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.,

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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.,

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- 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

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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.,

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