TABLE 1

Subject	Dose and route of administration	Time after dose (min)	Degree of blockade (dose ratio—1) Heart rate	Diastolic B.P.	dp/dt	Forearm flow
A	300 mg orally	100	13·0	12·9	40·3	
		165				29·6
		189	88·5	36·5	102·8	
B	300 mg orally	135	17·0	14·9	15·4	
		192				15·7
		212	15·4	12·4	10·1	
C	20 mg intravenously	46	4·8	4·0	6·7	
		73				17·2
		109	2·3	2·1	1·9	

Taking the blockade of heart rate as unity, the ratio of blockade of diastolic B.P. to heart rate was 0·81±S.E.M. 0·08 and forearm flow to heart rate was 2·19±1·44.

In two subjects given similar doses of practolol there was significant selectivity for the β_1 adrenoceptors; blockade of diastolic B.P. to heart rate (at maximum effect)= 0·26±0·11 and forearm flow to heart rate=0·18±0·03.

In the dog, however, after both intravenous and intraduodenal injections with M & B 17803A, isoprenaline vasodilatation was affected to a lesser degree than heart rate. In five dogs the blockade of diastolic B.P. to heart rate was 0·039±0·008 and femoral flow to heart rate was 0·058±0·016 indicating a 25·6 and 17·2-fold selectivity for the β_1 receptors respectively. In the sixth dog, there was no evidence of significant selectivity.

The explanation of these findings is not known; they may reflect either a species difference in receptor responses to M & B 17803A or, alternatively, variations in the pathways of its metabolism.

Effect of practolol on limb blood flow in anaesthetized patients with cardiac dysrhythmias

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The effect of practolol on limb blood flow was studied in four patients who developed cardiac ventricular dysrhythmias during an investigation of the peripheral vascular responses to anaesthesia. The patients were male volunteers between the ages of 40 and 65 years who were about to undergo elective surgery. After premedication with pethidine (1 mg/kg) and atropine (0·6 mg) intramuscularly, anaesthesia was induced with 2·5% thiopentone (5 mg/kg) given intravenously followed by suxamethonium (75 mg) to facilitate intubation. Before intubation the larynx was sprayed with 4% lignocaine hydrochloride (2 ml). Anaesthesia was maintained with a mixture of nitrous oxide and oxygen (6:3 l/min) administered through a Mapleson 'A' circuit and supplemented by halothane (1–4%) from a Dräger 'Vapor' calibrated vaporizer.

Forearm and calf blood flows were measured continuously by venous occlusion plethysmography using mercury-in-rubber strain gauges (Whitney, 1953) as the variable resistance of a bridge circuit. The outputs were transmitted from the operating room by telephone to an Elliott 903 digital computer where the blood flows were calculated in real time by a modification of a technique described previously (Hope, Carter, Horny & Wilcock, 1970). The analogue signals were also charted continuously on a Mingograf 81 recorder as were the ECG and B.P. records. The B.P. was measured

directly from a polyethylene catheter inserted percutaneously in the radial artery. Blood samples were removed at regular intervals for the determination of halothane concentrations and oxygen and carbon dioxide tensions. Environmental, skin and body core temperatures were measured by a YS1 46 Telethermometer.

When the inspired concentration of halothane had been raised to 4% four patients developed cardiac dysrhythmias (Pulsus bigeminus 3, unifocal extrasystoles 1). Within 5 min of the onset of the dysrhythmia practolol (4 mg) was given intravenously and in each instance sinus rhythm was restored (mean recovery time 34·7 s range 31–39 s). In addition to the restoration of normal rhythm the effect of practolol was to reduce blood flow in the forearm (mean reduction, 18·4%) and in the calf (mean reduction 22·7%). In a control group of four patients with sinus rhythm and not given practolol the forearm blood flow increased slightly (mean increase 7·8%) as did the calf blood flow (mean increase 15·8%) over an equivalent period of study. Thus a significant decrease ($P<0·025$) in limb blood flow occurred in those patients given practolol. This was associated with a significant decrease in blood pressure ($P<0·025$). Furthermore in those patients who developed dysrhythmias the mean blood pressures immediately before the onset of the cardiac disturbances were significantly higher than those in the control group ($P<0·0025$) despite the fact that the arterial pCo_2 values were not significantly different.

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Comparison of the symptomatic, electrocardiographic and haemodynamic effects of acute and long term β-blockade in angina pectoris

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In many patients with anginal pain during exertion, adrenergic β-receptor blockade induced by either intravenous or oral oxprenolol is associated with conspicuous symptomatic relief, reduction of the electrocardiographic S-T segment depression and haemodynamic changes chiefly characterized by a reduction in the exercising heart rate (Sharma, Majid, Galvin & Taylor, 1970). To confirm these preliminary findings and to establish the predictability of the response to the oral preparation from an acute intravenous injection of the drug, serial studies were made in six patients with uncomplicated angina pectoris.

Comparison of the control studies with those after intravenous oxprenolol and with those after oral oxprenolol demonstrated a conspicuous relief of anginal pain at the same level of exertion in more than half the patients after both methods of administration of the drug. Except for one patient, there was a close correlation between the symptomatic relief afforded by intravenous and oral oxprenolol. There was a significant reduction of the electrocardiographic S-T segment depression during exercise both after intravenous ($P<0·05$) and oral oxprenolol ($P<0·05$). There was a significant reduction in the exercising heart rate and cardiac output both after intravenous and oral oxprenolol; there was a reduction in mean systemic arterial pressure