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.

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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.

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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