Discussion. The experimental teratogenic effects of certain metals have been demonstrated in the golden hamster[3–5], and the toxic properties of indium have been studied in the rabbit[6] and rat[7]. The protective effect of ferric dextran on the hepatic lesions induced by indium alone led to the suggestion that ferric dextran stimulates the formation of a PAS-stainable material wherever ferric dextran is deposited in tissues[1]. This material might account for this protective effect against indium-caused liver damage. The teratogenic protection afforded by ferric dextran might be quite specific for it is the only agent out of several investigated, which protects against indium-induced liver damage[1].

The protective effect of certain substances against the known teratogenic activity of other substances has been documented previously. Thus, LANDAUER and CLARK[8] have shown that malformations in chicks produced by treatment with 6-aminonicotinamide can be prevented with the simultaneous administration of 3-acetylpyridine. As far as metals are concerned, zinc protects against the teratogenic action of cadmium in hamsters[4], and selenium protects against the teratogenic effects of both cadmium and arsenic[9]. These observations suggest that further intensive investigations concerning the interactions of various molecular teratogens will yield interesting and valuable information concerning the morphogenesis of congenital malformations[10].

Zusammenfassung. Nach Indiumnitratinjektion bei Goldhamstern mit 8-tägiger Schwangerschaft wird eine erhöhte Mortalität der Embryonen sowie Gliedmassenanomalie gefunden. Bei gleichzeitiger Verabreichung von Eisendextran (Imferon) werden die Embryonalschäden weitgehend unterdrückt.

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Dermal Toxicity of DDT[1]

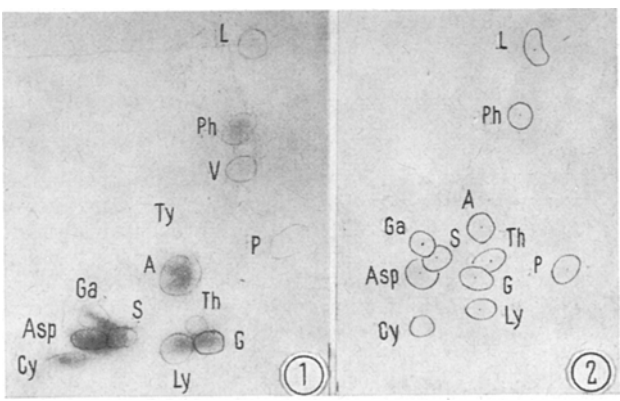
Various authors[2–9] in recent years have reported that the occupational poisoning by agricultural chemicals is more due to dermal absorption of the chemicals than to exposure by other routes. This indicates the degree of importance of the dermal toxicity studies and the amount of care and precautions needed in handling these chemicals. Among different insecticides, DDT perhaps ranks as the most extensively used and studied insecticide. Its application is diverse and well known. It is the best known, the cheapest and one of the most effective of the synthetic chlorinated hydrocarbon insecticides[10].

The present study has been made to show the biochemical alterations and the manner of damage that it may inflict on the cells of the skin tissue of guinea-pigs when applied dermally. There appears to be no literature on this point.

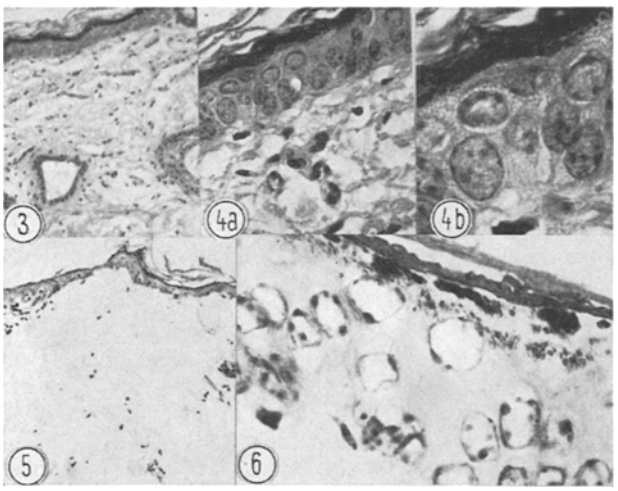
Materials and methods. ITRC bred guinea-pigs (body weight 350–400 g) were used throughout the experiment. The hair was removed on the latero-abdominal areas. DDT dissolved in absolute acetone was painted on those areas for a period of 3 weeks and 5 days in a week. The applied dosage of DDT ranged from 322 mg/kg to 400 mg/kg – a dosage 8–6 times less than the known acute dermal LD_{50} values for the female rats (Dermal LD_{50} values of DDT to female rats is 2,510 mg/kg). The animals of the control group received only the acetone painting for the same length of period. At the end of the experiment the animals were sacrificed and skin of the painted regions was removed and processed for the qualitative estimation of free amino acids according to the methods of AWAPARA[11]. Details of paper partition chromatography for the identification of free amino acids are reported elsewhere[12]. Histopathological observations of the skin tissue were also made with the help of paraffin sections, stained with iron haematoxylin and eosin.

