given a preoperative medication such as diazepam? This would not interfere with their being discharged in the early afternoon. The availability of contact with the gynaecological house surgeon if needed before subsequent appointments is a most reassuring facility.

With the change in attitude by the lay public towards abortion it is a great pleasure to feel that genuine efforts are being made by members of the profession such as Dr. Lewis and her co-workers to minimize the mental and physical trauma inherent in this procedure.—I am, etc.,

HENRY FITZGIBBON

Penticton, B.C.,
Canada

Anticoagulants in Mitral Valve Disease

SIR,—In your leading article (11 March, p. 641) on "Anticoagulants in Mitral Valve Disease" you quote us as finding that there was a 35% general incidence of embolism.¹ This figure in our paper was, in fact, 25%.—We are, etc.,

H. A. FLEMING
S. M. BAILEY

Regional Cardiac Unit,
Papworth Hospital,
Cambridge

¹ Fleming, H. A., and Bailey, S. M., *Postgraduate Medical Journal*, 1971, 47, 599.

** We regret this error.—ED., B.M.J.

Serum Hepatitis Hazard in Biochemical Control Sera

SIR,—Drs. A. D. Evans and K. W. Davies (11 March, p. 691) refer to the finding of H.A.A. in one of our company's products, Versatol Diagnostic Reagent batch no. 0089027. In view of the obvious concern which may be felt by laboratory staff, may I bring the following points to your attention.

The Versatol batch quoted was manufactured five years ago. At that time there was no awareness of the danger of hepatitis from reagents made of human sera and no testing for this antigen was done. No reagent of this batch number has been despatched to laboratories in Britain since early 1968 and, in the unlikely event that any hospital still holds any in stock, I would be pleased to exchange it for current material.

The following precautions are now taken by this company in manufacturing all freeze dried serum of human origin.

(1) These products are prepared in our American manufacturing plant from plasma obtained from blood banks. No unit of plasma is accepted without a certificate stating that the donor has been tested for the presence of Australian antigen. Further, pooled batches of plasma are tested again immediately before any further processing is undertaken. At these stages the method used for testing is the "Spectro-biological" electrophoretic method, and any material found to be positive is rejected.

(2) As a further precaution, finished manufactured products are now being tested on arrival in Britain by an independent virology laboratory, and no batches are released without a satisfactory report. The methods used for testing in the United Kingdom are electron microscopy, complement fixation test, immuno-electro-osmophoresis, and gel diffusion technique. This testing procedure has also been applied to all human plasma

based reagents which have been distributed in Britain bearing a manufacturing date from January 1971.

I hope you will agree this demonstrates our concern and that we are taking all possible precautions to eliminate any risks associated with our reagents.—I am, etc.,

JOHN M. MCGILCHRIST,
Medical Director,
William Warner and Co. Ltd.

Eastleigh, Hants

Sustained Relief of Hemiballismus

SIR,—The violent involuntary movements of hemiballismus—occasionally termed apoplectic chorea because of the frequency of a vascular basis—may in the acute phase be of such constancy and severity as to occasion a degree of exhaustion sufficient to endanger life. The rapid and persisting relief which attended the use of thiopropazate hydrochloride (Dartalan) in the present patient would appear to offer good prospects for its successful application in this condition.

A widow of 75 years of age suddenly developed involuntary movements of the right arm and leg. At first these were not of great severity, but two weeks later their intensity abruptly increased to the classical thrashing movements of hemiballismus. The blood pressure was considerably elevated, while the blood urea was normal; little else could be gleaned from the physical examination. The violence of the movements continued unabated and her general condition showed considerable deterioration. Various measures, alone or in combination, failed to effect an ameliorating influence, and included phenytoin, diazepam, L-dopa, amantadine, phenobarbitone, and chlorpromazine. With the difficulties of adequate oral feeding, intravenous fluids were required. Gradually the patient's general condition improved, but the involuntary movements remained little altered. All medication was discontinued. A gradual spontaneous improvement ensued over the next nine months without any treatment.

At that time she was still displaying very frequent wide amplitude throwing movements of the affected arm, making dressing and feeding impossible. The disability was considerable, and had remained more or less the same for about five months. Thiopropazate hydrochloride was prescribed in small dosage—2.5 mg twice a day. The response was remarkable. Within a week the involuntary movements had become infrequent. This effect has been fully maintained for more than five months without any untoward reactions.

A more aggressive therapeutic approach towards involuntary movements, whether these arise as a result of disease or are drug induced, has recently been taken. Thiopropazate hydrochloride is a phenothiazine and bears close relationship to chlorpromazine. Its present application in the control of choreiform movements has been reviewed by Singer and Cheng,¹ and includes Huntington's chorea, non-hereditary chorea, and Sydenham's chorea activated by oral contraceptives. Since thiopropazate hydrochloride may itself produce Parkinsonism the dose should be kept at as low an effective level as possible; the very small amount required in the present case is well below the average 15 mg three times a day em-

ployed in the study of Singer and Cheng,¹ a dosage considered to be excessive in the light of their subsequent experience.

