provide medical care for nomadic pastoralists. They state, however, that among the Somalis iron deficiency is rarely fatal. This is not true in the North-eastern Province of Kenya, where 250 000 Somalis live. In 1974 Bonte¹ pointed out that the North-eastern Province was unique among the provinces of Kenya in that blood diseases came top of the causes of death in hospital. Severe anaemia is the commonest single cause for hospital admission in the provincial and district hospitals.

Community studies have shown the high prevalence of anaemia.² Of 787 Somalis living in the bush, 190 (24%) had haemoglobin levels less than 8 g/dl and 33 (4%) values below 5 g/dl. Many of these people continue their daily activities with no symptoms, but their reserve is small. In the event of injury, childbirth, or acute malaria (all common events) the value may fall to 2 or 3 g/dl very suddenly. They then die or, if fortunate, survive a journey of 100 miles (160 km) to arrive in hospital with severe heart failure.

Professor Murray and his colleagues suggest that it may be unwise to correct iron deficiency in the face of quiescent infection. It is true that tuberculosis is a major problem and that brucellosis is common. The possible risks of reactivating infection, however, must be weighed against the at least equally serious risk of ignoring severe anaemia. The note of caution is an invitation to nihilism. Those who are building up services for Somali nomads will turn their attention to the anaemia and the pellagra and xerophthalmia which also result from the all-milk diet. They will also turn their attention to the infectious diseases. For a professor of medicine to arrive in a refugee camp of 6000 people bringing the facility for laboratory investigations but only 7000 iron tablets is only comparable to a Lord of the Admiralty reaching the sinking *Titanic* equipped with radar but in a four-seater rowing boat.

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¹ Bonte, J, in *Health and Disease in Kenya*, ed L C Vogel, et al, pp 75-90, Nairobi, East African Literature Bureau, 1974.

² Greenham, R, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1978, **72**, 72.

Rethinking antenatal care

SIR,—I am sure that I was not the only reader whose eye was caught by the title of your leading article (28 October, p 1177) only to be disappointed by its wholly technical content. As it correctly pointed out, there is as yet no satisfactory explanation for the inverse relationship between numbers of antenatal clinic visits and peri- and neonatal morbidity and mortality rates. However, unless and until a causal association is definitely disproved practitioners and health authorities have a responsibility to do everything possible to encourage early and continued attendance at antenatal clinics.

The Department of Health has laudably acknowledged this responsibility, and has recently published the highly informative proceedings of a conference it held around this topic in conjunction with the Child Poverty Action Group in April of this year.¹

The characteristics of late attenders have been well known for some time^{2,3} and there is much that can be done to reach them within

existing resources—for example, improvement of communication between general practitioners and obstetricians,⁴ reorganisation of antenatal clinics, redeployment of community midwives,⁵ and health education initiatives specifically aimed at the women concerned, such as the youngest primigravidae. Elsewhere you have recently demonstrated your awareness of the importance of the expectations of the patient,⁶ and it is now time for the profession to follow in rethinking not only the content but also the style of antenatal care.

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¹ Department of Health and Social Security Child Poverty Action Group, *Reaching the Consumer in the Antenatal and Child Health Services* (issued with Health Notice HN(78) 108). London, DHSS, 1978.

² McKinlay, J B, *British Journal of Preventive and Social Medicine*, 1970, **24**, 52.

³ Robertson, J S, and Carr, G, in *In the Beginning*. London, Nuffield Provincial Hospitals Trust, 1970.

⁴ Heward, J A, and Clarke, M, *British Medical Journal*, 1976, **1**, 1202.

⁵ Willmott, J A D, *Midwives Chronicle and Nursing Notes*, 1976, **89**, 236.

⁶ *British Medical Journal*, 1978, **2**, 188.

Smoking and deep-vein thrombosis

SIR,—Mr J K Clayton and others (5 August, p 402) have presented convincing evidence of the "protection" of cigarette smokers against postoperative deep-vein thrombosis and the increased risk associated with overweight for height. They conclude that the explanation for the "protection" of smoking patients provided they are lean remains obscure.