Normal skin of female guinea-pigs contained the following free amino acids: alanine, aspartic acid, cysteic acid, glycine, glutamic acid, L/n-leucine, lysine, phenylalanine, proline, serine, threonine, tyrosine and valine. Of these, leucine, proline, serine, threonine, tyrosine and valine were present in 'trace' levels while the levels of the remaining amino acids were above normal. The significant changes in the relative concentration of the ninhydrin reacting constituents of the skin of the control and DDT-painted female guinea-pigs were very clearly detectable on the chromatograms (Figures 1 and 2). A tremendous decrease in the level of almost all amino acids of the skin was witnessed in the DDT-painted guinea-pigs.

WITTER and FARRIER[13] reported that DDT, when administered orally to albino rats, did not show any significant effect on levels of glutamic acid, alanine and



Figs. 1 and 2. Effect of DDT on free amino acids of guinea-pig skin; (1) control, (2) DDT-painted. A, alanine; Asp, aspartic acid; Cy, cysteic acid; G, glycine; Ga, glutamic acid; L, leucine; Ly, lysine; Ph, phenylalanine; P, proline; S, serine; Th, threonine; Ty, tyrosine; and V, valine.



Figs. 3–6. Effect of DDT on the skin. 3, 4a and 4b showing the normal cells. 5 and 6, vacuolization and degeneration of cells (DDT-painted).

glutamine of brain. DDT when applied dermally to female guinea-pigs did, however, show certain interesting findings which included the depletion in the levels of different amino acids of the brain and kidney[12]. ROBERTS and TISHKOFF[14] reported a fall in the level of free amino acids of the tumors. These workers advocated that the pattern of free amino acids may be used as an appropriate tool in the identification of carcinomas from the non-malignant epidermis.

Histopathological findings also show that a constant application of DDT on the skin of guinea-pigs induces certain changes in the cell structure of the tissue. Thus, in comparison with the skin of control animals, DDT-painted skin showed the proliferation of hair follicles and increased degree of keratinization. Cytological observations also showed features of disruption and degeneration in the cells of the basal layer. Cells of the stratum malpighi carried vacuolated nuclei and 1–2 eosinophilic bodies indicating the early signs of damage (Figures 3–6). Depletion in the level of amino acids have a bearing on the structural changes of the cells observed under light microscope and electron microscope. While normal cells carry a highly developed endoplasmic reticulum, the same in the cells of the poisoned animal largely disappears and presents a vacuolated condition (details in COHEN et al.[15, 16]).

Zusammenfassung. Auf die Haut von Meerschweinchen appliziertes DDT bewirkt eine Verminderung im Aminosäuregehalt des Hautgewebes. Histopathologisch wurden Veränderungen im Bereich des Gewebes und der Zellen festgestellt.

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[1] 1,1,1-Trichloro-2,2-*bis*(P-chlorophenyl ethane) (P-P'DDT). P-P', isomer of 99.8% purity was generously supplied to us by J. R. Geigy & Co., Basle, and their help is gratefully acknowledged by the authors.
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Influence of Sodium on the Ability of Tyramine to Release Norepinephrine in Isolated Guinea-Pig Left Atrium[1]

It has been suggested that certain drugs are capable of enhancing the effects of norepinephrine and decreasing the effects of tyramine by blocking the uptake of both amines into adrenergic nerve endings (TRENDELENBURG[2]; FURCHGOTT et al.[3]; JOHNSON and KAHN[4]). More recently COMMARATO et al.[5] have presented evidence which supports the hypothesis that norepinephrine and tyramine are taken up by adrenergic nerve terminals through the same uptake system. If this were indeed the case one would expect that sodium deprivation, which has been shown to block the uptake of norepinephrine (IVERSEN and KRAVITZ[6]; GILLIS and PATON[7]; HORST et al.[8]; BOGDANSKY and BRODIE[9]), would also block the release of catecholamines induced by tyramine. The present experiments were undertaken in order to test this possibility.

Methods. Left atria from guinea-pigs were prepared and mounted, as previously described by FURCHGOTT et al.[3]. In each experiment one half of the atrium served as a control. The bathing solution was Krebs bicarbonate containing 10 m*M* glucose and 10^{-5} g/ml of ethylenediaminetetraacetic acid (EDTA). A mixture of 95% O_2 and 5% CO_2 was bubbled through the bathing solution. All preparations were electrically driven at a frequency of 30 beats/min. Atria were attached to force-dispacement transducers (Grass, Model FT.03) and mechanical activity was recorded by means of a Grass Polygraph. When low-sodium solution was used, the osmotic pressure of the solution was maintained with equivalent amounts of sucrose.

The catecholamines analysis was performed according to the method of ANTON and SAYRE[10]. Results are expressed as µg of norepinephrine base per g of tissue. All values reported in this paper are corrected for the degree of recovery.

The doses of drugs used (Iproniazid phosphate, norepinephrine bitartrate and tyramine hydrochloride) are expressed in terms of g of salts per ml of medium in the muscle chamber.