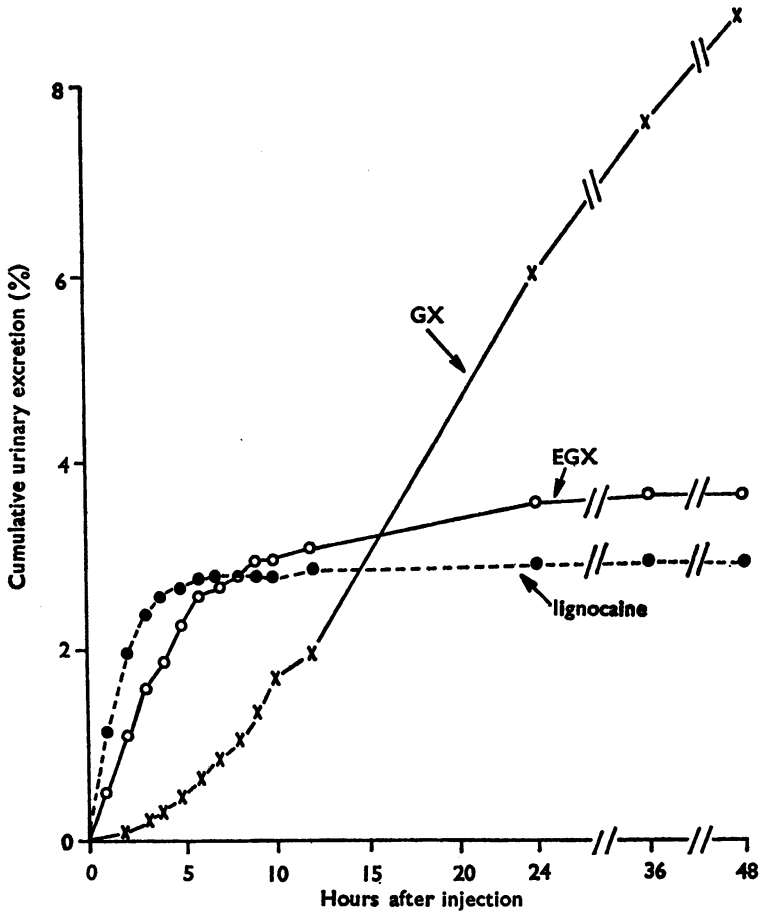

FIG. 1. Mean cumulative urinary excretion of lignocaine, ethylglycylxylidide and glycylxylidide in four healthy male volunteers after intramuscular injection of 200 mg lignocaine hydrochloride.

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The effect of AH 5158, pindolol, propranolol, D-propranolol on acute exercise tolerance in angina pectoris

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Numerous reports have established that propranolol and other β-adrenoceptor blocking drugs improve exercise tolerance in angina pectoris. Benefit is progressive as dosage is increased (Prichard & Gillam, 1971).

In the present study we have assessed the effect on acute exercise tolerance in angina pectoris of the β-adrenoceptor blocking drug pindolol, LB 46 (Saameli, 1967; Hill &

Turner, 1969), and AH 5158, a drug with some α-blocking effect as well as β-blocking action (Farmer, Kennedy, Levy & Marshall, 1972; Boakes, Knight & Prichard, 1971). Propranolol was also administered, as was a larger dose of its D-isomer. Small doses of D-propranolol have been found previously to be ineffective (Wilson, Brooke, Lloyd & Robinson, 1969).

Five volunteer patients exercised on a cycle ergometer at constant work load before (control) and after injection of drug or saline, at weekly intervals under standardized conditions. A second post-injection exercise was performed 5 min after pain from the first post-injection exercise subsided. Gradually increasing doses of each drug were administered in a run-in period, and patients were accustomed to the experimental procedure. The trial proper involved the randomized double blind administration of saline, D-propranolol 80 mg and graded doses of propranolol, 10 mg, 40 mg, 80 mg, pindolol, 1 mg, 4 mg, 16 mg, and AH 5158, average 30 mg and average 55 mg. Some

TABLE 1.
Duration of exercise (seconds, mean ±S.E.)

n=5 Drug:	Control (C)	Post injection	Increase on C
Saline	196 (26·3)	200 (23·0)	4 (7·0)
Propranolol (10 mg)	199 (32·6)	*263 (37·3)	*****64 (10·4)
Propranolol (40 mg)	171 (18·5)	**274 (28·3)	**104 (22·4)
Propranolol (80 mg)	180 (13·0)	*296 (28·4)	****116 (26·7)
Pindolol (1 mg)	211 (16·7)	****271 (26·6)	*60 (21·8)
Pindolol (4 mg)	198 (21·6)	****293 (28·2)	***96 (17·6)
Pindolol (16 mg)	184 (19·1)	*243 (18·9)	**59 (17·6)
AH 5158 (av 30 mg)	201 (26·6)	**283 (29·0)	***82 (23·7)
AH 5158 (av 55 mg)	229 (30·0)	***281 (36·7)	++52 (32·0)
D-propranolol (80 mg)	190 (15·5)	++207 (26·2)	++17 (16·6)

P with respect to saline
* < 0·05 ** < 0·025 *** < 0·01 **** < 0·005 ***** < 0·001 ++ > 0·10

of the results are given in Table 1. All drugs produced a significant increase in exercise tolerance with the exception of D-propranolol. There is a less clear dose response relationship with pindolol and AH 5158. This may be due in the latter instance to its increasing hypotensive action with larger doses. Pindolol although it has high potency, has a flat dose response curve (Boakes, Boeree & Prichard, to be published).

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Preliminary studies on the pharmacology of an antidysrhythmic, Kö 1173, in man

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Kö 1173 is a new antidysrhythmic drug (Singh & Vaughan Williams, 1972; Allen, Kofi, Ekue, Shanks & Zaidi, 1972) resembling lignocaine in structure. It can be administered intravenously and is well absorbed after oral dosage. Blood levels were measured