respectively. Thus it would seem that the mortality following transplantation is grossly underestimated on the basis of the Edinburgh data (however, other transplant survival data are available).

Secondly, there are several minor errors in the text and Tables. For example, in Figure 3 the numbers of patients surviving in the first five months bears little relation to the percentage survival graph. Also, in the paragraph on dialysis survival, it is stated that a survival of 0·98 has been used in states 7, 15, 23, and 25; this is not true of state 25.

Finally, it would seem that some explanation of the derivation of the 95% confidence limit is necessary. As I understand forecasting by a Markov process a 95% confidence limit is calculable on the basis that each parameter behaves as a random variable subject to predetermined probabilities. However, each probability, based on observation of past data, is subject to error and an estimation of these errors is desirable before confidence limits are applied to a forecast. As indicated above, I consider that several of the more important probabilities have been assigned values in error.—I am, etc.,

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Long-acting Phenothiazines in Schizophrenia

SIR,—I have belatedly received the 23 January issue of the *British Medical Journal* and was most interested in your leading article on "Long-acting Phenothiazines" (p. 189).

This article mentions "no double-blind controlled investigations of long-acting fluphenazines have been reported." At least six are known to me, of which three compare an active oral phenothazine with fluphenazines enanthate.[1-3]

Despite this oversight the writer rightly interprets the remaining data as indicative of their usefulness. This is important since we should not make a mystique out of the controlled trial. The necessity for their use in certain areas should not blind us to the information available from other approaches, particularly in this type of patient.

In the first study of fluphenazine decanoate in man we concluded that it was a most useful potent agent, longer acting, and with fewer side effects than fluphenazine enanthate; this in an open-study of 12 patients.[4] No evidence has appeared to contradict the above statements, and indeed in two controlled studies of fluphenazine enanthate versus fluphenazine decanoate both concluded that fewer extrapyramidal side effects are produced with the decanoate, although the results were less conclusive about the greater length of activity.[5,6]

The incidence and control of side effects has been detailed elsewhere, but are not necessarily as frightening as has been suggested.[7]

The range of improvement which appears greater than with oral preparations may be related to bypassing the gut and the liver therefore avoiding absorption and possibly early metabolic breakdown. Finally, the question of depression may be related to the more rapid improvement noted with this drug. As the article states, depression is a common feature of schizophrenia, but an alternative explanation is the "depression with insight" which often occurs with the rapid removal of symptoms.—I am, etc.,

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Antibiotic Sensitivity Testing

SIR,—Your recent leading article (22 May, p. 416) drew attention to the difficulties and lack of agreement in the interpretation of antibiotic sensitivity tests. This is hardly surprising considering that in any one organism each type of drug resistance shows different characteristics and that the level of resistance detected by standard dilution methods or inferred from zone diameters in diffusion tests depends on such a variety of factors peculiar to the organism.

Very little decisive information has been collected on the significance—in terms of interference with therapeutic response—of several of the commoner types of drug resistance seen in hospital strains of *Staph. aureus*. In trying to simplify the situation we probably err on the side of over-caution in some of our assessments of resistance—in particular with the penicillins—and may consequently not benefit to the full from some of our basic antibiotics.

At the present time the emergence in hospitals of new types of *Staph. aureus* showing a temperature-dependent tolerance to all penicillins and cephalosporins—usually referred to as methicillin resistance—has added to the difficulties in sensitivity testing. The distinction between cultures of full sensitivity and those showing this, the only type of naturally occurring resistance, is clear-cut in disc diffusion tests with methicillin carried out at 30°C. In similar tests at 37°C no clear picture emerges, there being a continuous range of zone sizes from apparently "sensitive" to apparently "resistant" in tests on nutrient agar media without added salt.[1] It may well be, however, that there is a better correlation between response to therapy and apparent sensitivity in disc diffusion tests at 37°C—particularly in those patients with otherwise unimpaired resistance to infection. Benner and Kayser have used the term "basal resistance" in an attempt to relate levels of methicillin resistance to in vivo therapeutic response.[2]

In the absence of comparative clinical trials it seems that there are two ways in which clinically relevant information on this and similar difficulties could be obtained. Firstly, for clinicians in hospital or general practice and pathologists advising on chemotherapy to attempt an unbiased retrospective analysis—from patient records—of the outcome of chemotherapy in patients where the infecting microbe was subsequently demonstrated to harbour a specific type of resistance to the drug used. Secondly, for a central laboratory to examine in detail collections of cultures from specific types of infections where the outcome of single course antibiotic therapy is known—whether successful or not—irrespective of what previous interpretation had been made of sensitivity tests.

