"Placebo." If one compares the mean pre-treatment blood pressure with mean "placebo" blood pressure in Table 1 there is a fall in blood pressure of 26/9 mm. Hg which is very similar to our own results, 26/10 mm. Hg, when patients were receiving a diuretic alone.

The authors consider various explanations for the failure of the blood pressure to rise to untreated levels when propranolol was stopped. As almost all were still on diuretic therapy during this time it would seem that no other explanation need be considered.

The results presented in Fig. 1 of their paper suggest that the maximal effect of propranolol is seen in less than six weeks, and does not support their initial hypothesis that some trials have failed to show an effect of propranolol because the duration of treatment was not long enough.

The authors say that they selected the 32 patients for study from more than 300 on the drug, the grounds of selection being that they had responded to propranolol in a dose of less than 320 mg. daily. If patients are selected for inclusion in a trial on the ground that they had already responded well to the drug the result is bound to be biased in favour of the drug under study, and no amount of care in trial design will eliminate this bias.—We are, etc.,

C. T. DOLLERY.

Department of Clinical Pharmacology,
Royal Postgraduate Medical School,
London W.12.

J. W. PATERSON.

Institute of Diseases of the Chest,
London S.W.3.

REFERENCE

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Tetrabenazine for Extra-pyramidal Movement Disorders

SIR,—Dr. W. A. G. MacCallum (21 March, p. 760) expresses the hope that tetrabenazine may well be an alternative in some cases to L-dopa. I do not feel that the pharmacological effects of tetrabenazine warrant such a statement. Though tetrabenazine reduces choreiform movements, this effect does not minimize the possibility of production of other extra-pyramidal symptoms. An analogy exists in that drugs such as reserpine, phenothiazines, and butyrophenones, which reduce the choreiform movements of, for instance, Huntington's chorea, are themselves capable of producing severe extra-pyramidal side-effects.

Dalby¹ noted that in contrast to the beneficial effect of tetrabenazine in choreiform and hemiballistic motor activity, patients with Parkinsonian tremors and those with intention tremors due to spinocerebellar degeneration experienced the opposite effect. Thus, the use of the drug is limited, and as other drugs have an equivalent amount of effect in controlling choreiform movements, there is no benefit in resuspecting the drug. Tetrabenazine, being a benzoquinolizine derivative, resembles reserpine in chemical structure and pharmacological and biochemical actions leading to depletion of noradrenaline and serotonin concentrations in the brain, and its side effects such as depression, postural hypotension, and extra-pyramidal symptoms are similar to those of reserpine.

Owing to these side effects caution must be exercised before re-introducing it into clinical practice.—I am, etc.,

R. THAVASOTHY.

Saxondale Hospital,
Nottingham.

REFERENCE

- 1 Dalby, M. A., *British Medical Journal*, 1969, 2, 422.

Long-term Anticoagulant Treatment after Myocardial Infarction

SIR,—Your leading article entitled "Long-term Anticoagulant Treatment after Myocardial Infarction (28 February, p. 514) seems to me so one-sided that it is difficult to believe it was written by an "un-biased observer".

The author referred to the work of the international review group (an analysis of the results on nine controlled trials between 1950 and 1965) in one sentence "...[they] could not reach an agreed decision." This in a way is correct, but certainly leaves the reader with an incorrect impression of what the international group said. Permit me to repeat that the group found a 20% reduction in mortality in men in the anticoagulant treated group compared to the control group. The mortality per 100 patients per month was 0.63 against 0.79, respectively. This difference is statistically significant ($p < 0.01$). The effect seemed to last several years in both older and younger men. The group concluded "Most of us considered that the consistency of the findings warranted a conclusion that anticoagulant therapy probably prolonged survival at least over two years . . .". "Two of us were not convinced that long-term therapy prolonged survival." It is worth mentioning that the two were authors of one of the nine trials under review.

Your leader writer states: "G. Aspenström and K. Korsen-Bengsten concluded that there was no difference in mortality between patients treated with long-term anticoagulants and untreated controls." What they actually found was 39 deaths in the treated group against 50 deaths in the control group, and their own conclusion was that "... the mortality through second to fifth years was in all probability significantly reduced in poor risk patients on dicumarol ($p < 0.05$)."

