required a very much larger clinical trial. This is exactly the cause of the equivocal results obtained by Mr. G. E. Moloney and his colleagues (24 October, p. 244).—I am, etc.,
F. S. A. DORAN
Bromsgrove General Hospital, Bromsgrove, Worcs

Cholera Again
Sir,—I venture to disagree with some of the points in your leading article on 'Cholera again' (3 December, p. 2). The 5/4/1 Daccsa solution can be used only for cholera or choleraic dysentery. It is absurd to stockpile specialized fluid of this kind when equally good results are obtainable by the simple right-angled solution, provided that the extra potassium and alkalai needed for full replacement therapy are given orally, either as a four-hourly or six-hourly dose of KCl, 3 g, and NaHCO₃, 4.5 g. As lactated Ringer is used for the intravenous therapy of many conditions, it is widely available, and any stock of it can be used. So easy is it to see when the patient has been given enough fluid that we usually delegate the decision when to stop to the nursing staff—after they have had a little supervision over the first case or two—that it is not difficult in deciding correctly. Surely what our nurses can do a physician in England can also do? I deprecate forsaking observing physical signs in exchange for reading laboratory results.

My account of the 1965 Brunei cholera epidemic may be of assistance to those who wish to know more of the practical aspects of cholera therapy. A second epidemic on a smaller scale has been dealt with subsequently in an identical manner, and we have yet to see one of our patients succumb to cholera. As a matter of practical experience, therefore, the simpler methods recommended in my article are difficult to improve on.—I am, etc.,

P. L. DE V. HART

General Hospital, Brunei Town, State of Brunei, Borneo.


Cataract Spectacles
Sir,—As an aphakic motorist I am writing to thank you for your leading article (12 December, p. 634) describing methods of overcoming the difficulties that we have because of the limitation of our visual fields. As you say, the full-aperture lens with its comparatively wide visual field does have an inconvenient peripheral ring scotoma, but this scotoma is so far out to the side that the motorist wearing full-aperture spectacles has no trouble at road junctions or in reversing.

Unfortunately, aphakic motorists are commonly prescribed "pebble" lenses which are about 2 cm in diameter. With these not only is the visual field very limited but their peripheral ring scotoma is dangerous as it lies so far forward that cars coming from the side suddenly appear without warning in front of the motorist approaching an intersection. Reversing is both difficult and dangerous with these small lenses. In my experience, pebble lenses do not give clearer vision than full-aperture lenses.

Full-aperture lenses should be prescribed for all aphakic motorists so that they will have as wide a visual field as possible.—I am, etc.,

J. B. MORWOOD

Public Health Department, Banstead, Surrey

Vision and Accidents
Sir,—In your editorial (12 December, p. 634) you state that the Medical Commission on Accident Prevention says that available evidence suggests that defective visual acuity is not important in the causation of accidents. As accidents occur more frequently after dark, more frequently in foggy weather, and people are required to have approximately a visual acuity of 6/12 before being allowed to drive, it seems that a prima facie case is made out that good sight is necessary for safe driving and that present standards should not be relaxed whatever the "available" evidence is.

I feel that the "evidence" is likely to be unsound for various reasons, one being that eye tests are not performed on cadet officers. An article in your book (281) on the place of gold therapy was knocked down as she stepped on to a crossing, complaining ten days later that the accident had caused defective vision in her right eye. She had had no head injury, her right peripheral vision was intact, but she had previously been cataractous and had contributed some of the eyesight that was lost. It was clear that her previously unnoticed poor vision in the right eye, far from being the result of the accident, was contributed to by the accident itself.

Unless the eyesight of all people involved in accidents, including those at night whose dark adaptation is known at the moment of impact, is recorded, I do not see how reliable statistics can be obtained.—I am, etc.,

P. A. GARDINER

London W.1

Gold in Rheumatoid Arthritis
Sir,—In your recent Current Practice article on rheumatoid arthritis (5 December, p. 603) the place of gold therapy was briefly reviewed. Reference was made to the possible value of estimating gold levels in biological fluids and it was claimed that toxic effects are associated with excessive plasma gold levels.