Hemiballismus is of infrequent occurrence; the present example of its successful treatment with thiopropazate hydrochloride appears to be the sole record but the rapidity and degree of its alleviation encourages its future use, not only in the established chronic situation but also during the acute phase.—I am, etc.,

J. SHAFAR

Burnley General Hospital,
Burnley, Lancs

¹ Singer, K., and Cheng, M. N., *British Medical Journal*, 1971, 4, 22.

Arteriovenous Anastomosis for Convenient Chemotherapy

SIR,—In advanced Hodgkin's disease—stage III and IV and group B (symptomatic)—combination chemotherapy is rapidly becoming the treatment of choice. Six courses consisting of 24 injections of caustic substances are usually given, followed by multiple booster or maintenance courses over a period of years. Practitioners of this mode of treatment are at times frustrated in their efforts by the absence of superficial or accessible veins. The following exercise may be of assistance to those so confronted.

A corpulent 19-year-old girl had recurrent Hodgkin's disease with high temperature and pleural effusion. She was accepted for quadruple chemotherapy, but the absence of palpable or visible veins made this impossible. She was referred to a vascular surgeon, and the following operation performed in August 1970.

Under local anaesthesia a small vein of less than 1 mm diameter was exposed on the anterior aspect of the right forearm. This was anastomosed to the radial artery, but because of the small calibre, microvascular techniques had to be used. Twenty-four hours later there was a loud bruit over the anastomosis. A remission in the Hodgkin's disease was induced by corticosteroids, so the anastomosis was not used, although the vein was usable within a month of operation. By November 1971 this remission had come to an end, and in December she started combination chemotherapy consisting of vincristine, mustine hydrochloride, prednisone, and natulan.

Up to the time of writing no trouble has been experienced in the intravenous administration of the cytotoxic agents, the veins proximal to the anastomosis being easily visible and palpable 16 months after the operation (Fig. 1). No complications have

resulted from the anastomosis, and it is interesting to note the dilatation of veins in the contralateral shoulder (Fig. 2).

I should like to thank Dr. John Dalby for referring his patient to my care and Mrs. Averil O. Mansfield for performing the operation.
—I am, etc.,

M. J. GARRETT

Liverpool 1

Iatrogenic Bone Collapse

SIR,—Further to your leading article (4 March, p. 581), may I draw the attention of your readers to another cause of bone collapse commonly observed in orthopaedic practice but seldom referred to in the literature? Murray and Jacobson¹ have pointed out that radiological changes in bone similar to that seen following both oral administration and intra-articular injection of steroids can also follow the administration of drugs of the phenylbutazone group, especially when used for the treatment of degenerative joint diseases. This is most frequently seen in the hip joint—"crumbling hip syndrome"—in which bone collapse of the femoral head, indeed complete disintegration of the joint, can develop with remarkable rapidity following prolonged therapy with drugs of this group. Joint disintegration in an extreme case can even mimic a neuropathic joint.

The exact cause of this is uncertain. One of the factors responsible may be that relief of pain, even partial, can lead to an increase in the activity of the patient, and possibly as a consequence the work-load of the joint is increased.—I am, etc.,

S. MULLICK

Wessex Regional Orthopaedic Centre,
Lord Mayor Treloar Hospital,
Alton, Hants

¹ Murray, R. O., and Jacobson, H. G., *The Radiology of Skeletal Disorders*, 1971, 553. Edinburgh, Churchill Livingstone.

Nephrotoxicity from Methoxyflurane

SIR,—Several important issues relating to the nephrotoxicity of methoxyflurane anaesthesia have been raised (11 December 1971, p. 661, and 8 January, p. 81).

As Drs. E. A. Proctor and F. L. Barton (11 December 1971, p. 661) pointed out, our initial study indicated that methoxyflurane

nephrotoxicity may be dose-related in man.¹ We have subsequently developed an animal model for methoxyflurane nephrotoxicity in rats and with it have shown that changes in renal function and pathology are dose-related.² Intraperitoneal injection of sodium fluoride produced a syndrome biochemically and morphologically similar to that seen following methoxyflurane administration, while injection of oxalic acid in doses up to 10 times the amount resulting from methoxyflurane metabolism did not produce polyuria. These studies lead us to believe that inorganic fluoride is the primary nephrotoxic metabolite of methoxyflurane. The degree of nephrotoxicity is related to serum inorganic fluoride levels and in turn to total methoxyflurane dosage. Our most recent clinical studies confirm these findings in man.^{3,4}

It would appear that maintenance of low methoxyflurane dosage would prevent the occurrence of nephrotoxicity. However, the report by Drs. Proctor and Barton of nephrotoxicity following the administration of repeated low-dosage methoxyflurane and concurrent tetracycline draws attention to important issues: (1) Methoxyflurane is known to be capable of inducing its own metabolism; (2) serum levels of inorganic fluoride are raised for more than 10 days after a single administration of methoxyflurane; (3) there are marked individual variations in metabolism of methoxyflurane and sensitivity in inorganic fluoride as a nephrotoxin; and (4) toxic interaction between methoxyflurane and other drugs with nephrotoxic potential such as tetracycline is known to occur. Thus it is not surprising that a patient having methoxyflurane analgesia at daily intervals and also receiving tetracycline developed nephrotoxicity.