Studies of this type might help in our understanding of which levels of resistance are likely to compromise successful therapy in particular categories of infection. In the case of methicillin resistance in staphylococci, for example, they might help to tell us which types of infection are amenable to treatment with penicillins (for example, cloxacillin) alone, and which require supplementary or other therapy. A similar study would be useful in the case of outpatients in whom infections are often caused by *Staph. aureus* strains producing small amounts of penicillinase. Many of these infections are still amenable to treatment with penicillinase-labile penicillins.[3,4]

In a subject where there is little factual information to rely on it would seem prudent to make use of all possible sources of information. It would be of interest to hear if anyone has access to material that might be of value in the types of assessment described.—I am, etc.,

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Cyclophosphamide and the Bladder

SIR,—A point referred to in your leading article (26 June, p. 726) merits amplification. It relates to the distinction between cyclophosphamide-induced cystitis and bladder malignancy.

Your leading article reinforces the manufacturer's recently circularized note about haemorrhagic cystitis, drawing attention to the occurrence of this side effect of the drug in some 10 to 20% of patients receiving large amounts of cyclophosphamide. Increased awareness will reduce the possibility of misinterpretation of the cause of haematuria when this is not accompanied by the more usual dysuria or increased frequency of micturition. Even cystoscopy, biopsy, and cytology can be misleading. Liedberg *et al.*[1] say "The cytologist and the clinician should be aware of the fact that pictures suggesting malignancy may appear during treatment with cyclophosphamide. The polymorphous, tumour-like granulation tissue sometimes seen on cystoscopy may be mistaken for metastases or primary bladder tumour both macroscopically and microscopically, particularly in very small biopsy specimens." Goldman and Warner[2] also emphasized the importance of recognizing the atypical

epithelial elements as the result of drug metabolite toxicity rather than as malignant change.

Cyclophosphamide, in common with other cytotoxic agents, can under experimental conditions produce malignant change in laboratory animals. However, it is not one of those that has been known to produce malignancy in humans treated with cytotoxic drugs for non-malignant disease or for suppression of homograft rejection. However, one case of a second malignancy (myeloblastic leukaemia) occurring in a patient on long-term cyclophosphamide for a first malignancy (of the ovary) has been reported,[3] and though this hazard may be less with cyclophosphamide than with certain other cytotoxic drugs, it should be borne in mind.—I am, etc.,

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Organ Donation—Valid Consent

SIR,—Reference was made in Council's Report (*Supplement*, 8 May, p. 62) to organ donation. Patients often ask how they can help medical science and others by donating an organ or their bodies. The following notes may be of assistance.

(1) A would-be donor must be at least 16 and mentally sound.

(2) If the deceased wished to leave his body or parts of it for medical purposes, this amounts in law only to a request to which his executor is not bound to give effect.

(3) If there was no mention of his wishes, surviving relatives have a right, so far as it is practicable to consult them, to object to the disposal of his body for medical purposes.

(4) The person "lawfully in possession" of a body has to dispose of it. This person is the owner of the premises until the executor or a relative claims the body, becoming the person "lawfully in possession."

(5) Even if the next-of-kin or a relative has indicated prior to the deceased's death that they do not object, the executor still has the power to decide against disposal of the body for medical purpses.

(6) If a person dies in an institution without relatives, the institution decides on disposal. Being intestate or having made no mention in a will is not crucial. The institution may bequeath the body only if it has no reason to suppose, after inquiry, objection by the deceased in his lifetime.

(7) An instrument of donation may not be so formal as a will. The would-be donor should leave with his papers a written statement of his desire to benefit medical education in this way.

(8) As soon as possible after death of the testator, the executors should telephone H.M. Inspector of Anatomy (01-407 5522) and post to him at the Department of Health and Social Security a notice (under the Anatomy Act) and medical certificate of cause of death.

