stated) and Morgan et al., also noted a rise in blood pressure in a few cases. Thorpe reported a rise in blood pressure (to 240/140 mm Hg) in a patient who took over 500 mg of pindolol in a suicide attempt.

It is difficult to estimate exactly how often a hypertensive effect occurs, but our experience with 200 patients treated with pindolol suggests that it may occur in about 5% of cases. We believe that pindolol is a useful and effective drug but that the initial dosage should be low (for example, 2.5-5.0 mg twice daily) and that if after 25-30 mg daily to be ineffective, then dose reduction should be tried. The blood pressure may then fall to satisfactory levels. If it remains unchanged, or if it falls but is still unsatisfactory, then some other drug should be added. We are, etc.,

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1 Simpson, F. O., Drugs, 1974, 7, 85.
2 Currey, R. I., Current Therapy, 1975, 2, 13.
3 Currey, R. I., Current Therapy, 1973, 14, 185.
4 Murphy, T. A. et al., Medical Journal of
Australia, 1972, 2, 509.
5 Thorpe, P., Medical Journal of Australia, 1971, 1, 1422.

Gold Therapy in 1975

Sir,—Your leading article (26 April, p. 156) has attracted only two cynical letters. One does not deny that gold is a toxic drug, but concede that beneficial effects should not be denied. I would disagree with your interpretation of the results of three trials. It should be stressed that in the E.R.C.
trial, gold was given as a "course" for five months and in all parameters assessed, excluding radiological evaluation, "the gold-treated patients improved to a greater degree than the controls from the third month onward, and this improvement was still apparent 12 months after the last injection was given." It is in the light of this limited course of injections that one should interpret the results of the trials. The advantage seen in the gold-treated series at month 18 had disappeared. I should add that the next part of the above sentence reads "though by some criteria the gold-treated series still remained significantly better than the control series, albeit by only a slender margin.

Tolamol in Treatment of Angina Pectoris

Dr. S. — We were interested to read the favourable report by Dr. Graham Jackson and his colleagues (29 March, p. 708) on tolamol in angina pectoris. We have recently completed a similar study using higher doses given for longer and our results are similar.

Ten patients completed our double-blind crossover trial. Diagnostic criteria for admission were identical with those of Dr. Jackson and his colleagues except that one of our patients had long-standing maturity-onset diabetes mellitus. After a run-in period to establish rapport and familiarization with the clinic and record cards each patient was seen every four weeks for 36 weeks. At each attendance records were made of the number of anginal attacks, trinitrin consumption, and evidence of heart failure and exercise tolerance. Clinical examination and resting electrocardiography were followed by standardized exercise on a treadmill (20% elevation) with continuous electrocardiography (V5 position) until an end-point was reached (angina, fatigue, breathlessness, or ST-segment depression). Patients received, in random order, capsules of identical appearance containing tolamol 100 mg, propranolol 20 mg, or placebo, each given for three consecutive months (successively one, two, or three capsules thrice daily unless side effects prevented an increase in dose. Patient compliance was measured using returned capsules.

The same "blind" observer saw patients throughout the trial and he assessed which treatment appeared to give best overall response: six patients were rated best on tolamol, two on propranolol, and two on placebo. Formal statistical analysis was not performed, but at the end of the last month of each treatment (that is, when on maximum dose). The number of attacks of angina (measured by mean consumption of trinitrin) during each active treatment period was less than during the placebo period but the difference was not statistically significant. The results of the exercise test in nine patients (one was excluded because he developed atrial fibrillation during the trial and required digitalization) were analysed as shown in the table.

Routine haematological, biochemical, and clinical observations each month did not detect any adverse effects other than the common minor side effects of propranolol. Six patients took tolamol 300 mg thrice daily; four took only 200 mg thrice daily because of exertional dyspnoea, bradycardia, or diarrhoea. Similarly, six patients tolerated the maximum dose of propranol (60 mg thrice daily).

We have shown that tolamol is an effective treatment for angina but we place no importance on its greater apparent benefit compared with propranolol because this is probably entirely due to the doses selected. The results of Dr. Jackson and his colleagues show that we should use double the dose of propranol. Tolamol may have an additional advantage in angina pectoris in that our patients 900 mg daily was equally acceptable to 180 mg of propranol. We suggest that further studies should be undertaken to assess tolamol in patients who require large doses of beta-blockers.

We are grateful to Pfizer Central Research for supplying tolamol.

We are, etc.,

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In reply to Dr. S. Oran and his colleagues (21 June, p. 686) I am well aware that bradycardia is a well-documented side effect of beta-blockers. What I question is the sagacity of excluding from any further discussion four patients, three of whom subsequently died, who deteriorated during the trial—all during treatment with the test compound tolamol (is this a coincidence?). No mention is made of these deaths in the results section. The author has altered their statement to "our mortality was of the order of 4%" without an annual figure. From the figures in the original paper, ignoring the fact that all incidents occurred on tolamol, three deaths among 47 patients each followed for 26 weeks (not 10 months) would give an annual mortality of 12.8%—three times the expected yearly mortality quoted. If one carried out an arithmetic to obtain an annual figure, what was the purpose of the authors in quoting an annual figure and equating it with their results? Is the fact that these reactions (three leading to death) occurred on only tolamol a coincidence or not? Surely further study with a large group of patients is required to clarify the point. If severe bradycardia is to be excluded, it would be useful to assess any side effects of beta-blockers which lower blood pressure by a "malignant" reflex.