It seems fair to suggest that the "apparent" protection of smoking was due to the "real" protection of lean body habitus, known to be associated with smoking, and was unrelated to smoking per se.

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Postoperative pain

SIR,—We welcome your excellent leading article on this subject (19 August, p 517) because this neglected area of therapeutics has concerned us for some time. Despite the ready availability of potent analgesic drugs patients still rank postoperative pain high on their list of unpleasant perioperative memories. This is not surprising, because very little is known about the relationship between the pharmacokinetics and pharmacodynamics of even the oldest agents.¹

Using pethidine as a model, we investigated the hypothesis that poor analgesia was due simply to inadequate and variable blood concentrations of the analgesic drugs.² We found a direct relationship between blood pethidine concentration and analgesic effect. The minimum therapeutic concentration for postoperative pain was found to be 0.45-0.55 mg/l. This is more than double the value previously reported after a single injection³ administered immediately after emergence from general anaesthesia. Repeated (4-7) intramuscular injections of pethidine resulted in fluctuating and often inadequate blood pethidine concentrations. Peak pethidine concentrations varied fivefold among patients and

twofold within patients. The time to reach peak concentrations varied by a factor of 8 among patients and by a factor of 2 within patients. Blood pethidine concentrations fluctuated markedly above and below the minimum therapeutic level and this was reflected in the analgesic response. Time above the minimum therapeutic concentration varied from 0 to 100% (mean $\pm$ SD = $35 \pm 36\%$) for the four-hour period after each injection.

However, in a subsequent study it was shown that only a twofold difference in clearance occurred among patients,^{4,5} suggesting that variation in absorption from the intramuscular site is the major reason for poor analgesia. Using a pharmacokinetic simulation system, an intravenous infusion regimen was designed to avoid the variability in absorption rate and to provide stable therapeutic blood concentrations.⁴ Controlled continuous intravenous infusion of pethidine produced stable blood concentrations which were maintained above the therapeutic level for postoperative pain and provided excellent pain control. Severe pain was not experienced by any person after three hours and analgesia continued for the duration of the two-day study. The continuous intravenous infusion technique has been successfully used in intensive care for up to 10 days and is currently being evaluated for other uses.

We conclude that (1) pethidine has a therapeutic blood concentration of 0.45-0.55 mg/l for pain following abdominal surgery; (2) variable response to intramuscular injection results from inadequate and fluctuating blood concentrations; (3) the intramuscular route of administration alone is the major cause of the variability in response; and (4) controlled intravenous infusion of pethidine provides continuous analgesia and may offer a significant advance in pain management.

The plethora of new parenteral agents which the pharmaceutical companies have introduced over the past 20 years is not a reminder that we have not found the right drug but a reminder that we had not found the optimal mode of administration of perfectly adequate analgesic drugs.

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¹ Mather, L E, et al, *British Journal of Anaesthesia*, 1975, **47**, 1269.

² Austin, K L, Stapleton, J V, and Mather, L E, Meeting of Australasian Society of Clinical and Experimental Pharmacologists, Melbourne, 1978, abstract No 18. (Paper in preparation.)

³ Shih, A P L, Robinson, K, and Au, W Y W, *European Journal of Clinical Pharmacology*, 1976, **9**, 451.

⁴ Stapleton, J V, Austin, K L, and Mather, L E, *Anaesthesia and Intensive Care*. In press.

⁵ Mather, L E, Austin, K L, and Stapleton, J V, Meeting of Australasian Society of Clinical and Experimental Pharmacologists, Melbourne, 1978, abstract No 19.

Crohn's disease—40 years on

SIR,—I was interested in your leading article (21 October, p 1106) and wish to make some further comments. As you suggest, crude recurrence rates are meaningless and they must be related to time.¹ Even then some interesting points may be missed. Although it is now agreed that related to time the recurrence rate for ileal disease is higher after a

bypass operation than after resection,^{2,3} the rates after five years following the first operation are similar.³ The bypassed bowel is being resected at a second operation, converting the bypassed person into a resected person who then carries the recurrence "risk" of a resected patient. The "bypassed" recurrences thus roughly equal the "resected" recurrences plus one for each patient.

