked grid floor. Twenty-four hours after dosing, each animal was tested individually. The number of squares traversed per minute was recorded for a 5 min period. The average minute activity was used as the exploratory activity.

Exploration by the Aroclor 1254 groups was determined in circular photoactivity chambers (18" diameter x 15" high). Twenty-four hours after dosing, each mouse was placed in a photoactivity chamber and the number of light beams crossed per minute for 5 min was recorded. The average minute activity was used as the exploratory activity.

MONS 029499

In order to gauge the rate at which the mice were habituating to the novel environment during their 5 min exposure, the difference between the average activity of the first 2 min and the last 2 min was calculated. A large difference (the average activity of the last 2 min being smaller) was taken to imply a rapid suppression of motor exploration, i.e., a high degree of habituation; conversely, a smaller difference would indicate relatively little motor suppression or habituation to the novel environment. The use of a decline in exploratory activity over a period of time as an index of habituation is based on the methods of Carlton (1).

DDT was given in doses of 0, 1.0, 10.0, and 25.0 mg/kg (total number of mice = 60). Aroclor 1260 was administered at 0, 1.0, and 10.0 mg/kg (total number of mice = 39). Aroclor 1254 was given at doses of 0, 0.5, 1.0, and 10.0 mg/kg (total number of mice = 48).

Passive Avoidance. - Fear-induced suppression of motor activity (passive avoidance) was measured in a standard passive avoidance situation (2). The apparatus consisted of a small Plexiglas chamber (3.5 x 6.5" with a grid floor) adjoining a larger chamber (13.5 x 13.5" with a grid floor) with a door between them. Four hours after dosing, each mouse was placed in the small chamber facing away from the door. The door was immediately opened, thereby activating a timer. The time (latency) to enter the larger chamber was recorded. As soon as the animal stepped into this chamber, the door was closed and an 8 ma/0.2 sec shock was delivered through the grid floor. The mouse was then returned to its home cage. On the following day the animal was given a single post-shock (fear) test. The latency to enter the large "shock" chamber was recorded but no shock was given.

DDT (80 mice), Aroclor 1260 (81 mice), and Aroclor 1254 (48 mice) were administered in oil in single oral doses of 0, 0.5, 1.0, and 10.0 mg/kg.

Maximum Electroshock Seizure. - Four hours after dosing, maximum electroshock seizure was induced by a 30 ma/0.2 sec pulse delivered via saline wetted corneal electrodes. The durations of the following seizure components were measured: tonic flexion, tonic extension, and clonus. In addition, the ratio of tonic flexion/tonic extension was calculated.

The following doses of DDT (61 mice), Aroclor 1260 (46 mice), and Aroclor 1254 (40 mice) were given: 0, 0.5, 1.0, and 10.0 mg/kg.

MONS 029501

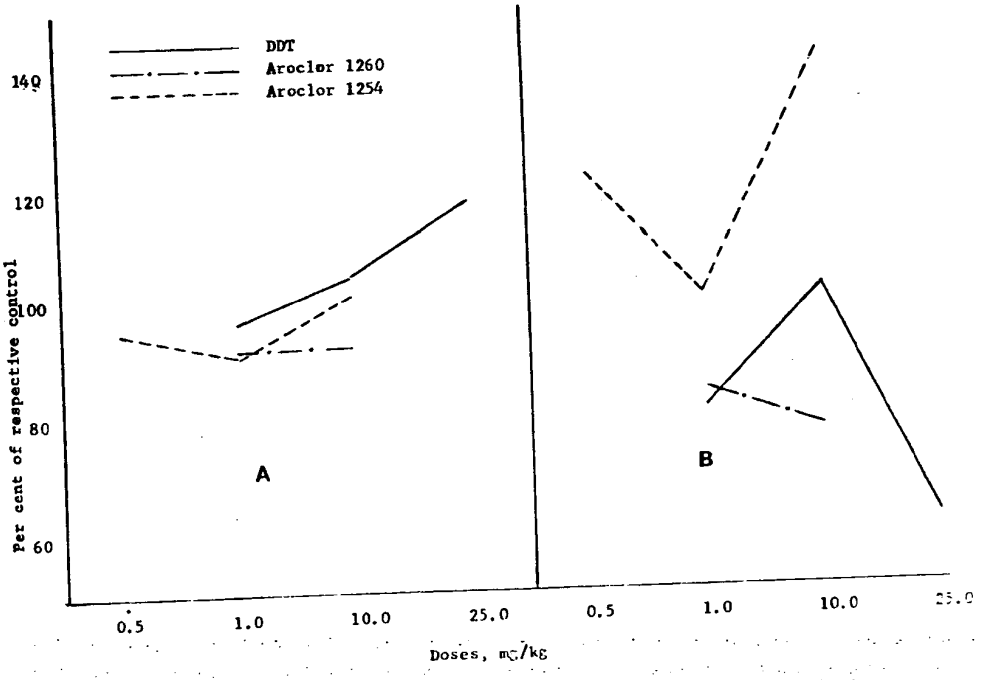

FIG. 1--Effect of DDT, Aroclor 1260, and Aroclor 1254 on (A) exploratory behavior and (B) habituation (4 hr pretreatment).

