recommendation and we think it appropriate to give details of those cases of severe paracetamol poisoning treated with methionine that have been reported to us.

In a three-year period we have accumulated information on 116 patients who had high plasma paracetamol concentrations (falling above a line joining 200 mg/l at four hours and 80 mg/l at 12 hours post ingestion when plotted on a semi-logarithmic paracetamol concentration-time scale) and who were treated with methionine. Seventy-four patients were given methionine within 10 hours of ingestion of the overdose and had serial liver function tests performed. Thirty-eight of 74 patients showed no abnormality of liver function and nine patients only had plasma aspartate aminotransferase (AAT) concentrations in excess of 250 IU/l; three of these patients had maximum AAT concentrations in excess of 1000 IU/l. All 74 patients made a satisfactory recovery with the exception of a 30-year-old woman who also ingested Dalmane, Indocid, and Tandalgesic besides paracetamol, and who died 53 hours after admission following a grand mal fit; the maximum plasma AAT concentration recorded was 53 IU/l. A further 28 patients with high paracetamol levels received methionine within 10 hours of ingestion but did not have liver function tests performed; all 28 patients made a satisfactory recovery. In contrast, 14 patients with high paracetamol levels received methionine more than 10 hours after ingestion; 10 of these 14 patients recovered, but four patients subsequently died from liver failure.

Although cysteamine is effective in the treatment of paracetamol poisoning,² the adverse effects make a less toxic alternative desirable.²⁻⁴ The early results obtained by Prescott *et al* (1 April, p 856) for intravenous N-acetylcysteine are promising, but we believe that there is sufficient evidence to continue recommending oral methionine as the treatment of choice for severe paracetamol poisoning.

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¹ Crome, P, *et al*, *Lancet*, 1976, 2, 829.

² Prescott, L F, *et al*, *Lancet*, 1976, 2, 109.

³ *British Medical Journal*, 1977, 2, 481.

⁴ Hughes, R D, *et al*, *British Medical Journal*, 1977, 2, 1395.

What kind of cot death?

SIR,—Your leader "What kind of cot death?" (18 March, p 671) brought the welcome news that, for reasons yet obscure, the frequency of cot death in Britain may be declining. It is likely that the increasing frequency of breast-feeding accounts for this trend.¹⁻³

Sudden infant death syndrome (SIDS), the term applied in the United States to cot death in the baby who clinically and pathologically appears to have been well, also appears to be declining⁴ and, correspondingly, breast-feeding in the United States has been on the increase.⁵ For some years Sweden has had strikingly fewer cot deaths and substantially more breast-feeding than Britain or the United States.⁶ Furthermore, babies from lower socioeconomic classes everywhere are more likely to suffer cot deaths and less likely to be breast-fed.^{1, 6}

Discussion of the role of infant feeding in cot death or SIDS has been discouraged in some quarters in spite of the evidence.⁷ Confusion has occurred because, until recently, too few babies were exclusively breast-fed through the period of greatest risk to permit

adequate comparisons. One question to be answered is, "How many deaths have occurred prior to six months in infants breast-fed with no cow milk formula supplements?" One hopes that the DHSS multicentre study of postneonatal mortality has asked this question and that the mother-infant feeding histories will be sufficiently detailed to provide an answer.

Of the epidemiological factors implicated, the infant feeding method is the one most amenable to change in any programme aimed at preventing cot death. Even if ongoing research into neural and cardiorespiratory mechanisms reveals the chain of events preceding unexpected death, we must still ask, "What is to be done?" Differences between breast- and bottle-feeding have important implications for the infectious,^{8, 9} immunological¹⁰, metabolic,^{11, 12} neural, and anatomical¹³⁻¹⁵ correlates proposed for cot death. We could therefore expect reductions in all three cot death categories if babies are breast-fed longer and more exclusively.

Cot death can be seen as the large tip of the infant morbidity-mortality iceberg. It is important that we know, in very practical terms, what accounts for its decline.

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¹ Sloper, K S, Elsdon, E, and Baum, J D, *Archives of Disease in Childhood*, 1977, 52, 700.

