ARTICLES

2,2-BIS(p-CHLOROPHENYL)-1,1,1-TRICHLOROETHANE (DDT) DETERMINATIONS IN TISSUES, BODY FLUIDS AND EXCRETA OF HUMAN SUBJECTS[1]

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The recent unfavorable reports from publications of articles dealing with the toxicity of DDT have caused considerable public alarm concerning the hazards of using this substance as an all-purpose insecticide.

Since its widespread introduction in 1943, the Armed Services have utilized many tons of DDT in the control of insect and disease-bearing vectors throughout the world. The employment of specific insecticide crews in these programs over long periods of time presented excellent opportunities for the potential buildup of toxic tissue levels.

Extensive experimentation by various workers has produced conclusive evidence that DDT can be readily determined in animals by chemical analyses when toxic or sub-lethal doses are administered orally. Studies by Laug (1) indicate that DDT can be detected chemically in tissues, body fluids and feces of animals acutely poisoned by oral doses of DDT in digestible oil. The insecticide was reported in all fat examined but was concentrated in the perirenal fat in amounts 50 to 100 times greater than in other tissues. Toxic doses produced characteristic neurologic symptoms and the concentration of DDT in organs was explained on the basis of their specific fat content. Laug and Fitzhugh (2) reported the results of studies on rats chronically exposed to DDT for periods of six months to two years. The survivors from this chronic exposure *(oral feeding)* exhibited only moderate tremors during the initial phase of the experiment and later appeared to recover completely.

Prolonged exposure and contact with this agent in its various diluents or solvents had further increased the speculation that sufficient quantities may be absorbed through skin or mucous membranes to produce clinical symptoms of DDT poisoning.

In view of the active participation of military personnel in preventive medicine programs on overseas bases and in the Continental United States, a preliminary study was conducted by the investigators on a long series of laborers presenting unusual and prolonged environmental contact with DDT. A special effort was made to obtain the cooperation of those

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persons who presented histories of lengthy contact without regard to medical examination as the primary method of separation. Selected individuals most likely to demonstrate DDT concentrations in fat deposits of the body were taken from experienced malaria, insect pest and rodent control personnel. Their chief occupations consisted of compounding and mixing DDT-oil formulations, the dissemination of these solutions by means of the DDT-fog generator, the application of larvicides and adulticides by means of knapsack and power sprayers or the distribution of DDT dusts by hand-operated dusters in routine pest control operations.

In contrast to the many "disturbances" of body function as reported by Biskind (3) in a highly uncontrolled study, there were no signs or symptoms of illness attributable to DDT in any of our subjects. Biskind attempted to correlate reported exposures to DDT with cases of gastro-enteritis and the elusive "virus x" appearing in a series of patients examined by him. He neither confirmed the presence of a virus as the etiologic agent producing symptoms simulating those reported for DDT poisoning nor did he demonstrate by chemical means the presence of DDT in tissues, body fluids or excreta in this same series of patients. His conclusions, based solely on obtaining confirmative reports of exposure to DDT of any type, do not agree with the complete laboratory findings, case histories and results of specific chemical analyses obtained by us.

The present study represents the first effort chemically to detect DDT in biopsied fat from apparently healthy human subjects. In addition to tissue examination, twenty-four hour urine samples, feces and whole and citrated blood were obtained for chemical analyses. *In the first series recently completed, no DDT was detected in the material under study from sixteen (16) individuals detailing histories of exposure by contact for periods varying from six months to three years;* one subject presented a history of daily contact for a period of five years.

In a personal communication, Laug suggested that the presence of excessive quantities of nonsaponified fat or oxidative byproducts formed during analysis would seriously interfere with the detection of DDT. Thus any small quantity of DDT (possibly expressed in fatty tissue examined by one of us [L.J.B.]) would be difficult to evaluate by the usual colorimetric procedures. In these instances, the technique of Clifford (4) was followed whereby pancreatic lipase, prepared in the laboratory from fresh hog pancreas, was used as a lipolytic agent for the biopsied fat and fat-containing tissues. Specimens were subjected to a forty-eight hour period of lipolysis and extreme care was taken to eliminate interfering oxidative by-products. By this method, one gram of abdominal fat was reduced to approximately 50 milligrams of a nonsaponifiable residue. This material was then nitrated and analyzed by the procedure of Schechter et al. (5) in view of the extreme accuracy of their method in determining small quantities of DDT in suitable extracts.

In this series of human subjects having past histories of lengthy exposures, and in whom the DDT needed to be absorbed through the skin or inhaled from dusting or from aerosol operations for final detection, none could be demonstrated in any sample. The animals used for controls were sacrificed upon termination of the experiment and DDT was reported in amounts indicating a definite correlation between tissue and oral dosage levels.

These negative results obtained from human volunteers are important and significant observations. Since DDT is preferentially contained in fat, its presence represents actual storage rather than passive or temporary "flooding" of organs or fatty tissues. We are led to conclude, therefore, that (a) handlers utilizing normal precautionary measures not only fail to exhibit symptoms of DDT poisoning, but, (b) show no chemically detectable accumulation of DDT in body fat as a result of prolonged external contact with this agent. It likewise indicates that

malaria control operators can safely utilize the services of personnel over long periods of time without fear of developing toxic tissue levels of DDT.

Military personnel and their dependents exposed to DDT in areas where nightly fog applications are made have not exhibited any untoward reactions to oil fog or DDT proper. In many instances these subjects have been residents of "endemic" fog areas for three years or longer. It is felt that the cross-section of population represented on three large Marine Corps bases provided a significant sample from which our epidemiologic and clinical observations were made.

It must be stated, however, that DDT, like many insecticides, is lethal to man when ingested in high dosages; yet many of the deaths recorded in the literature are due in reality to pathologic alterations in tissues produced by the solvents ordinarily used such as kerosene or other organic diluents. It seems unlikely that the average individual would ingest sufficient DDT by accidental means to produce death as a result of changes in the central nervous system or in other vital organs. Individual sensitivities to this agent must also be considered. These individual idiosyncrasies must be eliminated by a systematic and careful analysis in determining plausible explanations for new disease entities.

Adequate personnel protection as practiced by insecticide distributors, the consideration given to recommendations for use, and the careful indoctrination and rotation of exposed individuals through varied duties within the organization have been in part responsible for the small number of toxicities known to date.

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