In this connexion two patients who developed blood dyscrasias having received 810 and 780 mg Myocrisin (sodium aurothiomalate) respectively have been studied at the London Hospital. Both patients were receiving Myocrisin 50 mg by intramuscular injection at monthly intervals when the toxicity was observed. One patient had received weekly injections of 50 mg to a total dose of 730 and 580 mg respectively, during which time serial serum gold estimations had been performed. The mean serum gold levels (taken one week after the previous injection and after the patients had received a total of 330 and 360 mg Myocrisin) were 339 and 248 μg/100 ml, while in a group of nine patients who responded to gold without evidence of toxicity the mean level was 610 μg/100 ml.

Clearly, in these two patients there was no evidence of significantly raised serum gold levels. The levels of gold found in the serum vary widely depending on the size of the dose administered, the frequency of the injections, the interval after the last injection, and the total amount of gold given. If it is felt that a serum gold determination might be helpful in a patient with a genuine or suspected toxic reaction to gold a random blood sample estimation could not be interpreted correctly unless all these factors were considered.
were taken into account. As long as 1941 Freyberg et al.,\(^1\) wrote that they were unable to demonstrate any relationship between serum gold levels and the response to therapy, and the development of toxic reactions. Because more recent reports\(^2\) have suggested that there may be a relationship between these factors the results of serum gold are of interest. In a group of 37 patients are being analysed. Preliminary results so far are in agreement with Freyberg in failing to provide useful data regarding the response to therapy. Detailed results will be published shortly.—I am, etc.,

J. D. JESSOP
Department of Physical Medicine and Rheumatology, The London Hospital, London E.1


Combined Triiodothyronine and Thyroxine

Sir,—We wish to reply to the comments of Dr. J. A. Weaver (7 November, p. 366) on our clinical trial (17 October, p. 145). We have conformed to both administration of triiodothyronine and thyroxine using the 1:4 ratio (20μg T-3:80μg T-4) because this formulation had been recommended\(^3\) and adopted in commercial preparations in Europe and the United States. In a double-blind cross-over study it was essential that the number and appearance of the tablets in each treatment period were identical. Unfortunately, the two hormones differ in metabolic activity and, in addition, their rate and degree of absorption so that the dosages, dictated by the available formulations, were not equipotent. Preparations with equal biological effectiveness will be difficult to obtain. Theoretically, the recent formulation (15μg T-3:45μg T-4)\(^4\) offers a better approximation to the metabolic activity of one thyroxine tablet (100μg) and, therefore, would facilitate the cross-over study but this preparation was not available when the study was planned. On the other hand, calculations of metabolic activity may be spurious in clinical practice where the level of the two hormones in plasma and tissues is dictated by many variables which will finally determine the relative contributions of the two hormones to their total metabolic activity in patients. Apart from differences in their individual absorption and metabolism, the concurrent administration of the two hormones may influence the absorption of each and erratic medication, as detected in the trial, will constitute another variable. In these circumstances, we accepted the limitations in the choice of dose.

We avoided offering a statistically-orientated conclusion because a clinical interpretation was needed. In fact, analysis of the patients’ preferences gives a significant difference, using a \(x^2\) test, which Dr. Weaver may have had in mind. Fuller consideration of the variable factors in this trial, as in most clinical studies,\(^5\) illustrates the difficulty of interpreting the findings and suggests caution in analysis. About half of the patients had no preference for either treatment and this may be the correct clinical conclusion from the data. The additional observation that untoward symptoms were more likely to occur during treatment with the combined preparation was unexpected and, in our view, is inherent when using triiodothyronine either alone or in combination. From the protagonists’ point of view the onus of establishing greater clinical benefit remains; their studies offered no attempt to assess clinical well-being in comparison with thyroxine therapy. We argued that their emphasis on “normal” thyroid function as a sign of combined treatment is unsound as a guide to replacement dosage. Since the paper was submitted there has been further evidence that a proportion of exogenous thyroxine is converted to triiodothyronine in the tissues.\(^5\) Accordingly, efforts to formulate a fixed-ratio preparation containing the “correct” proportions of the two hormones are not necessary, and we contend that thyroxine alone has overall advantage in clinical practice.—We are, etc.,