Results

All results are expressed as per cent of control. Figure 1A depicts the changes in exploratory activity induced by DDT and Aroclor 1260. At 1.0 and 10.0 mg/kg there does not appear to be any marked differences between the effects of the 2 compounds. The Aroclor 1260 groups do, however, tend to exhibit a slightly lower exploratory activity. A similar low exploration is seen with the Aroclor 1254 group at 1.0 mg/kg.

The habituation scores seen in Fig. 1B similarly do not differentiate between DDT and Aroclor 1260. Aroclor 1254 does induce a facilitation of habituation. But this effect cannot be validly compared with the DDT or Aroclor 1260 groups since different apparatus was used.

In contrast to exploratory and habituation scores, a clear distinction between DDT and both of the Aroclor compounds is seen in the passive avoidance behavior. As shown in Fig. 2, the DDT-treated mice entered the shock (stress) chamber faster, while the Aroclor

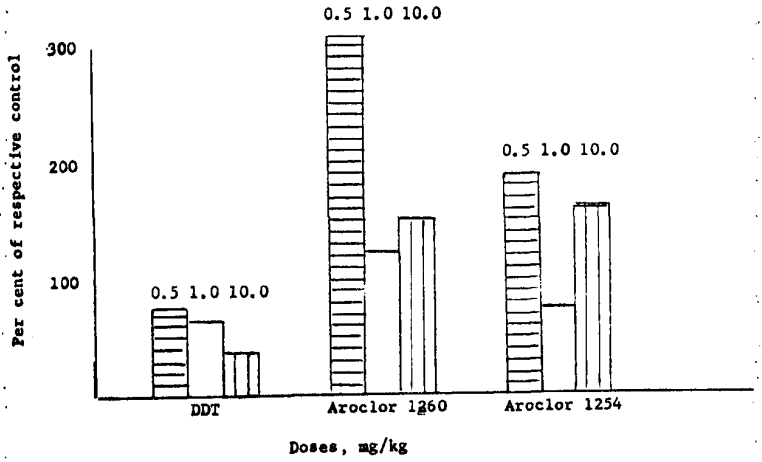

FIG. 2--Effecto of DDT, Aroclor 1260, and Aroclor 1254 on latency to enter a shock-stress chamber (all agents were given 24 hr before shock and 48 hr before testing latency to enter shock chamber).

