my comments to Mr. Wallace's letter

(1) Respiration is affected. Section was made just anterior to the pons through the peduncles, lamina quadrigemina and through the cerebral aqueduct ~~might through lower portion of midbrain~~ eliminating therefore almost all of the midbrain in addition to the cerebral hemispheres.

(2) It is difficult to interpret ~~sectioning~~ sectioning in frogs in regions between optic lobes, cerebellum and medulla, because the cerebellum is a very narrow structure. Interpretation of results is therefore difficult. (Besides we want information on higher animals.)

Is it not possible that motor pathways ~~are~~ could have become affected in the medulla, ~~and not~~ even though the circulatory and respiratory centers in this area are apparently not altered?

(3) The effects of DDT are delayed in the living animal; the results ~~are~~ might therefore be somewhat difficult to interpret particularly if one has to consider anesthetics in addition.

(4) Blood pressure and respiration were determined in unanesthetized animals in our case, and this I believe explains some of the differences.

(5) Our suggestive mechanism for the hypoglycemia is correct. This is indicated by glycogen analyses run recently.

Control rats showed normal glycogen content of the liver (3.8, 4.4, 3.6 and 3.5 g./100 g.).

Livers of severely poisoned rats contained only traces of glycogen (0.07, 0.13, 0.09 and 0.07 g./100 g.).

(6) If DDT had a marked effect upon the heart, I am sure that certain irregularities would have been noted since a concentrated solution was injected into the heart of the turtle.

The wing of severely poisoned animals contained only occasional traces of adhering substance

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Dr. William B. Deichmann
University of Cincinnati
College of Medicine
Cincinnati 19, Ohio

Dear Doctor Deichmann:

I have gone over very carefully the revised manuscript of your article on DDT. There were, as you know, many objections made to the original manuscript and I think that if the revision is circulated among the associate editors there still would be some objections. I realize that you have spent a great deal of thought and time in planning and carrying out your experimental work and I am taking the liberty of telling what I think could be done without very much difficulty to improve the manuscript in a way to your ultimate advantage. I am putting down then how the general problem appears to me and how your experimental work applies to it.

In the literature on DDT poisoning it is agreed that the principle action is on the central nervous system. This is shown in the animals tested by a state of general hyperexcitability with accompaniment of tremors and convulsions. The most characteristic symptom is the wide spread tremor. In considering the sites of action on the central nervous system there would be considered the cerebral hemispheres, mid-brain, medullary centers and spinal cord.

In your experimental work you show that after removal of the cerebral hemispheres tremors persist and this occurs also after removal of the cerebellum. In regard to the medulla, as shown by the experiments on respiration and blood pressure, there is no general stimulation here. On section of the cord tremors are absent in muscles supplied by nerves coming from below the cut level. In the peripheral nervous system on stimulation of the sciatic nerve a normal response is found which shows that there is no action on conductivity or on muscle. It would seem then that the part of the central nervous system which is primarily responsible for the occurrence of tremors is in the mid-brain. Various types of stimuli from without give rise to these tremors.

In the frog the convulsion is the typical toxic symptom. The location of action here can be shown easily by an experiment corresponding

to that demonstrating the location of action of picrotoxin. In this, serial sections are made from the cerebrum downward and the location of action is shown by determining at what stage in the sectioning the convulsions stop. In the mammals the relationship between the occurrence of convulsions and the occurrence of asphyxia is shown by the fact that the convulsions are stopped by artificial respiration.

In determining the action on smooth muscle it is necessary to show that DDT is in contact with the muscle in adequate amounts. It will be questioned whether your method allows the DDT to leave its oil solution and get into the muscle tissue in adequate amounts. In vivo experiments, with the DDT brought to the tissues through the general circulation, would be much more convincing and would show to what degree the response of the intestine and the uterus in poisoning differs from that of the control unpoisoned tissue. There are commonly used techniques for such experiments.

As actions on the blood pressure and respiration have been described by the Calvery group what should be brought out is the differences between your results and theirs.

In the blood sugar effects the initial rise could easily come from adrenaline action. In the hypoglycemia the exhaustion of available sugar caused by muscle activity seems unlikely as an explanation and since the DDT has an effect upon the liver, it is much more probable that interference with the glycogen breakdown has occurred.

In describing the action on the heart there will be the same objection raised to the experiments on the turtle and rabbit heart described in paragraph 1 on page 7. On this account this paragraph might well be omitted.

Finally, the expression that is used several times, "signs of illness" is too vague and could well be replaced by "toxic effects" or "signs of poisoning."

I think you will see from what I have written that what I have in mind is an orderly and convincing presentation of your experimental work.

Very sincerely yours,

George B Wallace

George B. Wallace
Managing Editor

GBW:vj
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