aspirin, while opiates and their derivatives cause unwanted central nervous depression. Indomethacin seems to provide effective analgesia without making the patient drowsy, and based on this limited experience I strongly recommend it for this purpose. Other similar drugs which combine analgesic and anti-inflammatory properties might prove to be equally effective.

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¹ McGinn, J T, Rosati, M, and McGinn, T G, *New York State Journal of Medicine*, 1970, **70**, 1783.

Quality v quantity in children

SIR,—In your leading article on "Birth weight" (9 July, p 79) you state that obstetricians, paediatricians, and mothers "are increasingly concerned about the quality rather than the quantity of children." I have always considered this overworked phrase to be the rather silly and empty-headed catch cry of women's lib and the Family Planning Association, but when it comes from the *BMJ* it gives me pause and makes me wonder if my judgment was too peremptory.

Could you please explain for your less enlightened readers exactly what you mean? I can understand that if one has £x to spend one could choose one Rolls-Royce rather than five cheaper cars (*pace* British Leyland), but when it comes to human beings how is the fashionable two-child family of higher quality than a six-child one? Or, if parents have two high-quality children and then unpatriotically add a few more, does the quality of the original fortunate siblings gradually decline? I cannot see how in human affairs quality and quantity are mutually exclusive—unless one has the temerity to observe that, in general, the poor have more children than the rich.

There ought by now to be experimental evidence to show that the offspring in modern two-child families are of higher quality than those of the less pessimistic prewar days. To my simple observation the proof of your proposition is completely lacking; but its frequent restatement does harm to the confidence of parents and even to the nation itself.

H P DUNN

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. In this context quality implies lack of defects; the change in attitudes has come from a realisation that perinatal morbidity is just as important as perinatal mortality and that there is no profit in preserving the lives of very small infants unless they grow up free of gross physical or mental handicap.—Ed, *BMJ*.

Fatal chlormethiazole poisoning in chronic alcoholics

SIR,—I should like to reply to Dr M M Glatt's letter (22 October, p 1088), in which he misquotes the opening statement of my report (3 September, p 614), and to suggest, with respect, that he himself misses the point.

Nowhere in the report is it stated that chlormethiazole is an antidepressant, although condensation of the paper into a short report may have led to some loss of clarity. The opening statement was: "Chlormethiazole edisylate (Heminevrin) is a sedative, hypnotic,

and anticonvulsant drug widely used in the treatment of depression." A depressed patient may need treatment with a sedative or hypnotic drug in addition to any antidepressant therapy.

The manufacturers (Astra Chemicals Ltd) state that it is a drug of low toxicity.¹ This may have led some general practitioners to believe that a patient who is depressed and has suicidal tendencies may come to little harm if an overdose of the drug is taken. The drug is packaged in bottles of 100 tablets and the pharmaceutical chemists to whom I have spoken say that in their experience this is the quantity in which the drug is usually prescribed. In two of the fatal cases I described a bottle which had contained 100 tablets of chlormethiazole was found near the body of the deceased.

The point of my report was to show that chlormethiazole is potentially dangerous, especially when taken with alcohol. It is surely logical to conclude that this is not a drug which a general practitioner may safely prescribe for someone who is depressed, has suicidal tendencies, and above all is an alcoholic. Chlormethiazole is a useful drug for the treatment of withdrawal symptoms in alcoholics in hospital *under strict supervision*. This is not the situation with which my report dealt.

A fifth case of chlormethiazole poisoning has recently occurred in the Bedford area, but the results of the analysis arrived too late for inclusion in the report.

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¹ *Data Sheet Compendium*. London, Association of British Pharmaceutical Industry, 1977.

Outpatient chemotherapy for breast cancer

SIR,—In their recent paper on chemotherapy for carcinoma of the breast (22 October, p 1064) Drs J H Goldie and L A Price have shown that an excellent response can be obtained by giving the drugs on only one day in every three weeks. Unfortunately their regimen necessitates admission to hospital and this alone may deter doctors in very busy district hospitals where the use of hospital beds is under severe pressure from using it.

The major reason that the patients need admission is for the infusion of the methotrexate. This, however, could be given as a single intravenous injection together with the other drugs. The therapeutic blood level would last only about 4 h as opposed to 16 h by infusion, but it is unlikely that this change would make a marked difference to the tumour response rate. Thus the regimen could be changed to giving intravenously vincristine 1 mg/m², cyclophosphamide 600 mg/m², 5-fluorouracil 500 mg/m², and methotrexate 100 mg/m² on one occasion every three weeks; 30 mg of folinic acid should be taken by mouth 18 h later. Alternatively the methotrexate could be given by mouth—50 mg at the time of the injection and 50 mg 6 h later. This would give longer-lasting therapeutic blood levels. The folinic acid rescue would also need to be extended, possibly by giving a further 30 mg at 24 h. This scheme would require a very dependable patient.

If the advantages of such chemotherapy for breast cancer, with its good response rate and low morbidity, are to be offered to patients

throughout the country, then it must be easy to administer on an outpatient basis. The above modified regimens would fulfil these requirements.