R. N. SMITH
Upjohn Center for Clinical Pharmacology, University of Western Michigan, Ann Arbor, Michigan, U.S.A.

S. A. TAYLOR
Department of Pharmacology and Therapeutics, University and Royal Infirmary, Sheffield, Yorks.

J. C. MASSEY
Department of Chemical Pathology, United Sheffield Hospitals, Children’s Hospital, Sheffield, Yorks.

Blood Transusions for Leukaemic Patients

Sir,—While offering our congratulations to Dr. D. Crowther and his colleagues (28 November, p. 513) for their interesting paper on the treatment of acute myelogenous leukaemia in adults, we may be permitted to add a cautionary note. We hope helpful rider? Although appreciating the editorial pressures put upon authors to limit the size of an article, we were nevertheless somewhat dismayed at the complete lack of information, indeed the absence of any comment, on the blood transfusion requirements of these patients, all 23 of whom developed severe bone marrow depression during the course of therapy. We presume that this information is readily available to the group as the absence of an acknowledgment to the local regional blood transfusion centre suggests that blood requirements were met from the hospital’s own department of haematology’s donor resources.

At the time of publication Dr. Crowther and his colleagues had treated a total of 37 patients, recording an enviable remission rate of 62%.\(^6\) It would seem likely, therefore, that sufficient experience will have been obtained in the near future to provide clinical settings and definitive answers to the management of thrombocytopenia seen before and/or during intensive therapy. On the assumption that blood transfusion was necessary during at least some of the periods of severe bone marrow depression perhaps we might ask the following questions: What were the indications for platelet replacement? What was the total number of donations used for platelet therapy in the group of 37 patients? Did all the patients require platelet support and what was the average number of donations required per remission? Were ABC and Rheus-compatible platelets used exclusively? And, finally, did occasions arise when the lack of supportive treatment constituted a serious threat to life (Case 10) or delayed the introduction of a course of combined chemotherapy?

These questions are intended to be entirely constructive as our own experience with this aggressive approach to the treatment of acute leukaemia leads us to suggest that all patients for whom this type of regimen is indicated should be referred to centres that are functionally and perhaps geographically closely related to regional blood transfusion centres. Moreover, it seems possible that the heavy demands generated by these protocols, seven days a week, are not fully appreciated by the blood transfusion services.

Perhaps we could serve this opening dialogue best by recording the number of donations withdrawn for platelet therapy in Scotland and England 1968 (Fig.). During September 1969 the effects of “ablative” chemotherapy in the management of acute leukaemia were first realized. Despite intensive surveillance by the senior medical staff on all requests and excellent training of our junior staff, the number of units of whole blood processed for platelets has risen by over 600% since that time. To meet this demand radical reorganization at administrative and technical levels has been necessary. It is an important fact that the subsequent increase in the availability of platelet concentrates, at any time of the day or night, has resulted in marked increase in their use by our colleagues in the management of other thrombocytopenic conditions, notably aplastic anaemia. In the light of this experience we are bound to conclude that previous efforts to supply platelets for patients with thrombocytopenia unrelated to "ablative" chemotherapy were less than adequate. We believe that Dr. Zucker’s suggestion that most blood transfusion services should automatically process 10% of their fresh whole blood units for platelets is somewhat right.\(^7\)

The implications of these preliminary findings are many, but before our clinical colleagues race ahead with further advances in “ablative” chemotherapy we would ask them to consider seriously their blood transfusion requirements, so that funds to provide adequate facilities and staff at

5 Mainland, D., Clinical Pharmacology and Therapeutics, 1969, 10, 867.