were not treated at Hammersmith Hospital. This feature of the trial arose from the collaboration with other hospitals to ensure an adequate total intake. When a patient, first seen at another hospital, was allocated at random to receive conventional treatment it was often difficult to justify giving that treatment at Hammersmith rather than at the hospital of origin.

A comparison of the response of patients treated with photons at Hammersmith with those patients in the neutron series who would have received their treatment at Hammersmith, whichever form of treatment had been selected, was included in the first report on the trial.[1] The findings in this subtrial at September 1976 were as shown in the accompanying table. The findings in the subtrial are similar

Findings in subtrial of neutron and photon treatment at September 1976

	Neutron series (n = 20)	Photon series (n = 25)
Local control of tumour:		
No with continued complete regression	18	5
No with complete regression followed by recurrence		8
No with no or incomplete regression	2	12
Survival:		
% alive at 1 year (actuarial)	54	38
Additional treatment for suspected residual disease:		3
No given radiotherapy		3
No treated surgically		
No with severe complications in larynx or pharynx	3	1
Mean time-dose factor (TDF)	118	108

to those for the whole trial. The difference between the numbers with persisting local control is significant at the 0·1% level; the difference in mortality rates is not significant. In the subtrial the average time-dose factor (TDF) was about 10% higher for patients in the neutron series than for those in the photon series (compared with about 20% in the whole trial[1]). Nevertheless, as the reports of both trials indicate, persistent local control of the tumour among subgroups of patients who were receiving equivalent doses of the two types of radiation was much more frequent among the neutron-treated patients.

We hope that many of the difficulties of a multicentre trial will be avoided in the new trials which will be undertaken with the cyclotron which has recently been installed at the Western General Hospital, Edinburgh.

Finally, we would like to correct a misprint in the table in our more recent article (25 June, p 1642). Ten, not 16, neutron patients received supplementary surgery for suspected residual disease.

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[1] Catterall, M, Sutherland, I, and Bewley, D K, *British Medical Journal*, 1975, **2**, 653.

Relative activity of atenolol and metoprolol

SIR,—With the increasing interest in the clinical use of cardioselective β-adrenergic antagonists it is of fundamental importance that the relative potency of the individual compounds be established. Using propranolol as the reference substance, it has been shown that the ratio between equipotent doses of atenolol and propranolol[1] is 1:0·7 and that of metoprolol and propranolol[2] 1:0·8. These results would suggest that identical doses of the two selective β_1-receptor antagonists, atenolol and metoprolol, would give the same degree of β-blockade.

To test this hypothesis we have compared the β-blocking effects of the two drugs in a group of seven hypertensive patients who, after one week's placebo treatment, were given in random order, one week's treatment with atenolol 100 mg daily, atenolol 200 mg daily, metoprolol 100 mg daily, and metoprolol 200 mg daily. At the end of each treatment period an exercise test on a bicycle ergometer (5 min at 75 W) was carried out two hours after tablet administration, heart rate and blood pressure recordings being taken before, during, and after exercise.

Mean results on placebo showed a resting heart rate of 98/min and a resting blood pressure of 170/105 mm Hg rising to 145/min and 221/111 mm Hg at the end of exercise. The respective values after atenolol 100 mg were 59/min, 161/99 mm Hg, 96/min, and 188/106 mm Hg and after metoprolol 100 mg they were 61/min, 161/102 mm Hg, 97/min, and 195/110 mm Hg. After atenolol 200 mg the respective values were 63/min, 161/97 mm Hg, 92/min, and 191/105 mm Hg and after metoprolol 200 mg they were 62/min, 163/97 mm Hg, 93/min, and 189/104 mm Hg. This similar degree in the inhibition of exercise tachycardia following both 100 mg and 200 mg administration suggests the equipotency of these two compounds. It is also interesting that no significant difference was observed in the hypotensive effects of these compounds at rest and on cessation of exercise.

