adrenergic blocking agents lipophobic. Both the quaternary local anaesthetics (Herr, Nádor & others, 1953) and the adrenergic neuron blocking agents are characterized by their slow but persistent action. The relation between local anaesthetic and adrenergic neuron blocking activity was first observed by Hey & Willey (1954). The present work seems to confirm the statement of Boura & Green (1965): "the possibility remains that the depressant action of the adrenergic fibre terminals is analogous to the impairment of nerve conduction in nerve trunks caused by local anaesthetics".

Our results show that on the rectus abdominis muscle of the frog, guanethidine like the local anaesthetics, is a non-competitive antagonist to carbachol.

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The effect of diethyldithiocarbamate on brain amine levels in the rabbit

SIR,—Sodium diethyldithiocarbamate or its oxidation product disulfiram inhibit both dopamine β-hydroxylase and monoamine oxidase in the brains of rats or guinea-pigs (Yamada & Yasunobu, 1962; Goldstein & Contrera, 1961; Musacchio, Kopin & Snyder, 1964; Collins, 1965; Carlsson, Lindquist & others, 1966). While investigating the neurotoxic action of sodium diethyldithiocarbamate in the rabbit (Edington, 1967), I have found differences in the level of central nervous system amines in this animal.

Twelve adult male or female Dutch rabbits 1·8–2·4 kg, were paired in similar weights and given sodium diethyldithiocarbamate as a buffered isotonic solution (Sunderman, White & others, 1963) at 750 mg/kg or saline intravenously. Two hr after the injection the rabbits were killed in a cold room, the brain removed, sectioned sagitally, and one half placed in a preweighed homogenized tube containing 10·0 ml of ice cold acid butanol. This tissue was homogenized and subsequently diluted to 30·0 ml. Fluorimetric estimations of 5-hydroxytryptamine (5-HT) and noradrenaline were made on the homogenized sample. The treated animals (6) had an estimated 5-HT brain content of $0{\cdot}67 \pm 0{\cdot}08$ μg/g brain while the controls (6) had $0{\cdot}45 \pm 0{\cdot}07$ μg/g wet weight. Noradrenaline

(0·68 ± 0·11 μg/g wet weight) was only detectable in the controls. The monoamine oxidase activity of the other half of the brain was measured using the method of Green & Haughton (1961). The treated animals (6) had a monoamine oxidase activity (measured as extinction) of 0·07 ± 0·03 while the controls (6) registered 0·25 ± 0·14. Two hr after the administration of sodium diethyldithiocarbamate, monoamine oxidase activity in the CNS was severely inhibited, 5-HT levels were raised, and noradrenaline levels were depressed. Carlsson & others (1966), measured noradrenaline and dopamine levels biochemically in rats and showed that noradrenaline levels were depleted while whole brain dopamine levels were not altered by sodium diethyldithiocarbamate, nor was it found by histochemical techniques to cause detectable changes in noradrenaline, dopamine or 5-HT. The results in rabbits confirm the depression of noradrenaline levels in the brain by sodium diethyldithiocarbamate. They also indicate that there is a significant increase in 5-HT levels when measured biochemically, and this is presumably due to the decrease in activity of monoamine oxidase. This increase in 5-HT may well have been more pronounced in rabbits due to the larger dose (750 mg/kg compared with 500 mg/kg used in rats by Carlsson & others) and the more direct route of administration (intravenous as opposed to subcutaneous). That this is so is supported by the fact that in the rabbits used in the present work noradrenaline could not be detected biochemically after the intravenous administration of sodium diethyldithiocarbamate, whereas Carlsson & others recorded only a 70% depression in levels after a single subcutaneous injection and a 90% depression after a second subcutaneous injection. The action of sodium diethyldithiocarbamate on CNS amines was of particular interest as I have shown that, given by injection over a period of months, it produces a neuraxonal dystrophy in rabbits and in hens. Whether the neuropathological lesion and the changes in brain amine levels are related, remains speculative since it is also known that sodium diethyldithiocarbamate inhibits a wide range of enzymes (Thorne & Ludwig, 1962) and also produces abnormally high levels of copper in the CNS and liver when given repeatedly (Edington & Howell, 1966).

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