cur secondary to pathological changes in the stria vascularis, although a causal relationship has not been proven.

However, it is possible that injury to the stria vascularis, associated with melanin-induced drug accumulation there, could result in changes in endolymph composition and ultimate hair-cell damage. If this were the mechanism of action then, given the observed differences in strial lesions between albino and pigmented animals, differences would be expected in the degree of hair-cell damage and consequently in the degree of hearing impairment. This appears not to be the case.

It might therefore be interesting to discover whether the accumulation of ototoxic drugs in the strial melanin would be reflected in higher levels of the drugs in the endolymph of pigmented animals, where they could exert a direct effect on the hair-cells. If such differences in drug endolymph level were not observed it would argue for a more significant role of direct effect of the drugs on the hair-cells rather than one mediated through strial damage and would explain the failure to observe any differences in hearing impairment between albino and pigmented animals.

Pseudolymphoma of Skin Induced by Oriental Hornet (*Vespa orientalis*) Venom

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Summary. Intradermal injection of saline suspension of *Vespa orientalis* venom sac to 57 black mice caused a local nodule composed o flymphocytes, few histiocytes and plasma cells 10 to 12 days following the injection. This reaction simulates the pseudolymphoma reaction observed in humans following arthropode stings.

The histological lesions in arthropode stings have two distinct components which may or may not be combined. Changes in the epidermis manifested by pseudoepitheliomatous hyperplasia and dermal infiltration [1-3].The dermal inflammatory infiltration may consist either of necrotizing lesions with abundant eosinophilic leucocytes, or as a dense lymphocytic infiltration [1-3]. This dense lymphocytic infiltration can simulate lymphoma infiltrating the skin and the term 'pseudolymphoma' was used [1,2]. In an extensive study of the effect of oriental hornet (*Vespa orientalis*) venom on various organs, intradermal injection of oriental hornet venom was examined in various animals [4,5]. In guinea-pigs and rats, intradermal injection of the venom causes an acute inflammatory response with abundant eosinophils [4,5]. Injection of hornet venom into young black mice causes a dense local lymphocytic infiltration simulating lymphoma.

Twelve 10-day-old C 57 black mice were injected with a saline suspension of *Vespa orientalis* venom sac (150 mg/0.1 ml) intradermally in the back area. The animals were sacrificed at days 2, 4, 6, 10, 12 after injection and the

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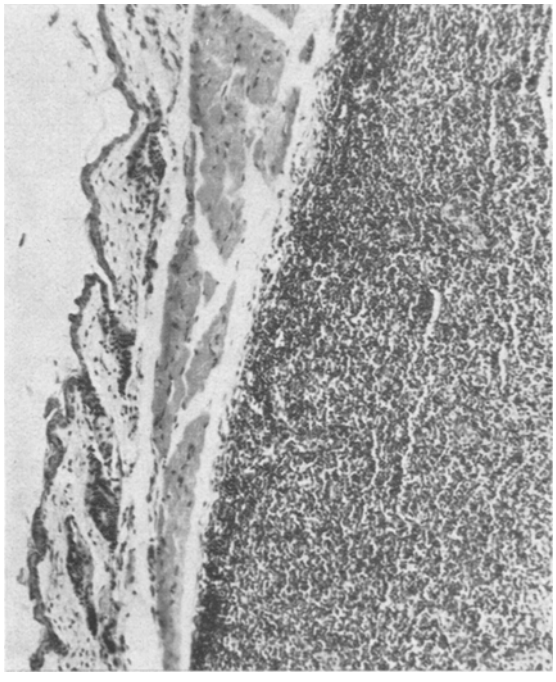

Fig. 1. Skin showing normal epidermis and upper dermis. A dense infiltration composed mainly of lymphocytes in the lower dermis. Hematoxylin-eosin stain. × 80.

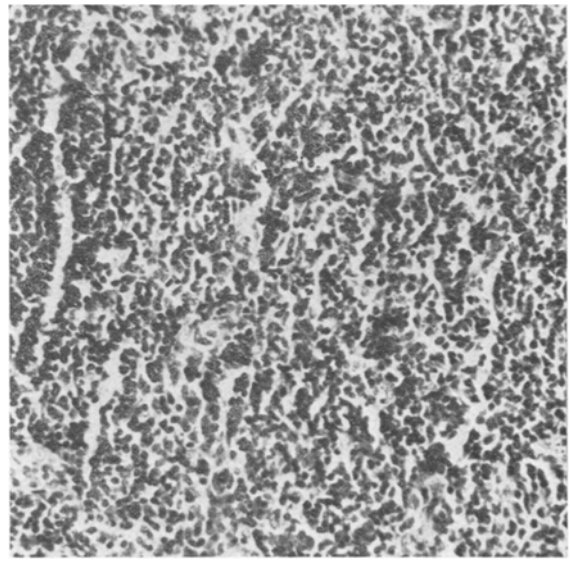

Fig. 2. Higher magnification of the dermal infiltration. Abundant small lymphocytes, few plasma cells and eosinophils. Hematoxylin-eosin. × 200.

skin taken from the site of injection for microscopic examination. The tissue was fixed in 10% formalin, embedded in paraffin and sections were stained with hematoxylin-eosin.