Moreover, it is only after the second operation that bypassed patients develop "recurrent" disease proximal to the site of the initial disease.³ This, together with Oberhelman's observations⁴ in relation to colonic disease, suggests that as long as a fertile soil remains, even in disconnected bowel, the disease does not macroscopically "spread" proximally. These observations must have a bearing on at least the perpetuation of the disease if not on its pathogenesis.

I am in no way advocating a return to a primary bypass procedure and its attendant risks but rather drawing attention to the greater information that may be derived from the available data.

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¹ Fielding, J. F., Cooke, W. T., and Williams, J. A., *Surgery, Gynecology and Obstetrics*, 1972, **134**, 467.

² Homan, W. R., and Dineen, P., *Annals of Surgery*, 1978, **187**, 530.

³ Alexander-Williams, J., Fielding, J. F., and Cooke, W. T., *Gut*, 1972, **13**, 973.

⁴ Oberhelman, H. A., in *The Management of Crohn's Disease*, ed. I. T. Weterman, A. S. Pena, and C. C. Booth. Amsterdam, Excerpta Medica, 1976.

Antenatal diagnosis of fetal duodenal atresia by ultrasonic scan

SIR,—Fetal ultrasound examination has been of substantial benefit, but the short report by Dr H. Gee and Mr U. Abdulla (4 November, p 1265) leaves me puzzled. They conclude, "Our case illustrates the importance of ultrasonic examination of the fetal abdomen." The diagnosis was confirmed only 12 hours after birth by an x-ray and no treatment was given. Also baffling is the suggestion that amniocentesis to look for Down's syndrome should be considered after ultrasonography has suggested the possibility of duodenal atresia. What action is to be recommended on the results at that late stage of pregnancy?

Would it not be better for energies and resources to be directed to expert neonatal care? Duodenal atresia would be diagnosed 12 hours after birth (as in this case) in the infant born after a pregnancy complicated by hydramnios, and many other anomalies would be diagnosed earlier and practical benefit would accrue.

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Thyrotoxic Graves's disease after primary hypothyroidism

SIR,—We were interested to see the report of spontaneous change from primary hypothyroidism to thyrotoxic Graves's disease described by Dr S. Olczak and others (2 September, p 666). We have been particularly interested in spontaneous change in thyroid function seen in patients with dysthyroid eye disease and have described five such cases.¹

Two of these were initially hypothyroid and subsequently became thyrotoxic.

Case 1—A 62-year-old man presented in January 1974 with an 18-month history of right proptosis. Clinically he was marginally hypothyroid with a low plasma thyroxine (T₄) concentration of 54.0 nmol/l (4.2 µg/100 ml) (normal range 51.5–108 nmol/l (4.0–8.4 µg/100 ml)) and a low radioiodine neck uptake (9.4% at 4 h (normal range 15–35%)). By September 1974 he was nervous and irritable and the plasma triiodothyronine (T₃) assays were 3.5 nmol/l (2.3 ng/ml) and 2.98 nmol/l (1.94 ng/ml) (normal range 12.3–24.6 nmol/l (8–16 ng/ml)), with a plasma T₄ concentration of 95.2 nmol/l (7.4 µg/100 ml).

Case 2—A 61-year-old man developed proptosis in 1972, affecting the right eye more than the left. In August 1974 he was first seen and had oedema of the right disc. At this time he was clinically hypothyroid with a plasma T₄ concentration of 30.9 nmol/l (2.4 µg/100 ml) and a free thyroxine index of 1.9 (normal range 3.6–8.9). Two months later he was clinically thyrotoxic; the plasma T₄ concentration was 123 nmol/l (9.6 µg/100 ml), the free thyroxine index 10.1, and ^{99m}Tc neck uptake at 20 min 4.5% (normal range 0.7–3.0%). He was treated with ¹³¹I.