MONS 029502

MONS 029503

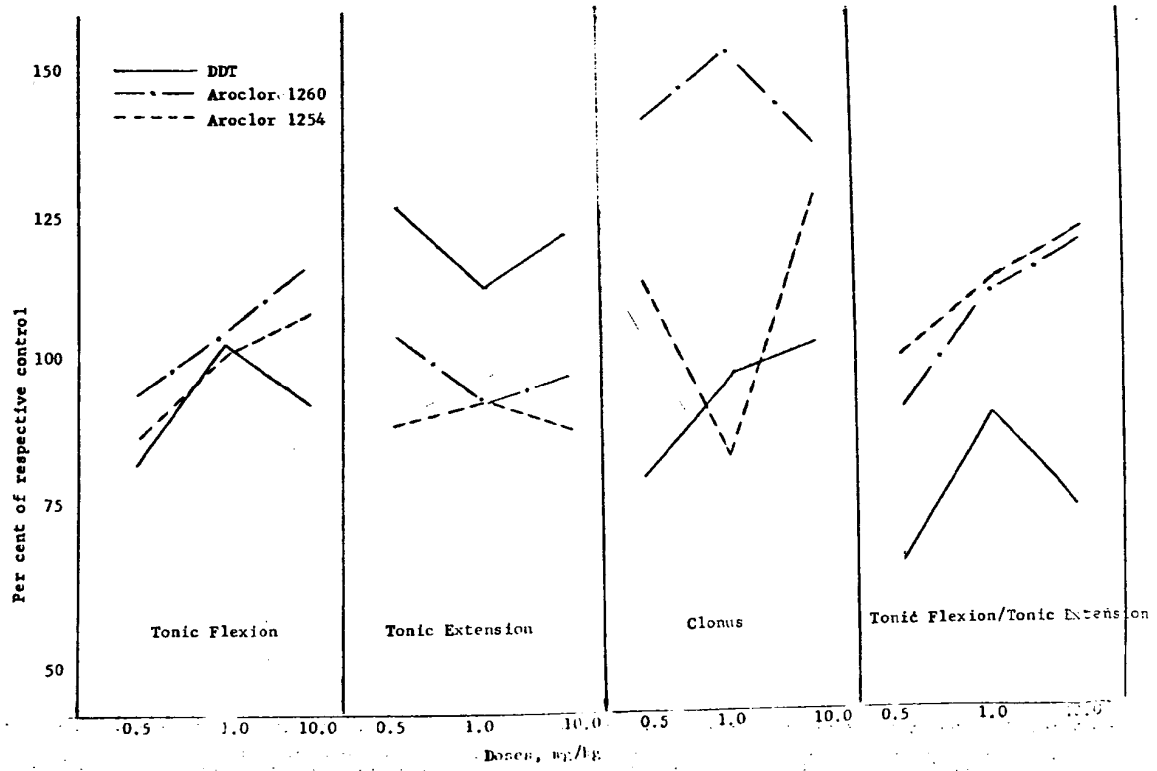

FIG. 3--Effect of DDT, Aroclor 1260, and Aroclor 1254 on maximum electroshock seizure 4 hr after dosing.

1260- and 1254-treated animals generally took a much longer time to enter the stress chamber when compared to their respective controls.

Further distinction between DDT and Aroclor compounds can be seen in their effects on MES pattern (Fig. 3). Mice treated with either Aroclor 1260 or 1254 exhibited a prolonged duration of clonus (Aroclor 1260 was more effective in this than was Aroclor 1254) and an increased tonic flexion/tonic extension ratio, and tended to have a decreased tonic extensor duration. Each of these effects is the opposite of that found after DDT treatment. Animals treated with DDT had a prolonged tonic extensor phase and a depressed tonic flexion/tonic extension ratio, and tended to have a decreased or unchanged clonic phase compared to controls.

Discussion

The present work has shown that DDT and polychlorinated biphenyls (specifically, Aroclor 1260 and Aroclor 1254) exert differential effects on the central nervous system. The behavioral inhibition induced by shock stress (3) is attenuated by DDT as seen by the facilitation of entrance into the shock (stress) chamber. The Aroclor compounds resulted in the opposite effect. These agents prolonged the latency to enter the shock chamber, thereby enhancing the inhibitory effects of stress.

The general level of central neuronal excitability is also differentially affected. The depression of the tonic flexion/tonic extension ratio (resulting from a decreased duration of tonic flexion and a prolongation of tonic extension) by DDT reflects an overall increase in brain excitability (4).

DDT also tended to exert a depressant effect on the clonic phase of MES. In contrast, the Aroclor compounds increased the tonic flexion/tonic extensor ratio (resulting primarily from the decreased duration to tonic extension). This reflects an overall decrease in central physiological excitability. The clonic phase, which is thought to be due to an active inhibitory system (5), is generally prolonged by the Aroclor compounds, especially Aroclor 1260.

The possibility exists that DDT may attenuate central inhibitory systems, while polychlorinated biphenyls may enhance central inhibitory systems, but further experimentation is necessary.

In summary, the present work not only has shown that the differential effects exerted by DDT and polychlorinated biphenyls distinguish these two classes of compounds, but also indicates that they exert opposite effects on the central nervous system.

References

(1) Carlton, P., in Progress in Brain Research, Vol. 28, Bradley, P., and Fink, M. (Eds.), Elsevier, New York, 1968, pp. 48-60.

(2) Weiss, J., McEwen, B., Silva, M., and Kalput, M., Science 163, 197-199 (1969).

(3) Stein, L., Chemistry of Reward and Punishment: Psychopharmacology - A Review of Progress 1957-1967, Public Health Service Publication No. 1836, Efron, D. (Ed.), U. S. Government Printing Office, Washington, D. C., 1968, pp. 105-123.

(4) Woodbury, D., and Vernadakis, A., in Methods in Hormone Research 5, Dorfman, R. (Ed.), Academic Press, New York, 1966, pp. 1-57.

(5) Gastaut, H., and Fischer-Williams, M., "The Physiopathology of Epileptic Seizures" in Handbook of Physiology (Neurophysiology), Section 7, Vol. 1, Field, J. (Ed.), American Physiological Society, Washington, D. C., 1959, pp. 329-363.