Dr. Michael Rosen and others (8 January, p. 81) concluded that methoxyflurane is not nephrotoxic when used as a self-administered obstetric analgesic. We believe this statement should be qualified. The agent appears not to be toxic under most conditions of low-dosage administration. It is not known if prolonged self-administration will lead to a large cumulative methoxyflurane dose with high serum inorganic fluoride levels. The concurrent administration of a nephrotoxic antibiotic might produce toxicity even if methoxyflurane dosage were low. Finally, the effects of the relatively high levels of serum inorganic fluoride on critical enzyme systems in the newborn have yet to be evaluated.—We are, etc.,

MICHAEL J. COUSINS

RICHARD I. MAZZE

Stanford University School of Medicine,
California

¹ Mazze, R. I., Trudell, J. R., and Cousins, M. J., *Anesthesiology*, 1971, 35, 247.

² Mazze, R. I., Cousins, M. J., and Kosek, J., *Anesthesiology*, 1972, in press.

³ Cousins, M. J., Nishimura, T., and Mazze, R. I., *Anesthesiology*, 1972, 36, 285.

⁴ Cousins, M. J., and Mazze, R. I., A dose-response study of methoxyflurane nephrotoxicity in man. In preparation.

Rapid Irregular Movements of Eyes and Limbs

SIR,—It was with great interest that I read the article by Drs. G. Pampielone and Maria Maia (19 February, p. 469) on the syndrome of rapid irregular movements of eyes and limbs in childhood. I was, however, disappointed that they did not record the blood lead levels in those patients who

showed no apparent aetiological cause for these signs.

I have recently returned from working as a medical officer for a lead smelting concern in a developing country, and was alarmed to find six unrelated African children under five years old who exhibited similar movements. In five of them the condition progressed to convulsions, coma, and death; and the survivor was mentally retarded. They all lived within half a mile (800 m) of the smelter. The children were found to have a blood lead level between 60 and 154 $\mu\text{g}/100\text{ ml}$ blood.

Facilities did not exist for E.E.G., poly-E.M.G. nor E.O.G. studies, but blood counts, skull x-rays, blood sugar, and electrolyte tests were unhelpful.

Treatment with intravenous calcium versenate (two patients) and penicillamine (four patients) failed to improve their condition. Corticotrophin was not tried.—I am, etc.,

M. J. NICKLIN

Gainsborough,
Lincs

Parenteral Long-acting Phenothiazines

SIR,—I would like to record a similar effect from fluphenazine decanoate to the one reported by Drs. R. N. Allan and H. C. White (22 January, p. 221).

The patient was a 61-year-old unemployed barman, who was admitted on 10 May 1971 with paraphrenia. Clinically he was myxoedematous and serum protein bound iodine was 1.7 μg per 100 ml. He was treated with thyroxine with great improvement in his mental and physical state and was discharged on 19 July. On 4 August he was re-admitted with a deep vein thrombosis which subsided rapidly on anticoagulants, and he was discharged on 23 August.

On 27 August he was re-admitted with grandiose delusions and was negativistic. He was now euthyroid. Medication with fluphenazine decanoate 25 mg fortnightly, benzhexol 5 mg t.i.d., haloperidol 3 mg t.i.d. was started on 27 October. His mental state improved rapidly. On 7 December he had a dystonic reaction relieved by procyclidine hydrochloride. On 12 January 1972, when he had received a total of 137.5 mg of fluphenazine decanoate as in the case of Drs. Allan and White's patient, he had extrapyramidal rigidity in all limbs. Procyclidine was given and haloperidol stopped. On 13 January he was worse. He was salivating profusely, could not swallow, and had a temperature of 39.5°C. The only other physical sign was scattered moist sounds in both lungs. He was treated by penicillin with streptomycin intramuscularly and procyclidine. The pyrexia subsided on the fourth day and the rigidity had disappeared by the seventh day. Chest x-ray on 26 January was clear. Five weeks after the last fluphenazine decanoate injection he was still excreting break-down products in his urine.

The interest of this case I feel is that the pyrexial reaction occurred with no more than an average dose of fluphenazine decanoate. Pyrexia does not appear to have been recorded as a complication of haloperidol treatment.

I should like to thank Dr. D. A. Toms for permission to report this case.
—I am, etc.,

J. B. DILLON

Nottingham