depolarizing smooth muscle cells; the anticholinesterases, physostigmine, and neostigmine, may have a similar action. This possible action should be borne in mind at any site where these anticholinesterases act as sensitizers.

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The action of propranolol on the dog heart

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Propranolol does not depress the isometric twitch of isolated skeletal muscle or isolated papillary muscle to electrical stimulation in concentrations associated with β-adrenoceptor blockade (Harry, Linden & Snow, 1971). Further evidence is presented here that propranolol in doses associated with β-adrenoreceptor blockade does not depress the myocardium of the intact heart of the dog.

Dogs were anaesthetized with chloralose and the chest opened in the mid-line. The heart was denervated by cutting the vagi in the neck and crushing both ansae subclaviae. The maximum rate of rise of pressure in the left ventricle (dP/dt max), measured at a constant heart rate and at a constant mean aortic pressure, was used as an index of inotropic changes in the heart (Furnival, Linden & Snow, 1970). In twenty-five dogs the resting dP/dt max measured $3{,}795 \pm 205$ mmHg/sec (mean; S.E.M.) and the resting heart rate 129 ± 3 beats/min (mean; S.E.M.). In twelve dogs which had received two injections of reserpine (0·5 mg/kg) subcutaneously 24 h apart, the resting dP/dt max measured $2{,}921 \pm 192$ mmHg/sec (mean; S.E.M.) and the resting heart rate 126 ± 4 beats/min (mean; S.E.M.). These results suggest that circulating catecholamines have no significant effect on heart rate but do affect dP/dt max. This suggestion was corroborated in further experiments; propranolol in doses up to 0·05 mg/kg was given to seven dogs which had not been pre-treated with reserpine and dP/dt max was reduced from $3{,}250 \pm 377$ mmHg/sec (mean; S.E.M.) to $2{,}425 \pm 309$ mmHg (mean; S.E.M.) but there was no significant change in heart rate.

In four dogs which had received reserpine the relationship between free heart rate and dP/dt max induced by isoprenaline in the presence of propranolol (0·1–0·5 mg/kg) was the same as in its absence. Thus propranolol produced no change in this relationship. This result is different from the results previously described by Harry, Kappagoda, Linden & Snow (1971) observed in denervated dogs which had not received reserpine; in these dogs the relationship was changed such that for a given heart rate induced by isoprenaline dP/dt max measured less in the presence of propranolol than in its absence.

It may be concluded that catecholamines present in the circulation of denervated dogs, which have not received reserpine, stimulate the cardiac muscle and not the sinu-atrial node and that propranolol in such dogs is acting solely as a β-adrenoreceptor blocking agent.

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Inhibitory α-adrenoceptors in guinea-pig vas deferens

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The response of the stripped guinea-pig vas deferens to noradrenaline (NA) consists of a rapid peak followed by a fade to a lower equilibrium level. At doses of NA giving a response greater than about 20% of maximal, an additional phase of the response appears: a relaxation phase which follows immediately after the peak and goes below the final equilibrium (Iijima & Reiffenstein, 1972). This relaxation phase appears to be due to active inhibition resulting from activation of α-adrenoceptors (Ambache & Zar, 1970). The peak responses of the tissue to both NA and methacholine are inhibited when these agonists are added during the relaxation phase due to a previous dose of NA. In contrast, if these agonists are added at the equivalent time during a methacholine-induced contraction, then only the response to methacholine and not that to NA is affected. Thus NA has a non-specific inhibitory effect, whereas the effect of methacholine is receptor-specific.

The effects of these inhibitory α-adrenoceptors also appear when excitatory α-adrenoceptors are maximally activated: if more NA ($2–20 \times 10^{-5}$M) is added during the equilibrium phase of a *maximal* contractile response to NA (2×10^{-5}M), then a transient but substantial relaxation occurs (without any initial contraction). Isoprenaline also causes a similar transient relaxaton but the latter appears to be due to β-adrenoceptor activation, since the relaxations caused by the two agonists can be selectively blocked by phentolamine (or tolazoline) and propranolol respectively. Thus the vas deferens of the guinea-pig appears to have three types of adrenergic receptors: excitatory α, inhibitory α, and inhibitory β. Rat vas deferens does not appear to possess the inhibitory α-adrenoceptors.

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