Heart rate was increased by 28 ± 3 beats/min (from 196 ± 7 beats/min), cardiac output by 44 ± 5 ml/kg body weight min (from 168 ± 16 mg/kg min) and local myocardial blood flow by a mean of 220%. Quazodine had similar effects in the infarcted animals, decreasing systemic pressure by 13 ± 3 mmHg (from 124 ± 6 mmHg) and diastolic pressure by 20 ± 3 mmHg (from 83 ± 6 mmHg). Heart rate was increased by 30 ± beats/min (from 201 ± 12 beats/min), cardiac output by 22 ± 5 ml/kg body weight min (from 133 ± 20 ml/kg body weight min) and myocardial blood flow by a mean of 34%. In the infarcted animals therefore quazodine produced a more marked decrease in systemic arterial pressure but the effects on cardiac output and on myocardial flow were considerably less than those observed in normal cats. Nevertheless, the degree of myocardial stimulation and the increase in coronary perfusion induced by quazodine, in animals with an ischaemic myocardium, suggest that it warrants further investigation in experimental cardiogenic shock.

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Muscle tremor produced by sympathomimetic bronchodilators

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Adrenaline, stimulation of the splanchnic nerves, and a variety of procedures that cause the reflex release of catecholamines from the adrenal medullae produce a decrease in the tension and an increase in the rate of relaxation of the maximal twitches of the slow-contracting soleus muscle of the anaesthetized or decerebrate cat. The effect is the result of a direct action on the muscle fibres, and is independent of concomitant cardiovascular changes (Bowman & Zaimis, 1958). The increased rate of relaxation means that the overall duration of the twitch is reduced, and this effect results in a pronounced decrease in the tension and degree of fusion when subtetanic contractions are evoked at frequencies of stimulation (5–15 Hz) that include the physiological range for this muscle. Adrenaline was effective in doses as low as 0·01 μg/kg intravenously. In different animals, noradrenaline was 50 to 200 times less potent.

Several sympathomimetic bronchodilators (isoprenaline, salbutamol, orciprenaline, terbutaline) have been shown to produce the same effect, and the use of relatively selective agonists and antagonists (sotalol, butoxamine, practolol) indicated that the adrenoceptors involved are β-receptors and that they resemble those of the bronchi (β_2 receptors) more than those of the heart (β_1 receptors). The same effect, occurring in the slow-contracting units of human muscles (Marsden & Meadows, 1968), probably accounts for the tremor that occurs in patients with phaeochromocytoma and that often accompanies the use of sympathomimetic bronchodilators. The cyclic AMP phosphodiesterase inhibitors, 3-acetamido-6-methyl-8-n-propyl-*syn*-(4,3-a) pyrazine (ICI 58,301), 3-acetamido-5-methyl-8-n-propyl-*syn*-triazolo (4,3-a) pyrazine (ICI 61,129), and 2-amino-6-methyl-7-oxo-8-n-propyl-*syn*-triazolo (4,3-) pyrazine (ICI 63,197), potentiated adrenaline and isoprenaline in their actions on the soleus muscle. ICI 63,197, effective in a dose of 50 μg/kg intravenously, was the most potent in this respect, whereas ICI 61,129, even in doses up to 10 mg/kg, was only very weakly effective. These compounds show the same rank order of potency in phosphodiesterase inhibiting activity (Somerville, Rabouhans & Smith, 1970), and the results are therefore compatible with the possibility that the effects of β-receptor agonists on the soleus muscle are mediated by cyclic adenosine 3′,5′ monophosphate, which in turn may be involved in the relaxation mechanism of the muscle.

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