² Jepson, M E, *et al*, *Lancet*, 1976, 2, 425.

³ Coles, E C, and Valman, H B, *Lancet*, 1976, 2, 583.

⁴ Peterson, D R, and Chinn, N M, *Pediatrics*, 1977, 60, 75.

⁵ Filer, L J, jun, *Hospital Practice*, 1978, 13, 87.

⁶ Vahlquist, B, *Environmental Child Health*, 1975, 21, 11.

⁷ Cunningham, A S, and Beckwith, J B, *Pediatrics*, 1976, 58, 467.

⁸ Downham, M A P S, *et al*, *British Medical Journal*, 1976, 2, 274.

⁹ Cunningham, A S, *Journal of Pediatrics*, 1977, 90, 726.

¹⁰ *British Medical Journal*, 1976, 2, 1167.

¹¹ Davies, D P, *British Medical Journal*, 1973, 2, 340.

¹² Raiha, N C R, *et al*, *Pediatrics*, 1976, 57, 659.

¹³ *Lancet*, 1977, 2, 1064.

¹⁴ Boat, T F, *et al*, *Journal of Pediatrics*, 1975, 87, 23.

¹⁵ Tonkin, S, *Pediatrics*, 1975, 55, 650.

Fetal malformation not associated with Debendox

SIR,—The report by Drs Dian Donnai and R Harris (18 March, p 691, and subsequent letters 8 April, p 925), drawing attention to an apparent association between the use of Debendox and an unusual malformation syndrome, is very interesting and could obviously be an important early warning of a new drug-induced abnormality. However, as is conceded in the article, Debendox has been widely used in early pregnancy with apparent safety for a long time, and with any such extensively used drug there will be the coincidental association of its use with malformation syndromes. We would like to report a further identical case, in which Debendox was *not* implicated.

A 32-year-old primigravida was delivered at term of a male baby who lived for an hour. Multiple congenital abnormalities were obvious, including complete exomphalos, absent right leg and right half of pelvis, absent right kidney, left hydronephrosis, abnormal lumbar spine, and small right hemithorax. No drugs were prescribed or taken in the first trimester apart from iron. There was possible contact with rubella in the first month, and at 13 weeks a flu-like illness was treated with ampicillin, codeine linctus, and paracetamol. Investigation of the baby showed a normal karyotype (including Giemsa banding) and no viruses were isolated. The mother had a rubella antibody (haemagglutination inhibition) titre of

1/16. No conclusive aetiological association was therefore established.

As a number of cases of this very unusual and apparently rare malformation syndrome, without any clear genetic or environmental aetiology, have been reported in a short time, we would suggest that this mini-epidemic be looked at more closely and that any other cases be reported until aetiological associations (Debendox or other) become established.

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SIR,—Drs Dian Donnai and R Harris (18 March, p 691) reported three cases in which an unusual congenital abnormality followed treatment with Debendox (dicyclomine hydrochloride 10 mg, doxylamine succinate 10 mg, pyridoxine hydrochloride 10 mg) in early pregnancy. We would like to report a case of a similar abnormality (exomphalos, reduction deformity of one leg, and thoracic kyphoscoliosis) in a patient who took no antiemetic, but in whom ovulation was induced with Clomid (clomiphene citrate).

The patient, a 21-year-old primigravida, was first seen in the gynaecological clinic in January 1977 complaining of secondary amenorrhoea and infertility. After investigation she was treated with clomiphene citrate, 50 mg daily for five days, and became pregnant after the first cycle of treatment. She took no drugs during the first trimester. She was admitted in November 1977 at 32 weeks' gestation because of premature rupture of the membranes. Two days later she delivered a male infant weighing 1470 g with multiple abnormalities, who died after 40 minutes.

Post-mortem examination showed exomphalos containing most of the abdominal contents. The right hip and upper part of the femur were absent so that the right lower limb was attached to the pelvis by skin and soft tissue only. There was a severe thoracic kyphoscoliosis and in addition hydrocephalus, anorectal atresia and an absent left kidney.