Three of 12 animals sacrificed at days 10 and 12 showed a pink coloured nodule at the injection site. Microscopic examination showed normally preserved epidermis and upper dermis. In the lower dermis and subcutaneous fatty tissue, a localized well circumscribed nodule, composed mainly of lymphocytes, was seen (Figure 1). Higher magnification (Figure 2) showed a dense collection of mature lymphocytes, few large histiocytes with large oval clear nuclei, and few plasma cells.

A recent study of the pharmacological activity of oriental hornet venom[6] showed that the venom possessed protease, hyaluronidase, released histamin from mast cells, caused hemolysis and was immunogenic. The antigenic effect of the venom might explain the clinical anaphylactic reaction attributed to the venom[7]. The similarity of pseudolymphoma of the skin to drug-induced pseudolymphoma is striking. Patients taking anticonvulsants, particularly diphenylhydantoin (Dilantin) and nephenytoin (Mesantoin) can develop lymphadenopathy which on microscopic examination may simulate lymphoma[8–10]. It has been suggested that this syndrome represents a drug-induced sensitivity resembling a serum sickness hypersensitivity reaction, or possibly a genetically determined enzymatic defect as seen in primaquine sensitivity[8,11]. The fact that venom injection to various animals did not show the pseudolymphoma reaction, whereas only C 57 black mice developed this reaction, supports the notion that this reaction is genetically determined.

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Acute Effects of Tolamolol on Renal Function in Hypertensive Patients[1]

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Summary. The renal haemodynamic effects of a single i.v. administration of tolamolol were studied in 9 hypertensive subjects. No change of GFR and ERPF was observed after tolamolol, while urine output decreased and urine creatinine concentration increased. A reduction of the heart rate was confirmed. Blood pressure was unchanged.

Tolamolol, a phenoxypropranolamine compound (Pfizer, UK-6558–01), is a new β-adrenergic blocking agent. Although preliminary studies have indicated that it exerts an antihypertensive action[4], there are no data available concerning its effects on renal function. This knowledge seems to be necessary before undertaking any further clinical investigations, since most antihypertensive drugs decrease the glomerular filtration rate (GFR) and the effective renal plasma flow (ERPF). The present study has been designed to examine the effect of intravenously administered tolamolol on renal function (GFR and ERPF) of hypertensive patients.

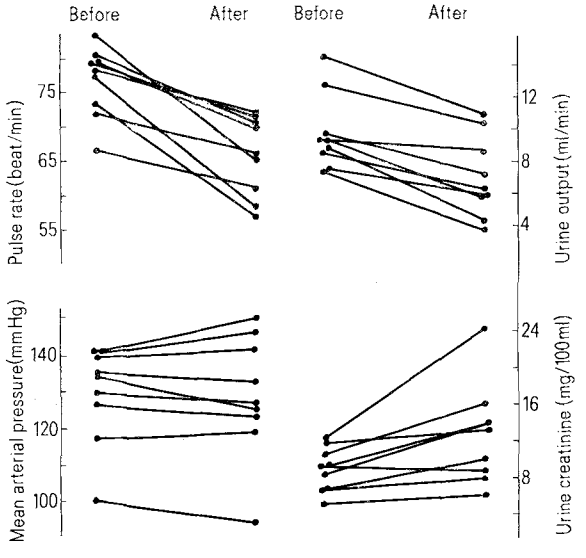

Fig. 1. Variations of different parameters in individual patients before and after tolamolol administration.

Material and methods. 9 hypertensive female patients (4 with essential hypertension, 1 with renovascular hypertension, 3 with pyelonephritis and 1 with nephritis) were examined. The age of the subjects studied was between 34 and 52 years (mean 43.11 ± 6.64 SD). At basal conditions their mean arterial pressure (MAP) ranged from 100.53 to 140.65 mm Hg (mean 129.57 ± 12.46 SD), GFR from 55.71 ml/min to 134.60 ml/min (mean 93.69 ± 22.99 SD) and ERPF from 227.08 ml/min to 600.28 ml/min (mean 410.35 ± 103.25 SD).

The patients were hydrated by administration of 1 l of water during the 60 min preceding the experiment. Thereafter each patient drank 200 ml of water every 20 min. Diatrizoate-I^{131} and hippuran-I^{125} were used for the measurement of GFR and ERPF respectively. Renal clearances were determined by continuous venous infusion of

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[2] We acknowledge with thanks Pfizer Central Research, European Group, Brussels, for supplying tolamolol. Our sincere thanks go to Dr. R. Panetta for his assistance in the preparation of the manuscript.
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