Effect of Parathion on the Skin of Guinea-Pigs

Parathion (0,0-diethyl O-(*p*-nitrophenyl) phosphorothioate) is being used extensively in the field of agriculture both as dusts and dilute sprays. Aerosol preparation containing 10% parathion is also being used in nurseries and green houses[1]. Occupational poisoning due to parathion is also common in workers engaged in the synthesis, formulation and application of this insecticide. Agricultural labourers like thinners, harvesters and irrigators frequently come in close contact with the insecticide. Literature on the histopathological changes in the skin of individuals repeatedly exposed to insecticide sprays and dusts is not adequate. Further physicochemical factors like temperature and environmental variations, apart from several other major factors (dosage, route of exposure, species, sex, nutritional status etc.), have been found to modify the absorption of the insecticide[2]. In the light of such variations, dermal application of insecticide under tropical conditions as in this country merits further study. This report, which is the continuation of our earlier observations[3], deals with the histopathological changes in the skin of guinea-pigs after they are exposed directly to the action of parathion.

Materials and methods. 40 female guinea-pigs (ITRC stock) with an average body weight of 250 g were used in the experiment. The lateroabdominal area measuring approximately 4 × 4 cm was previously made ready by hair clipping for parathion painting. Parathion (technical grade ICI 98.70% purity) was used after diluting it to 1 ppm strength with 50% ethanol. 1 ml of the solution was slowly transferred on the specified area of the skin with the help of a graduated pipette attached to a vaqupette. 30 animals were treated with 1 ml of parathion, daily for a period of 15 days (total number of skin paintings 15). 10 animals of the control group were painted with 1 ml of 50% ethanol. The animals were killed 24 h after 5th, 10th and 15th paintings. Paraffin cut sections of the skin were stained with haematoxylin and eosin and Masson's Trichrome for histopathological observations.

Results and discussions. No clinical symptoms of poisoning or death due to parathion painting on the skin were noticed in any of the animals during the period of experimentation. Macroscopic examination of the skin of these animals at the end of 15 days did not show dermatitis or any other noticeable changes.

Microscopic study of the insecticide painted skin, however, revealed various pathological changes which were absent in the skin of control animals (Figure 1). Hyperkeratinization of the epidermal layer and the thickening of the stratum corneum was observed in the animals painted for 5 days (Figure 2). In the 10-days painted animals, the dermis showed scattered infiltration of mononuclear cells. Subsequent application of parathion caused the mononuclear cells to become more localized in their distribution around hair follicles and sebaceous glands (Figure 3). In the earlier paintings, dermis also showed mild proliferation of connective tissue around hair follicles and sebaceous glands but further application of the insecticide increased the degree of proliferation (Figure 4). The Collagen and reticular fibres in the dermis were swollen and fused (Figure 5). Mild damage to the endothelial cells of the blood vessels was observed in the 5-day painted preparations, but additional paintings produced changes like the thickening of the wall of the blood vessels, and swelling of the endothelial cells. A mild perivascular inflammatory infiltrate was also present (Figure 6).

Exposure of the skin surface to different insecticides is a common phenomenon among workers engaged in insecticide formulations, spraying and dusting of fruit orchards as well as in public health. Carelessness on the part of workers to observe precautionary measures have increased the chance to absorb more of these toxicants through their skin[4,5]. Recently MAIBACH[6] has shown that pesticides are largely absorbed into the body through the skin.