The abnormalities found in this baby are strikingly similar to those described by Drs Donnai and Harris, and their occurrence in the absence of treatment with an antiemetic perhaps suggests either that the association with Debendox was fortuitous or that this combination of abnormalities is commoner than generally recognised.

We thank Professor H G Dixon for his permission to report this case.

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Effect of maternal diazepam on the newborn

SIR,—May I commend Dr R J Rowlatt's warning (15 April, p 985) on the hazards of diazepam in labour, which echo my own fears?¹ In addition to those he mentions is the effect on the fetal heart, which loses its beat-to-beat variation. It is suggested² that this reflects a loss of adaptive ability of the fetal heart and circulatory system, or is possibly due to a depression of the cardiac reflex centres in the brain. Moreover, the common metabolic pathway that diazepam shares with bilirubin (being conjugated with glucuronic acid) means that its detoxification could result in raised bilirubin levels and even kernicterus in the

neonate. Apart from these possibly deleterious effects of diazepam several authors³⁻⁵ have questioned its value in labour, and it is therefore difficult to justify its widespread use in the obstetric field.

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¹ Burn, J M B, *Midwives Chronicle and Nursing Notes*, 1974, **87**, 348.

² Scher, J, et al, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, **79**, 635.

³ Lee, D T, *Canadian Medical Association Journal*, 1968, **98**, 446.

⁴ Elder, M G, et al, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, **76**, 264.

⁵ Friedman, E A, *Obstetrics and Gynecology*, 1969, **34**, 82.

Side effects of cyproheptadine

SIR,—Recently cholestatic jaundice was reported (25 March, p 753) as a complication of treatment with cyproheptadine. At present we are evaluating the hypothalamic effects of cyproheptadine in various endocrine disorders and we have administered the drug to 20 patients for periods up to nine months in doses of between 16 and 32 mg daily.

Jaundice has not occurred in any of our patients and liver function tests have remained normal. The only side effects noted have been drowsiness and an increase in weight during treatment. The drowsiness is usually transient and lasts up to four weeks after starting treatment. The increase in weight has affected all our patients with only one exception. With a low dose of cyproheptadine (<16 mg daily) the increase in weight during a six-month period has been 2.9 ± 1.8 kg. With a larger dose taken for the same length of time the weight increase has been 4.2 ± 5.2 kg. Although Bayliss¹ noted that some patients with Cushing's disease became psychotic when given this drug and it has also been stated² that occasionally central nervous system stimulation leading to hallucinations may occur, we have not encountered these problems in any of our patients. In women whom we have observed closely for a period of months the drug has not led to any appreciable mood changes. Dryness of the mouth and other anticholinergic effects have similarly been conspicuous by their absence, but we are dealing with a young patient population of less than 40 years of age.

Our conclusion is that cyproheptadine is generally very well tolerated by patients and that it is associated with remarkably few side effects, a view shared by other workers.³

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¹ Bayliss, R, *Quarterly Journal of Medicine*, 1977, **46**, 553.

² *Lancet*, 1978, **1**, 367.

³ Delitala, G, et al, *Metabolism*, 1977, **26**, 931.

Alcohol and cirrhosis

SIR,—I wholeheartedly agree with the suggestion of your correspondent (25 March, p 789) that the deleterious effects of alcohol may have been seriously exaggerated, as well as the definite benefits minimised.¹

I would disagree with him, however, that the differing national cirrhosis rates necessarily

imply a specific constituent of wine absent from distilled spirits. One must surely take into account also the varying national alcoholic sex ratios (females being more liable to alcoholic cirrhosis²) as well as possible racial genetic differences. Thus it may well be that some races are more prone to cirrhosis than others, because of genetic predisposition. Recent evidence³ suggests that certain histocompatibility antigen patterns, so-called genetic markers, may reflect susceptibility to cirrhotic disease (we know that HLA subtypes reflect susceptibility to a myriad of afflictions⁴). Tissue typing may in the future show certain nations with a particular proclivity towards hepatic cirrhosis. This may well apply to the French.

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¹ Kinnell, H G, *British Medical Journal*, 1977, **2**, 1479.

² Morgan, M Y, and Sherlock, S, *British Medical Journal*, 1977, **1**, 939.