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Blood for antenatal tests

SIR,—An increasing number of serological and other tests are now required during antenatal care. Each test, except that for haemoglobin estimation, calls for 10 ml of clotted blood. Would a lesser quantity—say, 2 ml—be feasible? It should then be possible to perform all the tests from 8 or 9 ml of clotted blood collected in a single container using one 10-ml syringe, leaving the few remaining drops for the haemoglobin estimation.

The saving in time, space, containers, and syringes would be considerable.

L G HULL

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Association of autoimmune diseases with HLA-B8

SIR,—I was very interested to read the report by Dr B Hazleman and others (15 October, p 989) on their findings of HLA-B8 in 54% of their patients with polymyalgia rheumatica (PMR) and giant-cell arteritis.

Of the other suspected autoimmune diseases associated with B8 which they mention, chronic active hepatitis has not been associated with PMR, whereas a mild cholestatic hepatic dysfunction, described by different authors in recent years,¹⁻⁵ seems to be common in patients with PMR. However, the nature of the underlying hepatic lesion has not been well understood.

In our study⁶ of the 37 patients with PMR in whom it was measured, 23 (62%) had elevated activity of serum alkaline phosphatase (AP), mainly of hepatic origin, and bromsulphalein retention was abnormal in six out of 13 patients (46%). Fine-needle liver biopsy of the liver was performed on six patients, four of whom had elevated AP levels of hepatic origin. Three of the four patients for whom liver smears were stained for AP activity had an increased activity in their bile canaliculi that corresponded to a rise in the serum concentration of AP. In one of these three patients staining with naphthylamidase showed that the bile canaliculi had a calibre wider than normal and had irregular and granular walls. A partial reversal of these changes was shown in a second biopsy performed 10 days after corticosteroid therapy had been given. Mild fatty degeneration of the liver cells was seen in two other patients, whereas a patient with normal serum AP activity also had normal liver cells and bile canaliculi. The pathological structural changes observed in the wall of the bile canaliculi in one patient and the increased AP activity in this same patient and in two others may be evidence of a subclinical hepatic disease of variable severity associated with PMR. The increased number of lymphocytes and plasma cells observed in half of the biopsy specimens points to an immunological pathogenesis of this hepatic lesion.

In their report Dr Hazleman and his colleagues also refer to the prevalence of HLA-A10 and B8 in Hodgkin's disease shown in

some studies. As an example of a possible relationship between malignant lymphoma and PMR on this ground they refer to a case described by us^{6,7} in which malignant lymphoma occurred four years after the diagnosis of PMR was made. Among our 54 patients with PMR we have recently reported another case⁸ in which chronic lymphatic leukaemia developed five years after the onset of typical PMR. In this patient lymphocytic infiltration was detected in renal, liver, and muscle biopsy specimens at the time of diagnosis of PMR, when the number of lymphocytes in the peripheral blood and bone marrow was normal. The significance of the combination of the two diseases in this patient is unclear. It may simply be the coincidental coexistence of two diseases, both relatively common in elderly people. However, the clinical course does point to a more direct relationship. Histocompatibility antigens have been studied in patients with chronic lymphatic leukaemia, but, so far as I know, no increase in any specific HLA haplotype has been shown.

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- ¹ Terwindt, V A M. and Knoben, J M A, *Acta Medica Scandinavica*, 1966, **307**, 173.
- ² Hall, G H. and Hargraves, T, *Lancet*, 1972, **1**, 48.
- ³ Glick, E N, *Lancet*, 1974, **1**, 77.
- ⁴ Gibbs, P, *Lancet*, 1974, **1**, 351.
- ⁵ von Knorring, J. and Wasastjerna, C, *Scandinavian Journal of Rheumatology*, 1976, **5**, 197.
- ⁶ von Knorring, J, *Scandinavian Journal of Rheumatology*, 1972, **1**, 117.
- ⁷ von Knorring, J. and Somer, T, *Scandinavian Journal of Rheumatology*, 1974, **3**, 129.
- ⁸ von Knorring, J. and Selroos, O, *Scandinavian Journal of Rheumatology*. In press.

Renal failure associated with ergot poisoning

SIR,—In their case report on "St Anthony's fire and pseudochronic renal failure" (8 October, p 935) Drs C D Pusey and D J Rainford found no reports of acute renal failure in ergotism. I would like to report a case of acute renal failure in association with ergot poisoning.

A 37-year-old woman was admitted with a history of intermittent claudication associated with a very high intake of ergotamine tartrate tablets for the treatment of migraine. Both legs were cold, with absent foot pulses. The temperature of the left great toe was 23°C. She was treated with anti-coagulants, oral tolazoline, bilateral femoral, sciatic, and tibial nerve blocks, phenolamine and sodium nitroprusside, methylprednisolone, and low-molecular-weight dextran 40. Her systolic blood pressure dropped as a result of this treatment to an average of 60 mm Hg over the next 8 h and then rose to above 100 mm Hg. During this time she was given 20 mg of intravenous frusemide and passed 1 l of urine over the next five hours. The haemoglobin and blood urea were normal on admission. After her initial diuresis her urine output ceased and she went into acute renal failure with the blood urea concentration rising to 43 mmol/l (260 mg/100 ml) on the ninth day after admission, at which point peritoneal dialysis was begun. Renal function returned to normal, as did the skin temperature in both legs. An intravenous urogram and creatinine clearance done later were both normal.