Studies of FREDRIKSSON[7,8] have indicated beyond doubt that the present method of decontamination procedures of the exposed parts of the body through water and soap wash usually followed under field conditions does not minimise the insecticide hazards. Furthermore, an apparently long incubation period, often of several

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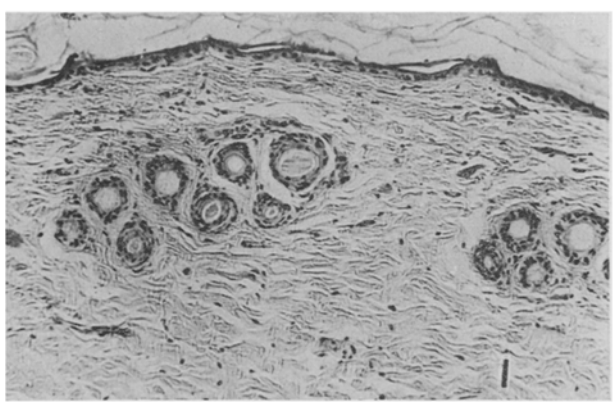

Fig. 1. Control (50% ethanol alone); H & E. × 124.

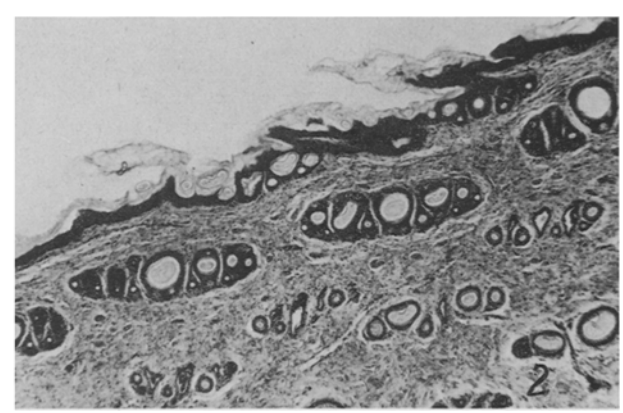

Fig. 2. Hyperkeratinization and thickening of the stratum corneum, H & E. × 47.

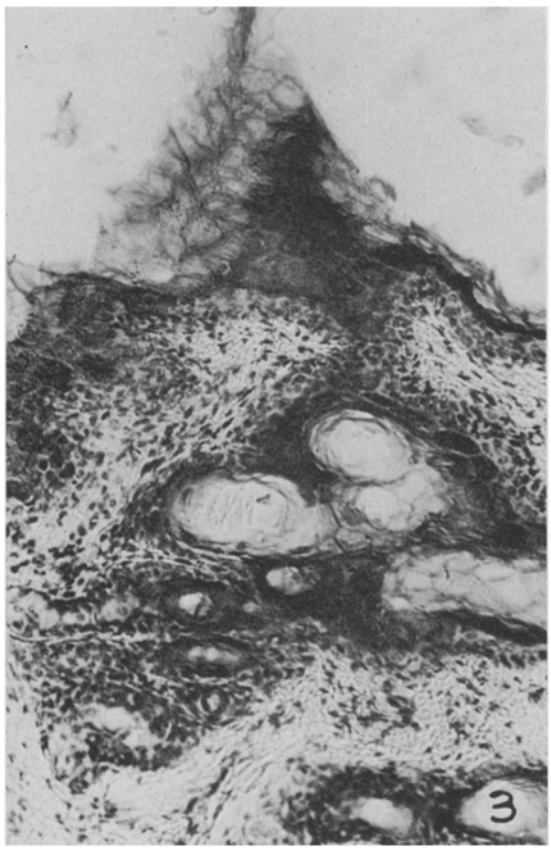

Fig. 3. Proliferation of mononuclear cells in the dermis; H & E. × 170.