³ Bell, H, and Nordhagen, R, *British Medical Journal*, 1978, **1**, 822.

⁴ Oliver, R T D, *British Journal of Hospital Medicine*, 1977, 449.

Bronchiectasis and cystic fibrosis

SIR,—The otherwise excellent article on bronchiectasis and cystic fibrosis by Dr Margaret Hodson (15 April, p 971) is seriously marred by the failure to emphasise that the advice on management and drug dosage is directed throughout to the adult and adolescent, and not to the child.

Firstly, tetracycline should not be prescribed for young children for obvious reasons; secondly, the dosage of all the antibiotics recommended is high for infants and small children; it would have been better to specify the amount to be given per kg/day. Oddly, gentamicin 2 mg/kg/day is lower than the dose usually required, which is more commonly 5-7 mg/kg/day; but of course if regular blood level monitoring is carried out as advised by Dr Hodson the amount can be regulated as necessary.

Bronchodilators are not routinely required for children and in fact only occasionally prove useful, but salbutamol 5 mg in 3 ml by inhalation would be an excessively high dose, 0.5-1 ml of 0.5% solution in 2 ml saline being more appropriate.

There are numerous other statements that are unsatisfactory in the context of childhood. For instance, physiotherapy really needs to be carried out three times a day if the child has cough or sputum. Force of circumstances only may cut this down to twice a day—that is, school, mother at work, and so on. Rectal prolapse must be treated by dietary care and increasing the pancreatin extract, or by checking that the latter is effectively used, in order to control the frequency and looseness of the motions. If this is done, resort to surgery is never necessary.

The final paragraph gives a pessimistic impression of an undoubtedly distressing condition by stressing the early mortality of the past and of many of the older patients of today, without noting the effect that early diagnosis—

perhaps as a result of neonatal screening—together with more effective treatment may have in the future on the quality of life and length of life. It is highly satisfactory that adult chest physicians are now showing an interest in cystic fibrosis, which in fact reflects the improving life expectancy and the increas-

ing number of young adults requiring their care.

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Hyperbaric oxygen

SIR,—With reference to your leading article (22 April, p 1012) may I draw your attention to the fact that the regional centre for hyperbaric oxygen for the West Midlands region is sited in this hospital? It has been so for the last seven years, and there are therefore four regional centres for hyperbaric oxygen in this country at the time of writing.

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Payment to clinical members of district management teams

SIR,—Certain important aspects of this matter have not been mentioned in recent correspondence on this subject in your columns.

DHSS circular DS 131/74 (paragraph 6), dated 15 May 1974, stated: "The rate of pay is regarded as provisional pending experience of the new management arrangements. The Department and the professions have agreed that inquiries should be made in due course to determine the amount of time clinical members of the DMT/AMT are spending on this work, and that the level of payment should be reviewed in the light of this information at that stage, any revised payment being backdated to 1 April 1974. We shall write to you again about this in due course."

In 1975 DMT payments were increased from £700 to £950 annually, along with the general increase in medical salaries at that time. I think that clinical DMT members believed, as I did, that the DMT increases were in fact just part of that general increase in medical salaries. However, DS 250/75, dated 28 July 1975, stated that "The increases notified in this letter have been agreed on the basis that any future increases related to workload, as envisaged in paragraph 6 of DS 131/74, should not be backdated to before 1 April 1975." Thus it seems that the 1974 agreement regarding the review of time taken on DMT work was revoked, as far as the first year of DMT work is concerned. I wonder how many DMT members were parties to the 1975 "agreement," or even knew about it.

The *BMA News Review* for March 1978 (p 140) states: "The GMSC, together with the Central Committee for Hospital Medical Services, is asking the Department of Health for payments to clinical members of District Management Teams to be based, in future, on two notional sessions per week instead of one." The words "in future" sound ominous to me: do they mean that the 1974 agreement is to be reneged on in respect of the second, third, and fourth years of DMT activity, as well as the first year?

Just what is being done to ensure that the DHSS does honour the agreement to which it was a party in 1974?

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*.*The Secretary writes: The claim referred to by Dr Penman is now with the DHSS,