This hepatotoxic effect of busulphan therapy appears to be rare and in this case was associated with prolonged therapy. However, we suggest that jaundice in patients under treatment for chronic granulocytic leukaemia may be attributable to busulphan therapy rather than severe leukaemic infiltration of the liver.—We are, etc.,

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Aerosols in Asthma

SIR,—We feel that the paper by Dr. L. H. Harris (5 December, p. 579) on the effects of isoprenaline plus phenylephrine given by pressurized aerosol requires comment. The final sentence of the summary is misleading. On the test day only 13 of the 23 patients showed any significant bronchodilatation, which does not support the statement that the combination aerosol has a satisfactory bronchodilator effect. This relative ineffectiveness of the combination aerosol as a bronchodilator has also been found by Pflug *et al.*¹ In their study Medihaler-duo was given to 13 patients with chronic airway obstruction, and in six of these there was either no change or an actual fall in FEV₁. Recent pharmacological studies (Simonsson, B. G., personal communication; Price, F. J., personal communication) have demonstrated that there may be alpha receptors in human bronchial muscle. Thus the addition of an alpha stimulant, phenylephrine, to an isoprenaline aerosol may well reduce its effectiveness as a bronchodilator.

Dr. Harris also claims in the summary of his paper that the aerosol is, "additionally safe if used by a severely hypoxic patient unaware of the seriousness of his condition." We believe that there is no aerosol that can be safely used by such a patient, if one defines safety in terms of avoiding a fall in arterial oxygen tension. It is of interest that in Dr. Harris's series of the three patients with the lowest oxygen tensions there was a slight fall in arterial oxygen tension in two of the subjects following Medihaler-duo. In addition, in the study previously quoted, by Pflug *et al.*,¹ nine out of the 13 patients showed a fall in arterial oxygen tension, following inhalation of Medihaler-duo and in five of these the fall was greater than 5 mm Hg.

We would not agree that a comparative trial with isoprenaline was unnecessary. We think that the effects of isoprenaline, and isoprenaline plus phenylephrine, should be compared in the same patients. All of the previous studies quoted for isoprenaline except that of Waddell *et al.*² were done either with wet aerosol isoprenaline (estimated doses being much higher than that contained in Medihaler-duo) or with intravenous isoprenaline. The study of Waddell *et al.* is the only study in which isoprenaline was administered by a

pressurized aerosol and we would estimate that oxygen tension fell by more than 5 mm Hg in only one out of 12 patients, and this would not be statistically different from the results that the author reports with Medihaler-duo. Similarly, under the results quoted for orciprenaline, two of the studies were performed with subcutaneous orciprenaline and one with a wet aerosol of orciprenaline, and only the study of Meisner and Hugh-Jones³ looked at the effects of a pressurized aerosol of orciprenaline, and in this study no patient showed a fall in arterial oxygen tension. Thus the grouping together of several papers to obtain average changes is really quite unjustified in view of the differences in diagnoses, doses of drug administered, route of drug administration, time of sampling of arterial blood, and degree of hypoxaemia in the different patients.

We would once again emphasize the danger of suggesting that any aerosol is safe in severely hypoxic patients. There is still no scientific evidence to suggest that any available bronchodilator aerosol has an additional margin of safety as regards changes in arterial oxygen tension. We would make a plea for future studies on this important topic to be carried out in a properly controlled manner, and in particular against the use of such data in advertising material.—We are, etc.,

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Practolol in Angina

SIR,—I wish to report briefly a double-blind trial of practolol (Eraldin) in angina pectoris. Practolol is a beta-receptor antagonist which is cardioselective and is therefore preferable to other beta-blockers in patients with obstructive airways disease. It lacks the "quinidine-like" or membrane-stabilizing action of propranolol, it has intrinsic sympathomimetic activity, and is less liable than other beta-blockers to produce or exacerbate cardiac failure. Results of controlled trials of practolol in angina have varied, suggesting that it is less effective in relieving angina than propranolol. George, Nagle, and Pentecost¹ found practolol almost as effective as propranolol, while Prichard, Lionel, and Richardson² demonstrated only slight relief of angina by practolol in oral doses up to 2.4 g daily. Westerlund³ found no reduction in the number of anginal attacks although there was improvement in the work performance with exercise tests. In addition, Atkins, Blomqvist, and Cohen⁴ have found recently that practolol was more effective than propranolol in improving exercise tolerance measured by bicycle ergometry.

Twenty-eight patients with stable angina pectoris which had been present for a minimum of 3 months (mean 3 years 8 months) were studied. These were 20 men and 8 women, with mean age of 59.5 years. The trial started with a run-in period of

one to three months, during which the dose of practolol was increased until subjective improvement of angina occurred. No patient was rejected owing to lack of improvement in this open part of the trial. The patients then entered the double-blind phase of the trial, consisting of two four-week periods in which they took either practolol or placebo in random order, later crossing over to the alternative preparation. The dose of practolol was that established in the open trial (range 200-800 mg/day, average 447 mg). Patients were seen at fortnightly intervals throughout the trial and the frequency and severity of angina, trinitrin consumption, and effort tolerance were recorded. A summary of the patient preferences in the 28 patients follows:

Better in practolol period	10
Better in placebo period	3
Improved in both periods	12
Worse or unchanged in both periods	3

Side effects were not troublesome. One patient, who was worse in both periods, could not take more than 200 mg practolol daily because of nausea.

These patient preferences—10 improved on practolol compared to three improved in control periods—are statistically significant at the 5% level. The order of the practolol and control periods did not influence drug preference. The large number of patients improving in both periods, 12 out of 28, may well be a feature of trials of effective drugs in angina, and is not seen in trials of inert drugs.⁵ The run-in period on practolol might well produce an improvement in exercise tolerance with improvement of cardiovascular reserve by increased exercise, which might persist into the control period.

I am most grateful to Dr. B. Nebenzahl, Dr. R. B. Royds, and Dr. R. A. Wiseman for help with this trial.

—I am, etc.,

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- 3 Westerlund A., *Postgraduate Medical Journal Suppl.* 1971, 47, 64.
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Long-acting Phenothiazines

SIR,—We would like to compliment you on your concise leading article on long-acting phenothiazines in schizophrenia (23 January, p. 189). The effect on hospital admission rates is demonstrated by our retrospective study of 212 chronic schizophrenic outpatients attending St. Clement's Hospital in which each patient was acting as his own control. A total of 103 patients fulfilled the criteria of this study, in that they had a follow up period of 12 months or more and a previous history of fully documented hospital admissions prior to receiving injections of long-acting fluphenazine. The remaining patients were excluded because they had received their injections for less than 12 months or had incomplete records. The number and duration of hospital admissions in the follow up period was compared with the number