An Adrenergic Neurone Blocking Action of Dimethylphenylpiperazinium

SIR,—Recent work in this laboratory has attempted to localise the site of sympathetic inhibition in the isolated small intestine of the guinea-pig (Wilson, 1962) using transmurally stimulated (Paton, 1955) "Finkleman" (1930) preparations set up in Krebs's solution at 37°. With two sets of platinum electrodes and different stimulation parameters, the parasympathetic cholinergic nerve plexuses in the gut wall and the periarterial sympathetic adrenergic fibres may be stimulated both independently and simultaneously. A base-line of just submaximal transmural twitches is first obtained (stimuli of 1 to 4 V; 0·3 msec.; 5/min.) and these may then be abolished by the simultaneous maximal stimulation of the periarterial sympathetic nerves (stimuli of 15 to 20 V; 1 msec.; 25 to 50/sec. for 10 to 20 sec.) That the origin of the transmural contractions and the site of the sympathetic inhibition are both distal to the parasympathetic ganglia is shown by the persistence of these effects in the presence of ganglion blocking concentrations of hexamethonium bromide (5×10^{-5} to 1×10^{-4}), or of DMPP (1,1-dimethyl-4-phenylpiperazinium iodide; 5×10^{-6}) held in contact with the intestine for 10 min.

But, if the intestine is left in contact with this concentration of DMPP for 10 to 30 min., another action of the drug is seen which is separate from its known ganglion stimulating and ganglion blocking properties. The inhibitory effect of sympathetic nerve stimulation now becomes progressively smaller and is finally reversed to a potentiation of the transmural twitch; in spite of repeated washings, this total blockade of adrenergic nerve inhibition remains unchanged for several hours, although (–)-adrenaline added to the organ bath still gives a complete inhibition of the transmural contractions. For the most part these findings agree with the results of Bentley (1962), who has shown a similar action of DMPP on the rabbit Finkleman preparation and the hypogastric nerve-vas deferens preparation of the guinea-pig. The only difference is Bentley's observation that in the rabbit Finkleman preparation, sensitivity to the inhibitory action of added (–)-noradrenaline is increased in the presence of DMPP, whilst in my experiments with the guinea-pig, greater than normal amounts of added (–)-adrenaline are needed to suppress the transmural twitches.

The evidence from both sources appears to establish a postganglionic adrenergic blocking action of DMPP which interferes in some way with the eventual release of the sympathetic transmitter substance. This action is of interest because DMPP is chemically distinct from the known adrenergic neurone blocking agents, xylocholine (Exley, 1957), reserpine (Burn and Rand, 1958), bretylium (Boura and Green, 1959) and guanethidine (Maxwell and others, 1960).

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August 25, 1962

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