Neither of the above patients was given thyroxine as medication before developing thyrotoxicosis.

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¹ Croft, D. N., et al., in *Scientific Foundations of Ophthalmology*, p 135. London, Heinemann, 1977.

Dexamethasone in acute stroke

SIR,—We read with interest the article on acute stroke and dexamethasone by Dr Graham Mulley and others (7 October, p 994). We have carried out a similar but smaller, previously unreported study. We looked at the effect of dexamethasone and mannitol upon the mortality of acute stroke. Thirty-six patients with an acute stroke were randomly allocated to a treatment or a placebo group. The active treatment group received dexamethasone 4 mg intravenously 8-hourly and 200 ml of 10% mannitol intravenously once a day for five days after admission. The exclusions from the trial and investigations were similar to those of Dr Mulley and his colleagues.

The overall mortality at three months was 45%. There was no significant difference in the mortality of the two groups (χ^2 , $P > 0.05$), which lends support to Dr Mulley's results.

We have analysed our data further as we wished to ascertain whether the use of oedema-reducing agents ought to be more selective. We therefore divided each group into those who were hypertensive before or on admission ($n=18$) and those who were normotensive (diastolic blood pressure < 110 mm Hg) ($n=18$). Patients who are normotensive are more liable to have had a large infarct, whereas those who are hypertensive are more liable to have had a haemorrhage or a small, deep infarct associated with the Charcot Bouchard aneurysm. We found no significant difference between the effects of treatment and placebo on the mortality of the normotensive group ($P > 0.05$). However, we found that the hypertensives who received active treatment had significantly more deaths than those in the placebo group ($0.05 > P > 0.01$). Thus it would appear that

dexamethasone and mannitol have little effect and perhaps even a detrimental effect on mortality in the hypertensive group.

As the study was carried out within a district general hospital with no immediate access to computerised tomography or echoencephalography to aid distinction between haemorrhage and infarct we feel that our findings endorse Dr Mulley's statement that there is no indication for the routine use of dexamethasone or mannitol in acute stroke.

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Iodine and acetone-containing plastic spray dressings

SIR,—The report by Dr J. O. Morgan-Hughes and Mr R. A. Bray (26 August, p 639) of severe erythema and blistering resulting from the use of Op-Site and Slek dressings on skin treated with iodine tincture was very puzzling. The only compounds that might be expected to react together are iodine and acetone to form iodoform. This, however, requires the presence of an alkali and would not be expected to produce the severe effect experienced.

Investigation in this laboratory showed that an intermediate is formed when acetone and iodine are warmed without alkali. This compound, triiodoacetone, was not isolated but would certainly be extremely irritant and lacrymatory since related compounds are used as chemical warfare agents. Formation of this compound, even in minute quantities, on the skin and its retention under an impervious layer would without doubt produce the results observed.

Only two clear plastic dressing sprays are currently available for human use: these are Op-site and Nobecutane. They both use the same acrylic resin, but the latter does not contain acetone. Our investigation indicates that it is the reaction of acetone with iodine that produces erythema and blistering, and the use of sprays containing acetone on skin sites previously treated with iodine tincture is not to be recommended.

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Communication with Asian diabetics

SIR,—I would like to take issue with Dr B. A. Leatherdale and his colleagues (28 October, p 1198), who conclude that some Asian patients—in fact 77% in their survey—lay false claim to literacy. The conclusion is based on a novel and hitherto untested way of proving literacy—that of observing multilingual hospital notices and signs.

I must now confess to public embarrassment that, although an occasional visitor to Dudley Road Hospital, I cannot recall the subject of even one sign in any Asian language. But there lies a cautionary tale. Most of those Asian diabetic patients accused of falsely claiming literacy may indeed be highly literate in reading and interpreting ancient and difficult religious scripts—the only familiar way they have learnt to use their literacy—and yet fail to comprehend the use