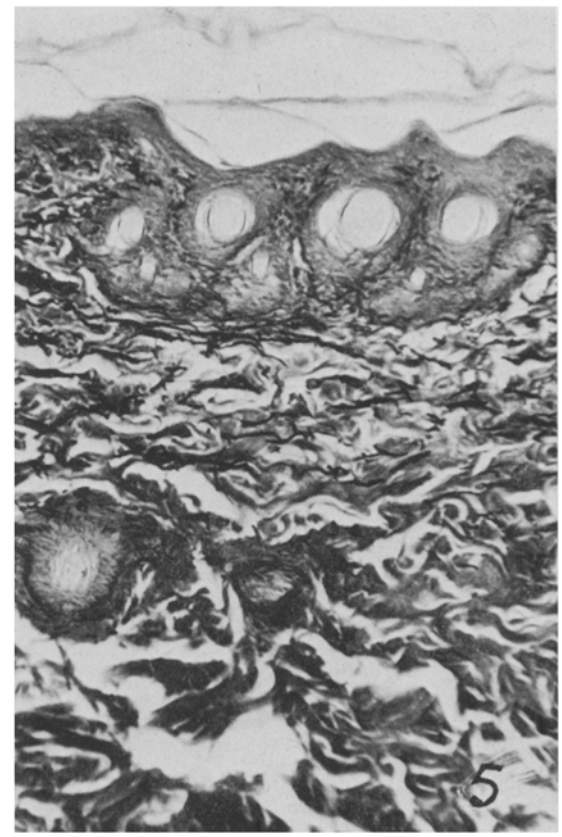

Fig. 5. Dermis with swollen and fused collagen and reticular fibres; Masson's trichrome, × 170.

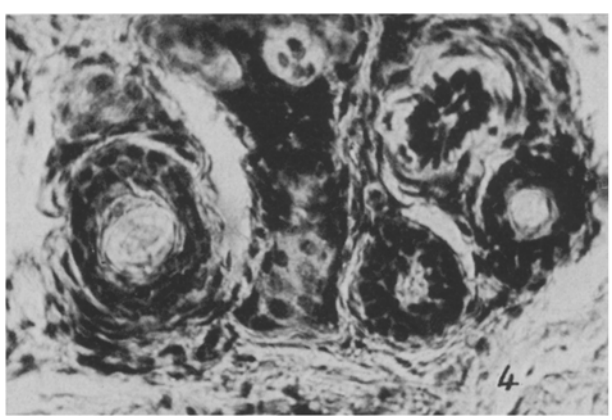

Fig. 4. Dermis showing proliferation of connective tissue around hair follicles and sebaceous glands; H & E. × 320.

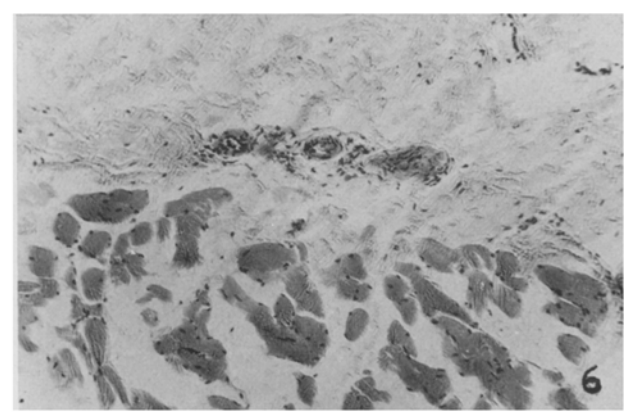

Fig. 6. Thickening of the wall of the blood vessel and mild perivascular inflammatory infiltrate in the dermis; H & E. × 80.

hours, follows between the initial contamination and actual wash and this makes skin decontamination quite unsuccessful. Though this is true for all insecticides, it is more so with parathion which is more stable[9].

The findings reported here are of considerable interest because of their possible relationship to cases of delayed poisoning through skin absorption under tropical conditions. Pathological changes that appear may not be the same among different species. Furthermore, the presence of chronic skin diseases in agricultural workers appear to augment the rate of absorption of the insecticide and result in skin lesions[10].

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Since the skin of guinea-pig differs from that of man in having mosaic pattern of hair growth, it should be understood that these abnormalities are not interpreted as an indication that the pathological picture would be similar in man also. However, information gathered through these experiments has thrown light on our further understanding of the possible types of tissue damage due to insecticides, and has emphasized due caution in their handling[11].

Zusammenfassung. Nach täglicher Applikation of Parathion werden histologisch Veränderungen der Meerschweinchenhaut festgestellt.

