Alprenolol has a β-adrenoceptive blocking potency similar to propranolol when administered intravenously, but possesses intrinsic sympathomimetic activity (Ablad, Brogard & Ek, 1967; Forsberg & Johnsson, 1967; Johnsson, Norrby & Sölvell, 1967). The effects of these two agents have been compared in ten patients with proven hyperthyroidism, all of whom had a heart rate of more than 90 beats/min at rest before the start of the investigation. Two doses of each drug (5 and 10 mg) were given intravenously to each subject, treatments being administered on different days in varying order, the smaller before the larger doses. In seven patients normal saline (5 ml) was also included among the treatments. A resting heart rate was determined by electrocardiogram for 5 min before, and every minute for 5 min and at 10 min after, each injection. Both drugs produced a significantly greater fall in heart rate than normal saline (Table 1), but although the 10 mg dose of propranolol produced a significantly greater fall than 5 mg, the effects of the two doses of alprenolol did not differ significantly from one another. The heart rate 10 min after injection was significantly lower after propranolol (10 mg) than propranolol (5 mg) or alprenolol (10 mg), and propranolol (5 mg) produced a significantly lower heart rate than alprenolol (5 mg). Neither drug produced an arrhythmia or increase in ectopic beats in any patients. These results are further evidence that β-adrenoceptor blocking drugs with sympathomimetic activity are inferior to a compound without such activity in the treatment of hyperthyroid tachycardia.

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A comparison of the effects of propranolol and practolol on the exercise tolerance in angina pectoris

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β-Adrenoceptor blockade improves the exercise tolerance of patients with angina pectoris (Hamer & Sowton, 1966; Grant *et al.*, 1966; Birkett & Chamberlain, 1966; Wilson, Brooke, Lloyd & Robinson, 1969). Propranolol has β-adrenoceptor blocking and local anaesthetic properties either of which might be responsible for its action. With the development of practolol, a β-adrenoceptor blocking agent devoid of local anaesthetic properties, an assessment of the relative importance of these two actions in the amelioration of the symptoms in angina pectoris can be made.

Six patients with long-standing angina pectoris were exercised on a treadmill to assess the effect of intravenous administration of propranolol (0·15 mg/kg), practolol

(0·3 mg/kg) or a placebo on their exercise tolerance. The same procedure was repeated after oral administration of propranolol (50 mg 8 hourly), practolol (100 mg 8 hourly) or a placebo. The treadmill is a reproducible test of exercise tolerance providing a situation similar to the normal daily life of the patient.

There was a significant increase in exercise tolerance ($P<0·05$) in the oral and intravenous study with both propranolol and practolol. No distinction could be made on the basis of exercise tolerance between either the drugs or their mode of administration.

A beneficial effect on exercise tolerance is observed in angina pectoris from β-adrenoceptor blockade. In the doses used the effect of propranolol is not related to its local anaesthetic activity, since a similar response was noticed with practolol. Practolol does not affect the bronchi and may be given to patients with obstructive airways disease and as it has a relatively slight effect on contractility may be better tolerated in the presence of cardiac failure.

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The effect of propranolol on the human and canine transmembrane action potential

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Many studies have been reported on the effect of β-adrenoceptor antagonists on the intracellular cardiac potential of the isolated mammalian heart. There is some divergence in the results; Dohadwalla, Freedberg & Vaughan Williams (1969) found no change in the rate of rise of the action potential after (±)-propranolol, whereas Shevde & Spilker (1970) found an increase in the rate of rise in a similar preparation, but only at low concentrations ($1·0\times10^{-6}$M).

Human tissue might provide a more applicable model of the clinical situation. We have used small pieces of human ventricular cardiac tissue excised at corrective cardiac surgery to study the effect of propranolol on transmembrane action potential. Cardiac tissue taken from identical sites in healthy mongrel dogs was also studied.

(±)-Propranolol (3×10^{-5}M) significantly decreased the rate of rise of the action potential in human ventricular tissue with no significant effect on other electrophysical events. There was a similar effect in dog ventricle at the same order of concentration of propranolol, in agreement with the work of Davis & Tempte (1969). There was no increase in rate of rise of the action potential at lower concentrations in either species.

The conclusion of Dohadwalla *et al.* (1969) that the measurement of the rate of rise of the action potential is a sensitive test of the activity of drugs on cardiac muscle is corroborated by our results, which extend the observations to human tissue.