You state: "E. A. Loeliger and colleagues found no difference in mortality but a higher rate of reinfarction in untreated patients." They found the incidence of cardiovascular death in the treated group to be 4.8% against 7.2% in the placebo group. True enough this difference is not statistically significant, but taken together with the statistical significant reduction of reinfarction rate the flat statement that Loeliger *et al.* found no difference in mortality is in my mind a slightly biased expression.

Further on you say: "It is agreed that long-term anticoagulants are of no benefit to women." It is correct that the difference in the mortality reported by the international group in women of 0.86 per 100 patient/months in the treated group against 0.93 in the control group could easily have been due to chance. We reported³ the results of a controlled clinical trial of long-term anticoagulant therapy in women after

their first infarction and could show a significant reduction in mortality and reinfarction rate in the treated group. Admittedly this is not a large study, including 159 patients only, but still by far the largest study of this treatment in women so far reported. It would not seem unreasonable to have at least referred to this study which throws some doubts on the old idea that anticoagulant therapy after infarction is effective in men only.

It seems to me fair to conclude that the majority of statistically well-controlled trials show a significant reduction in mortality and/or reinfarction rate in the treated group, that some studies have shown a trend in favour of the treated group, but that none has shown that the treated group did worse than the control group. But to state as your leader writer does that there is "... absence of any evidence of benefit" seems to be quite far from the truth. If one wants to abandon the long-term use of anticoagulants after myocardial infarction I should certainly use other arguments than "the absence of any evidence of benefit" of this treatment.

Such a leading article gives food for many thoughts. One is that I would have liked the article to be signed.—I am, etc.,

CHR. F. BORCHGREVINK.

Institutt for Almenmedisin,
Oslo, Norway.

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- 2 Aspenström, G., and Korsen-Bengsten, K., *Acta Medica Scandinavica*, 1966, 176, 563.
- 3 Borchgrevink, C. F., *et al.*, *British Medical Journal*, 1968, 3, 571.

Azathioprine in Psoriasis

SIR,—Cytotoxic drugs are widely used in the treatment of psoriasis which has failed to respond to conventional topical regimens. Most dermatologists have used methotrexate, but there have recently been several disquieting reports¹⁻⁴ of renal and hepatic damage following methotrexate therapy. Because of an earlier favourable report of 6-mercaptopurine in psoriasis⁵ we have carried out a preliminary study of the closely related drug azathioprine (Imuran) in this disease.

Ten patients were studied, all of whom has disabling psoriasis which had proved refractory to prolonged topical treatment. Methotrexate had earlier been given to six of these, but had been withdrawn in four because of failure to respond. In the remaining two methotrexate had been stopped because of toxic effects. The total daily dosage of azathioprine was 2.5 mg./kg. body weight and this was continued for six weeks. None of the patients studied was on any other systemic treatment for psoriasis during the period of study. The only local treatment prescribed was emulsifying ointment. All patients completed the six-week course of treatment.

Before beginning azathioprine haemoglobin, total and differential white cell counts and platelet counts, E.S.R., blood urea, and liver function tests were carried out, and were repeated at fortnightly intervals.

The results are summarized in the Table. Of the ten patients, five showed clearing of

Sex	Age	Previous Systemic Therapy	Response*	Toxicity
F	31	—	+++	—
F	57	Methotrexate	+	leucopenia
F	57	—	+	—
F	63	Methotrexate	+	raised bilirubin
F	39	—	+	—
F	73	Methotrexate	+++	anaemia, leucopenia
M	61	Methotrexate	+	—
M	52	Triamcinolone	+	—
F	38	Methotrexate	+	—
F	72	Methotrexate	+	—

*Grading of response:

○ = 0–25% reduction in area of involvement
 + = 25–50%
 ++ = 50–75%
 +++ = 75–100%

extent 25% or more. Improvement occurred at two weeks in two patients. In the remaining three improvement was not observed till four to six weeks. In three of the patients who had shown improvement azathioprine treatment was discontinued at the end of the six-week period. One month later relapse had occurred in two of these. In three of the 10 patients toxic effects were noted (leucopenia in two, raised serum bilirubin in one), but these reverted to normal on ceasing azathioprine.

Methotrexate given in daily oral dosage is effective in 70–100% of cases of chronic psoriasis,^{6,7} whereas in the present study only one-half of the patients showed significant clearing with azathioprine. Since, however, three of the remaining patients had failed to respond to methotrexate and one to systemic triamcinolone the comparison is probably misleading, and we feel our results are sufficiently encouraging to justify a more detailed study of azathioprine in psoriasis.—We are, etc.,

MALCOLM W. GREAVES.