(9) If the deceased wishes to leave an organ under the Human Tissue Act, he should make an oral declaration before two witnesses in his final illness. Alternatively, a simple written declaration will meet this Act if the intention is clear.

(10) If no executor exists nor knowledge of the deceased's intention, relatives or the person "lawfully in possession" can authorize a bequest for medical purposes.

(11) As to transplants, the organs must be removed very soon after death; hence only a medical institution would be able to help in such cases.

(12) The Royal National Institute for the Blind, 224 Great Portland Street, London W.1, keeps a register for corneal grafting. Potential donors might carry on their persons a note of their wish to make such a bequest.—I am, etc.,

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General Practitioner Obstetrics

SIR,—Some complaints about long waiting times at antenatal clinics may well arise out of unnecessary attendances. Obstetric consultants have a tendency to take over perfectly straightforward antenatal work from the general practitioner merely because a statistically increased risk necessitates booking one of their hospital beds for the confinement. Delivery of a grand multipara or elderly primipara may be safer in the general hospital 20 miles (30 km) away than in the local maternity unit, but the overall advantage in some cases must become very doubtful if arranging this with a consultant is going to let her in for regular 40-mile journeys (60 km) to his antenatal clinics, with an hour or so waiting about to be seen by a variety of obstetric personnel.

Under present foreseeable circumstances the consultants must compromize, and clearly should do so in a logical manner that would also avoid the overcrowding of their antenatal clinics and unnecessary journeying and waiting by mothers. There might even emerge a case for every primipara having the benefit of a second opinion at 36 weeks' gestation, but surely it would be found that the hordes of mothers who regularly attend hospital for no better reason than that they have booked their confinement there could well revert to the care of their own doctors for at least the first seven or eight months of gestation.—I am, etc.,

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Fractured Femur and Fat Embolism

SIR,—Mr. P. A. Ring (3 July, p. 46) seems to give tacit acceptance to the fact that fat embolism is not a complication of the nailing operation for subcapital fractures, but his statement that this operation "commonly ends in disaster" is something less than half the truth.

Such a statement would be valid only if it were confined to trifin nailing for displaced fractures of Stage III and IV.[1] As emphasized by Barnes[2] and many other observers, trifin nailing is quite inadequate for these fractures for which more rigid fixation is necessary. Several methods of internal fixation are in fact available[3-5] which have been shown to achieve a consistent union rate of about 85% in displaced fractures, and those experienced in their use believe internal fixation to be a far safer and more dependable routine method of treatment for these elderly patients than primary prosthetic replacement. This view was confirmed by a recent comparison of two series of patients treated at the Radcliffe Infirmary, Oxford, by internal fixation and prosthesis respectively, in which the results came out strongly in favour of the former, both as to primary operative mortality and postoperative morbidity.[6]

In a series of cases to be published shortly from this centre, confined to fractures of Stage III and IV and to one method of fixation (triangle pinning), there has been no primary operative mortality, no recognizable case of fat embolism, and, in a minimum follow-up of two years, no patient has required replacement surgery for avascular necrosis. The union rate among these patients was 86% and the evidence suggests that the remaining 14% of failures were attributable in every instance to an error, in either reduction or fixation, on the part of the surgeon, rather than to any inherent biological or mechanical qualities conducive to non union in the fracture.—I am, etc.,

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Induction Course for Hospital Medical Staff

SIR,—Induction programmes, formal or informal, have been developed to help newcomers learn about their hospital environment more easily, learn their tasks more quickly, and avoid disturbing errors. An effective induction programme is concerned with introducing the newcomer to physical environment, hospital personnel, duties to be performed, interrelationship with other departments, and background information concerning the hospital's place in the community, its goals and achievements. No newcomer can assimilate all this in one crowded and confusing day.

Though induction courses are run for some ancillary staff in some hospitals, this has not so far been done for professional and technical staff, and no formal induction course has yet been done for medical staff.

I carried out a survey of all the medical staff who had joined the Salford Group of Hospitals in the last 12 months. A questionnaire was sent to 37 doctors. 26 (17 English and 9 overseas) responded and the findings of the summary were:

Seventeen doctors were not told to whom they had to report on the first day of joining;
Seven were not told about the nature of their work;
Five only were taken to other hospitals nearby where they would work in close association;