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Complex Formation Between Bee Venom Melittin and Extract of Mouse Skin Detected by Sephadex Gel Filtration

We have been interested in the pharmacological properties of the venom of the honey bee (*Apis mellifera*), and of its isolated constituents. Melittin, the major component of the venom, has been studied by several investigators, since its isolation from whole venom by gel filtration[1,2]. The amino acid sequence of this polypeptide has been determined[3], some of its biochemical reactions have been studied in vitro[4], and its antibacterial properties have been recorded[5]. This unique, surface-active, cationic, histone-like moiety has been found to be slightly radio-protective in mice[6], and may be synergistic with the main radio-protective fraction of bee venom phospholipase A[7,8].

The cationic property of melittin partly accounts for its cytotoxicity with respect to mouse bone marrow stem cells, an effect observed in our earlier study[9]. In that work it was concluded that the stoichiometric relationship between the cell surface area and the weight of added melittin, vis-a-vis cytotoxicity of melittin, could be explained by the known charge on the polypeptide. This interaction between melittin and the cell surface raised questions about the ability of melittin to directly enter the body via the subcutaneous injection route. It was also found during this same study[9] that the addition of purified human serum albumin (fraction V) protected bone marrow cells from melittin cytotoxicity. The lack of such protection by other serum fractions suggested the possibility that a complex formed between melittin and fraction V.

The present work was undertaken to answer the question raised by these two observations, namely, whether: 1. melittin on s.c. injection enters the body as such or 2.

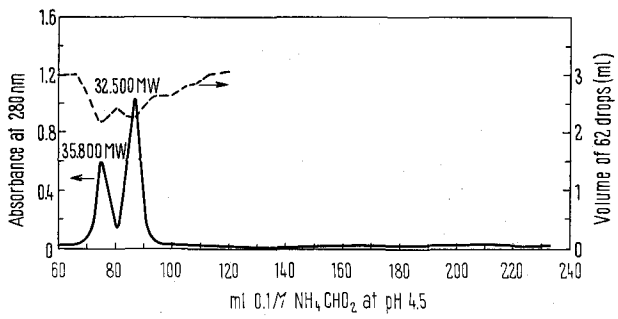

Fig. 1. Separation of the components of human serum albumin (fraction V) on a Sephadex G75-40 column.

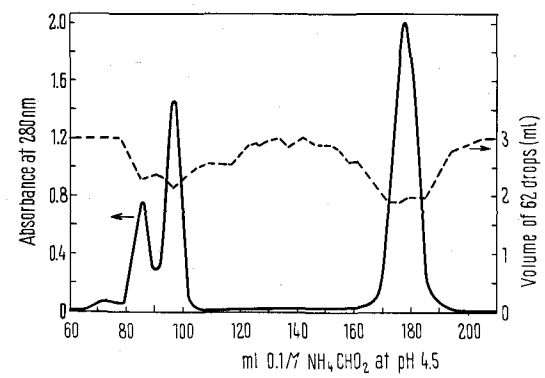

Fig. 2. Separation of the components of a mixture of 27.7 mg human serum albumin (fraction V) and 16.6 mg melittin on a sephadex G75-40 column.

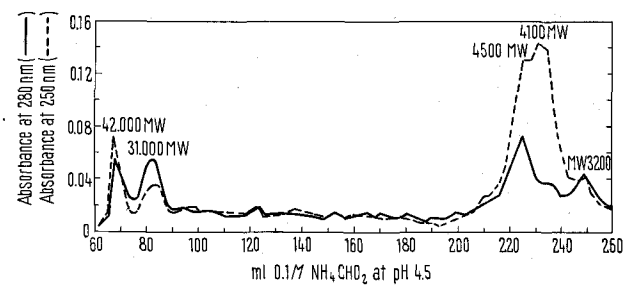

Fig. 3. Separation of the components of mouse skin extract on sephadex G75-40 column.

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