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[1] De Plaen, J F, Amery, A, and Reybrouck, T, *European Journal of Clinical Pharmacology*, 1976, **10**, 297.
[2] Bengtsson, C, *Acta Medica Scandinavica*, 1976, **199**, 71.

Poisoning with maprotiline and mianserin

SIR,—Since the introduction of tricyclic antidepressant drugs into clinical practice 20 years ago they have become an increasingly popular agent for suicide and self-poisoning. In 1974, the latest year for which figures are available, there were 323 deaths attributed to these drugs,[1] and this number has probably increased since then. In order to ascertain the incidence of serious toxicity from overdose we have followed up all cases of antidepressant poisoning referred to this unit in the year starting April 1976. Although analysis of this study is not yet complete, the report by Drs J Park and A T Proudfoot (18 June, p 1573) prompts us to report our experience of overdose with the two newly introduced quadricyclic antidepressants, maprotiline (Ludiomil) and mianserin (Bolvidon; Norval). Follow-up was achieved on 41 cases (36 in adults and five in children) of maprotiline poisoning and 20 cases (19 in adults and one in a child) of mianserin poisoning.

Of the adults taking maprotiline, 17 had ingested more than 1 g and 10 less than 1 g, and in nine cases the amount ingested was not known; 10 patients had taken additional drugs. All but two of these patients developed symptoms. These, in order of frequency, were: drowsiness in 24 cases, convulsions in eight, coma in seven, anticholinergic signs in five, tachycardia in five, bradycardia in three, cardiac arrest in three, hypotension in two, and hypertension in one. Two of the patients died, but their deaths were not directly attributable to the overdose; one died of a massive pulmonary embolus after making a full recovery from the overdose and the other died from a fall following the overdose. Two of the five children who took maprotiline developed symptoms. One was just drowsy, while the other, a girl of 4, had repeated convulsions after the ingestion of 525 mg of the drug.

The symptoms reported in the 19 adults who ingested mianserin were drowsiness in 13 cases, hypertension in three, coma in two, tachycardia in two, and hypotension in one. There were no reports of cardiac arrhythmias or convulsions. The two patients who were in coma had taken additional sedative drugs. There was one death. This patient, a woman of 72, had threatened suicide previously. She was admitted deeply unconscious having ingested about 600 mg of mianserin and an unknown quantity of lorazepam. She did not regain consciousness and died the next day. Necropsy revealed bronchopneumonia. Toxicological analysis confirmed that only these two drugs had been ingested. The plasma mianserin concentration on admission was 110 μg/l and that of lorazepam 500 μg/l.

From our as yet limited experience it would appear that the clinical features of poisoning with these two compounds differ. Overdose of maprotiline causes symptoms similar to those produced by the more conventional tricyclic antidepressants[2] and our findings are in accord with those reported by Drs Park and Proudfoot. Overdose of mianserin commonly causes drowsiness but the more serious complications of tricyclic antidepressant poisoning (convulsions and cardiac arrhythmias) were not reported. It is possible that if these patients had taken larger quantities of mianserin they would have exhibited more serious symptoms. The absence of anticholinergic effects with mianserin would suggest that physostigmine or other cholinesterase inhibitors should not be used in therapy.

We would like to thank all those physicians who completed our questionnaires and Dr Ian Bradbrook for the mianserin estimations.

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[1] Office of Population Censuses and Surveys, *Deaths from Poisoning by Solid and Liquid Substances, 1974*, London, OPCS, 1976.
[2] Noble, J, and Mathew, H, *Clinical Toxicology*, 1969, **2**, 403.

Whooping-cough immunisation

SIR,—As stated in your leading article (2 July, p 5), there have been differences in the estimates of the risks which may be associated with whooping-cough vaccine. As I have previously pointed out, in evaluating the vaccines available today "it is not acceptable to extrapolate from data collected from studies with other vaccines and different schedules, or from