pretation is further supported by the observation that all the tissues had greatly reduced noradrenaline levels after treatment with 6-hydroxydopamine whether assayed biochemically, or assessed by histochemical fluorescence microscopy. Furthermore, responses to the sympathomimetic amine, tyramine, were greatly reduced or abolished in those tissues (heart, ear artery, renal artery and portal vein) where its mode of action is known to involve the release of noradrenaline from sympathetic nerves.

It is concluded that pretreatment of rabbits with 6-hydroxydopamine according to the dose schedule described above, produces marked impairment of sympathetic neuronal function in the tissues examined.

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Prostaglandin E_2, inflammation and pain threshold in rat paws

D. C. KUHN and A. L. WILLIS

Department of Pharmacology, Hoffman-La Roche Inc., Nutley, New Jersey, U.S.A.

We have examined relationships between disappearance of injected prostaglandin (PG) E_2 from the paws of rats and the duration of the PG-induced oedema and hyperalgaesia.

Prostaglandin E_2 (1 μg, 0·1 ml), containing ^{3}H-PGE_2 (0·47 ng, 0·12 μCi) was injected into the subplantar surface of hind paws in rats. At various times after injection, 'pain threshold' (Randall & Sellito, 1957) was measured and the paws excised, weighed and frozen in liquid nitrogen. The prostaglandins were extracted (at pH 2·8) from crushed paw material into ethyl acetate. Radioactivity in the extracts was determined by liquid scintillation counting.

Extractable radioactivity, disappeared very rapidly from the paws, and when peak swelling was attained (20 min), the equivalent of only 25 ng of PGE_2 could be recovered. The oedema produced by the PGE_2 was short lived, decaying at a rate which was superficially similar to, but slower than disappearance of the injected PGE_2. In contrast, the hyperalgaesia developed more slowly and lasted for at least 6 h, even though the amounts of originally injected PG were apparently very low (equivalent to about 0·7 ng of PGE_2).

The occurrence of hyperalgaesia has been reported following or during injection or infusion (respectively) of E-type PGs into human skin (Solomon, Juhlin & Kirschenbaum, 1968 ; Juhlin & Michaelsson, 1969 ; Ferreira, 1972). However, chronic hyperalgaesia is produced after prolonged subdermal infusion of low concentrations of PGE (Ferreira, 1972) or within four days of repeated daily injections of PGE_2 (1–2 μg) in rat paws (Willis & Cornelsen, 1973). A little (equivalent to about 0·4 ng PGE_2) radioactivity could still be extracted from the paws at 24 h, and it is possible that some of the PGE_2 could have been converted to poorly extractable material. Thus the chronic hyperalgaesia in rat paws might be partly due to accumulation of PG metabolites which produce hyperalgaesia and this is being investigated.

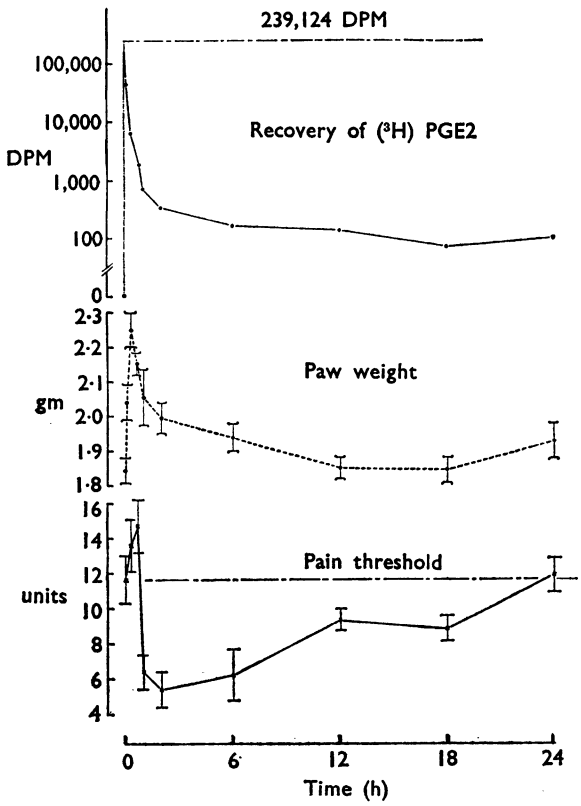

FIG. 1. Temporal relationship between disappearance of injected PGE_2, paw weight and 'pain threshold'. Results shown are means (±S.E.M.) for 16 pairs.

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A method for perfusing the whole rabbit ear with homologous blood

C. NICOL (introduced by A. G. H. BLAKELEY)

Department of Pharmacology, University of Glasgow, Glasgow G12 8QQ

Dutch rabbits of either sex, weighing 1·5–3·0 kg are used. The rabbit is anaesthetized with 4% Halothane in a 2:1 mixture of N_2O/O_2. The trachea, external jugular vein and carotid artery are cannulated. The rabbit is injected with 4,000 I.U. Heparin and 50 μg prostaglandin E_1 to prevent clotting of the blood and aggregation of the platelets, Blakeley, Brown, Dearnaley & Woods (1969). Approximately 30–40 ml of warm oxygenated Krebs' bicarbonate saline is infused into the rabbit and the animal is bled out. The ears are then cut off close to the head, one being used as a control. The skin is shaved over the central artery near the base of the ear. The artery is then exposed by blunt