day), or from (3) animals in which 1–2 cm of both hypogastric nerves were removed 1 or 5 days previously.

One day treatment failed to cause supersensitivity. Both 5-day reserpinization and 5-day decentralization resulted in a substantial increase in sensitivity to noradrenaline and methyl furmethide (Fig. 1). Similar results were obtained when histamine and potassium were used as stimulants, although the magnitude of the sensitivity increase to potassium (1·5-fold at the ED50) was considerably less than that to the other agents.

Fleming (1963) proposed, on the basis of indirect evidence, that an alteration of the electrical properties of the smooth muscle cell membrane might be involved in the development of supersensitivity. Since the vas deferens exhibits supersensitivity *in vitro*, as shown by the present experiments, a study of the electrophysiological behaviour and of the ion distribution in this tissue is now in progress.

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The inhibitory innervation of the bovine iris sphincter

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The presence of an inhibitory, as well as an excitatory, component in the innervation of the sphincter pupillae has been known for some years (Joseph, 1921). Anatomical evidence for adrenergic innervation to the sphincter is well documented for a number of species (Laties & Jacobovitz, 1966; Malmfors, 1965; Richardson, 1964). In this work the nature of the adrenergic innervation of the bovine iris sphincter has been further investigated. Isolated preparations of sphincter muscle were used to study the effects of transmural electrical stimulation and of directly acting sympathomimetics and the modification of these effects by blocking agents.

Eyes were removed from cows immediately after killing, and stored in Krebs solution at 3°–4° C until used (2–24 hr). Iris sphincter loops were dissected from the eyes and mounted in Krebs at 37° C aerated with 95% O_2/5% CO_2. Movements of the sphincter were recorded isotonically under a tension of 450 mg. Preparations were stimulated transmurally from a square wave stimulator. The parameters of stimulation were 150 V, 0·3 msec pulse width and frequencies of 2 to 80/sec for periods of 15 sec at intervals of 5·5 min.

Recordings were begun when the tissue had taken up a steady spontaneous level of tone (usually after about 2 hr). The sphincter then gave a biphasic response to transmural stimulation, the contractile phase of which could be abolished, at all frequencies used, by hyoscine (5×10^{-8} g/ml.). Eserine or neostigmine potentiated this component in concentrations of 10^{-6} g/ml. The α-receptor blocking agents phentolamine or piperoxan in concentrations up to 10^{-5}M had no significant inhibitory

action on the contractions, indicating the absence of an alpha excitatory component in this phase. This was supported by the results of experiments with noradrenaline, oxymetazoline and phenylephrine in the absence or abolition of tone.

The relaxant component of the response to transmural stimulation was strongly inhibited by guanethidine, bethanidine, dimethylphenylpiperazinium and debrisoquin. Inhibition of this component was also obtained with Sotalol (5×10^{-8} g/ml.), but propranolol was less potent. The ratio of the EC50s with (—)-isoprenaline, (+)-isoprenaline, (—)-adrenaline, (—)-noradrenaline (1 : 33 : 300 : 1,150), together with the blockade of (—)-isoprenaline by Sotalol (5×10^{-7} g/ml.-10^{-5} g/ml.) support the conclusion that a β-receptor is responsible for the mediation of the inhibitory component in the bovine iris sphincter.

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Enhanced release of transmitter during sympathetic nerve stimulation in the presence of angiotensin

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Angiotensin can influence sympathetic function in such diverse ways as excitation of ganglia (Lewis & Reit, 1965; Farr & Grupp, 1967; Aiken & Reit, 1968), increased biosynthesis of noradrenaline (Boadle, Hughes & Roth, 1969) and potentiation of responses to sympathetic nerve stimulation (Bennelli, Della Bella & Gandini, 1964; Zimmerman & Gomez, 1965; Sjöstrand & Swedin, 1968). The potentiation of postganglionic sympathetic nerve stimulation by angiotensin could be explained by either a facilitation of noradrenaline (NA) release (Zimmerman & Gisslen, 1968), or by the inhibition of the re-uptake process for NA (Palaic & Khairallah, 1967); both these possibilities have now been investigated.

Uptake of ^{3}H-NA was studied in rat isolated hearts perfused with Krebs solution; ^{3}H-NA (5 ng/ml., specific activity 7–9 c/mM) was infused for 2, 5 and 10 min periods. Angiotensin II amide (Ciba, 100–1,000 ng/ml.) did not reduce the uptake of radioactivity at any of the time periods studied, indicating that the polypeptide does not exert cocaine-like effects, even at the highest concentration used.

The rabbit portal vein was used to study the release of transmitter during transmural stimulation of intramural sympathetic nerves (Hughes & Vane, 1967). The vein was preincubated with ^{3}H-NA (50 ng/ml., 0·25 mc) for 2–3 hr; it was then mounted in air surrounded by a water jacket maintained at 37° C. The vein was superfused with Krebs solution at a constant flow of 4 ml./min and contractions of the vein were detected with an isometric transducer coupled to a direct writing ink recorder. The superfusate was collected at timed intervals and the radioactivity determined by liquid scintillation spectrometry. NA and its metabolites were separated by alumina and Amberlite resin procedures (Roth & Stone, 1968).