ROD DAWBER.

University Department of Dermatology,
 Newcastle upon Tyne.

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One-eye Viewing

SIR,—It has long been recognized that monocular clues such as perspective and the change in apparent colour of objects as they recede into the distance are of considerable importance in depth perception.¹ For several years I have illustrated this point in my teaching by asking students to view colour photographs or reproductions of representational paintings.

When viewed with both eyes open the pictures appear flat. Presumably this is because binocular clues provide the accurate information that all points in the picture are in the same plane. This predominates over any illusion of depth created by the monocular clues. When one eye is covered most subjects report a greatly increased impression of depth. This illusion is enhanced by

detailed inspection of the picture at close range. The phenomenon is quite striking and I am surprised that it is not better known. I presume it has been described before and I would appreciate information concerning previous reports in the literature.

The significance of this phenomenon is by no means trivial. I have spent many happy hours wandering through art galleries with the catalogue lightly covering one eye. I have been amazed at the extra life that this injects into most paintings. The impressionists especially respond to this

method of viewing. Also I wonder if even the most expensive stereoscopic apparatus can create a more realistic impression of depth than does a good quality colour photograph viewed with one eye?—I am, etc.,

R. B. CROSS.

Department of Physiology,
 University of Queensland,
 Brisbane, Australia.

REFERENCE

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Children in Intensive Care Units

SIR,—The interesting article by Drs. J. R. Harper and G. Varakis (28 March, p. 810) points the way to the logical utilization of the complicated and expensive facilities and specialized staff involved in intensive therapy units. In Peterborough we have gone one step further in that we admit all children requiring intensive therapy, including neonates, to the adult unit.

Peterborough District Hospital (opened August, 1968) has a seven-bedded intensive therapy unit with all the usual facilities, including a hyperbaric oxygen chamber. In the year preceding January, 1970, out of 462 admissions to the unit 50 were children under the age of 12 years with a simple statistical breakdown as follows:

	Total	Ventilated	Nasal Endotracheal Tube Only	Died	Average Length of Stay
Medical—Neonates	20	16	2	6	7.2 days
Others	15	7	2	4	4.2 days
Surgical—Head injuries	6	—	—	—	4 days
Postoperative	9	—	—	—	

Like our colleagues at Northampton we have found that the children were adaptable, and those old enough to comment gave no indication that they thought of the unit as being any more frightening than the other parts of the hospital. On the other hand we find that the children, especially the neonates, demand a great deal of attention, and this is occasionally disturbing to the adult patients on the unit, particularly at night. We are fortunate in that as part of the intensive therapy unit there is a separate environment-controlled room which is proving invaluable for nursing the smaller babies. We feel that, though still an intrinsic part of the adult unit, the paediatric portion should have a definite area where the relevant equipment can be concentrated, and not exist as an adaptation of whatever space is vacant at the time. Obviously, however, the unit must remain flexible to meet the occasional heavy demands of either paediatric or adult patients.

by the senior members has smoothed the initial difficulties and now children are welcomed as providing a more complete range of work. The children's ward staff have noticed the understandable "I.T.U.-itis" on transfer back from the unit, but state that the patients soon re-adapt to the ward atmosphere and that no real problems have been encountered.

In conclusion we agree, as already stated, that the duplication of these expensive facilities in separate areas for adults and children is not feasible in the district general hospitals, and hope our results help to prove that the alternative of treating all patients together can work.—We are, etc.,

R. ROBERTSHAW.

B. W. POWELL.

Peterborough District Hospital,
 Peterborough.

Allergy to Iprindole (Prondol) with Hepatotoxicity

SIR,—Dr. P. J. W. Young (7 February, p. 367) reported an allergic reaction to iprindole with hepatotoxicity. We would like to draw attention to two cases which have occurred in the last year in this practice where hepatotoxicity without obvious allergic phenomena was demonstrated.

The first was in a 30-year-old house-

wife who had had a long-standing history of depression and who had been on tranylcypromine until a fortnight before iprindole was prescribed on 24 December 1968. A week later she felt unwell and by 3 January 1969 she was jaundiced, had discomfort in the right hypochondrium, and had dark urine in which bilirubin and urobilinogen were