heart rate (Weissler, Lewis & Leighton, 1972).

Covariance analysis demonstrated that PEP shortened significantly (129 ms to 119.5 ms, $P<0.005$) while HR, LVET, QS_2 remained unchanged. Mean arterial pressure (calculated as diastolic pressure + pulse pressure/3) dropped from 96.6 mmHg to 94.8 mmHg ($P<0.005$). The plasma level of DTZ, at the third hour, was 175 ± 104 ng/ml (range 56–374).

Diltiazem 120 mg did not modify elementary parameters of the cardiovascular system in the supine or erect positions, nor adaptation to exercise in healthy volunteers. Diltiazem 180 mg produced a reduction in pre-ejection time, probably due to a slight peripheral vasodilatation (LVET and QS_2 unchanged—Gibson 1978; Lewis, Rittgers, Forester & Boudoulas, 1977). It does not seem to reduce venous return. The absence of reflex tachycardia may be due to the direct action of DTZ on the sinus node (Briley, Cavero, Langer & Roach, 1980).

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H. VALETTE & E. APOIL
Laboratoire d'Explorations fonctionnelles, Département de Physiologie humaine, UER Kremlin Bicêtre, Université Paris-Sud, 78, rue du Général Leclerc, 94270 Kremlin Bicêtre, France

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β-ADRENOCEPTOR BLOCKADE AND VENTILATION IN MAN

We were pleased to read the report of a further study of the effects of acute β-adrenoceptor blockade on ventilation in man (Leitch, Hopkin, Ellis, Clarkson, Merchant & McHardy, 1980) but were surprised that the authors referred only to our preliminary communication on one aspect of this topic (Patrick & Pearson, 1978) and not to our fuller paper (Patrick, Tutty & Pearson, 1978). We have also reported a rather similar study on the effects of β-adrenoceptor blockade in normal exercising subjects (Banks, Patrick & Pearson, 1978; Pearson, Banks & Patrick, 1979).

If we now bring together the five published studies of the effect of a single dose of 80–100 mg propranolol on the ventilatory response to CO_2 in man, we begin to see a pattern emerging despite the apparently contradictory conclusions drawn by individual authors. Table 1 summarises the mean values for CO_2-sensitivities for each study: the overall average, weighted by the number of subjects studied, shows a 12% decline in CO_2 sensitivity after propranolol. It is possible to extract values for 34 individual subjects from four papers (Keltz, Mathur & Stone (1977) give average values only), and these are shown in Figure 1. The scatter reflects the difficulty, mentioned by each of the authors, in obtaining stable values for CO_2-reponses and shows the wide inter-individual range. Nevertheless, there is a significant reduction in CO_2-sensitivity after propranolol, whether a paired t-test or a Wilcoxon signed rank sum test is preferred. This suggests that the respiratory effect of propranolol is modest but consistent, often hidden by the inherent variability in the data, and convincingly seen only if larger numbers of subjects are studied. It remains difficult to explain except on the basis of some central action of this drug which may be an undesirable side-effect, especially in patients whose ventilation is barely adequate.

We found that β-adrenoceptor blockade not only

Table 1 The effect of a single dose of propranolol on the slope of the ventilatory response to CO_2 in normal man. Average values found in studies from five laboratories are shown.

Study	Authors	Dose (mg)	Route	Number of subjects	Slope of CO_2-response line: Placebo ($l\ min^{-1}\ kPa^{-1}$)	Slope of CO_2-response line: Propranolol ($l\ min^{-1}\ kPa^{-1}$)	Ratio: propranolol/placebo (%)
1	Mustchin *et al.* (1976)	80	oral	6	26.2	14.0	53.4
2	Keltz *et al.* (1977)	0.15/kg	i.v.	20	26.3	24.8	94.3
3a	Patrick *et al.* (1978)	100	oral	8	20.9	18.0	86.1
3b	Patrick *et al.* (1978)	80	oral	7	27.5	28.4	103.3
4	Trembath *et al.* (1979)	80	oral	5	22.8	17.3	75.9
5	Leitch *et al.* (1980)	80	oral	8	16.3	15.0	91.7
	Weighted average			54	23.8	20.9	87.8

increased the unpleasantness of exercise but also reduced the work performed in a progressive exercise test taken to exhaustion (Pearson *et al.*, 1979). The failure of Leitch *et al.* (1980) to confirm this finding may be due to the fact that their subjects discontinued the test well below their presumed maximal work capacities at cardiac frequencies (on placebo) of only 166 beats/min.

J.M. PATRICK,
Department of Physiology and Pharmacology, Medical School, Queens Medical Centre, Nottingham, NG7 2UH

S.B. PEARSON,
Southampton Western Hospital, Oakley Road, Southampton, SO9 4WQ

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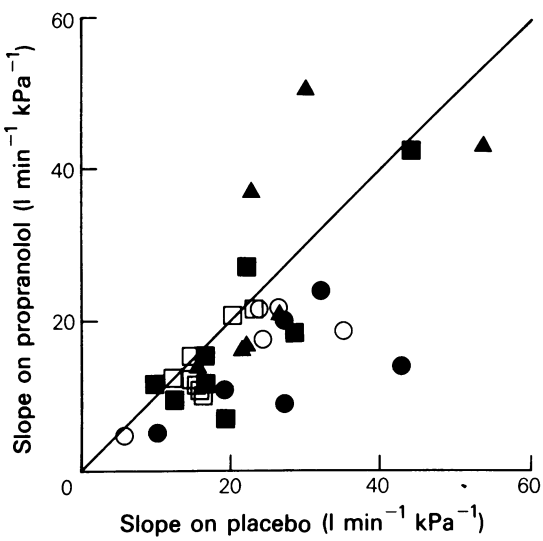

Figure 1 The effect of a single oral dose of propranolol on the slope of the ventilatory response to CO_2 in 34 individual subjects in five studies (see Table 1): ●,1: ■,3a; ▲,3b; ○,4 and □,5. The line of equality is shown.

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