Gabbai *et al*¹ in their description of an outbreak of ergotism reported blood urea concentrations rising to 10–20 mmol/l (60–120 mg/100 ml) and, in the four patients who died, blood urea levels of more than 25 mmol/l (150 mg/100 ml).

Hypotension in association with treatment with low-molecular-weight dextran is a well-recognised cause of acute renal failure.^{2,3} It is reasonable to postulate that this was an unlikely cause for the development of acute renal failure in a patient who was young, with normal kidneys. A combination of the hypotension, dextran infusion, and renal artery narrowing secondary to the ergot poisoning is a more likely cause of the development of acute renal failure. It is difficult to be sure which of the two contributing factors was of more importance, the ergot poisoning or the hypotension and associated dextran treatment. However, the possibility exists that the ergot poisoning was the most important of the contributing factors.

I would like to thank Dr Victor Parsons of King's College Hospital for allowing me to publish details of this case.

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- ¹ Gabbai, H, *et al*, *British Medical Journal*, 1951, **2**, 650.
- ² Mailloux, L, *et al*, *New England Journal of Medicine*, 1967, **277**, 1113.
- ³ Morgan, T O, *et al*, *British Medical Journal*, 1966, **2**, 737.

Mobilisation after myocardial infarction

SIR,—Your leading article on this subject (10 September, p 651) does not emphasise the ease with which a rehabilitation programme can be set up in a district general hospital.

We at Lewisham have, over the past 18 months, had 150 patients through our rehabilitation unit, and, although it is quite true that 20% or so usually drop out at some stage during the course, the majority gain considerable psychological benefit. Their increase in physical fitness and morale is testified to by all who come in contact with them, particularly their immediate family. Our unit is run by one of the physiotherapists with a doctor who meets once a week with a member of the medical team to iron out particular problems. It does not require any particular resources and has certainly not put any great strain on the finances of the hospital.

The enthusiasm of many of the participants has been such that they have started, with the help of the Inner London Education Authority, a coronary rehabilitation class at night school, which is well attended, and we hope to extend this aspect of the programme.

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SUSAN JOYCE

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Bilateral injuries in childhood: an alerting sign?

SIR,—You published a letter from Dr A R Buchan and me last year (16 October 1976, p 940) giving a preliminary warning of the possible suspicious nature of bilateral minor injuries in children under 5. At that time we reported the total absence of bilateral injuries in daily inspections of 481 children on the register of the 10 day nurseries in Leicestershire.

This research has now been completed and, although many aspects are not of general interest and are being published elsewhere, the final figures showed that during the 13-week

period from 1 November 1975 to 31 January 1976 20 896 inspections were made and 3709 injuries noted. Of these, only one was bilateral and it was clearly seen to be non-accidental and one of a series of incidents within that family.

S A LAING

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Treatment of depression

SIR,—I feel that your leading article on this subject (29 October, p 1105) left the unfortunate impression that the only treatment of depression is physical. The psychological aspects of depression are wholly ignored. Leading articles like this can only increase the over-prescribing of antidepressants which various recent studies have pointed out. All too frequently medications and physical treatments are used as a quick and short answer to the overwhelming needs of patients whose medical symptoms of depression have their roots in alienation, loneliness, or unhappiness in their lives. Perhaps the article should have been retitled "Physical treatments of depression."

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Propranolol and thyroid surgery

SIR,—We read your recent leading article (22 October, p 1039) with interest and believe your view as regards the use of propranolol as a preoperative measure in thyroidectomy for Graves' disease is ultra-cautious.

Our experience over the past 18 months is, admittedly, limited to some 15 cases. Propranolol was used as the sole preoperative measure in all, with satisfactory results. Technically, the gland is easier to handle at operation. The total time of the "illness" is cut to about ten days, which includes preoperative preparation and hospital stay.

If this drug is used it is important that a dose be given on the morning of operation and that it be continued postoperatively for some 5–7 days.

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Noxythiolin-resistant organisms

SIR,—I was interested to read Dr B Chattopadhyay's article (29 October, p 1121), but his conclusions cannot remain unquestioned.

Sensitivity discs are a test of sensitivity to antibacterial agents; resistance cannot be inferred. Sufficient concentration of noxythiolin may not be achieved by diffusion from discs to inhibit growth of those bacterial strains with a high minimum inhibitory concentration relative to noxythiolin. That such "resistant strains" are killed by relevant concentrations of noxythiolin was elegantly demonstrated by Dr Chattopadhyay. Employing dilutions of noxythiolin in broth culture to "simulate urinary tract infection" he found "resistant" organisms to be totally killed at a concentration of 1.25% noxythiolin. This is half the concentration recommended for treatment of