respiratory distress syndrome and which can be done only at birth or on the spot. Ventilation with high oxygen concentrations is best reserved for larger referral units to which babies requiring such treatment can be safely transferred either in utero if the risk is predictable or by flying squad if it was not. Their treatment requires practised staff round the clock, an adequate number of ventilators in working order, laboratory support for the measurement of blood gas tensions, bilirubin levels, and electrolytes, the maintenance of apparatus in working order, and chronic umbilical artery catheterisation of the infant, which is a hazardous procedure in unpractised hands, as well as other uncommon and potentially lethal complications.

It is our contention that all very sick babies suffering from medical, surgical, or cardiac conditions or any combination thereof should be referred to one regional unit for treatment in their own interests and in that of other babies in the referring unit. Those who enjoy such work should get a job there if they want to do it. There is plenty for the peripheral neonatologist to do that does not involve intensive care of very ill babies.

However, we do not entirely agree with the Oppé Report recommendations¹ and would advocate instead a policy whereby babies causing concern should be held under observation in an annexe to the labour ward until it becomes clear either that they are well enough to join their mothers or that they need intensive care.

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¹ Department of Health and Social Security, *Report of the Working Party on the Prevention of Early Neonatal Mortality and Morbidity*. London, DHSS, 1974.

Intensive investigation in management of Hodgkin's disease

SIR,—The excellent study by Dr S B J Sutcliffe and others (4 December, p 1343) confirms the value of laparotomy and splenectomy in the staging and management of patients with Hodgkin's disease.

We have reported cases of fulminating septicaemia following splenectomy in our own experience and discussed the possible significance of changes in serum immunoglobulin levels (particularly the fall in IgM) following operation and treatment¹; longer-term studies are in progress. Serious infection following splenectomy is probably not common² and Dr Sutcliffe and his colleagues do not comment on this particular point, though they have had some morbidity related to the operation itself. What would be helpful would be to try and identify patients who may not need exploratory laparotomy.

Total cellular anergy is infrequent, but in our studies so far it has been found to be invariably a feature of generalised disease.³ We have now assessed 78 untreated patients by four techniques (skin and leucocyte migration inhibition testing with recall antigens, lymphocyte transformation with phytohaemagglutinin, E-rosette studies). Total cellular anergy as judged by subnormal response in all tests was seen in only five cases (6%). In three of these patients disease was obviously generalised (clinically stage

IIIB in one and stage IVB in two). The other two patients were in clinical stages IA and IIA respectively but were found to be in stage IVA after laparotomy and splenectomy.

If it were to be confirmed that total cellular anergy always implied generalised disease (that is, that the patients were in the chemotherapy group), then these patients, in whom retention of the spleen may prove beneficial in the long term, could be excluded from laparotomy regardless of apparent clinical stage.

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¹ Hancock, B W, *et al*, *British Medical Journal*, 1976, 1, 313.

² Desser, R K, and Ultman, J E, *Annals of Internal Medicine*, 1972, 77, 143.

³ Hancock, B W, *et al*, *Clinical Oncology*. In press.

Dangers of corticosteroids in phaeochromocytoma

SIR,—We were very interested to read the case report by Drs Peter Daggett and Stephen Franks (8 January, p 84) describing a patient with phaeochromocytoma who experienced hypertensive episodes while on a high daily dose of 45 mg prednisone, given to treat concurrent giant cell arteritis, but not when the dose was reduced to 5 mg. They also observed marked hypertension when 100 mg hydrocortisone was given parenterally. A similar observation was made by Cowley *et al*¹ when 100 mg hydrocortisone was given before the removal of a phaeochromocytoma.

A peripheral interaction may partly explain these observations since there is good experimental evidence that corticosteroids have a permissive role in, and may also potentiate, the smooth-muscle response to corticosteroids.² However, we suggest that corticosteroids when given in high doses may have a significant direct action on the adrenal medulla. We have shown that concentrations of hydrocortisone in the range 20–200 mg/l release catecholamines from isolated perfused dog adrenal glands³ and we would expect a dose of 100 mg hydrocortisone given parenterally to reach an initial plasma concentration of approximately 30 mg/l, assuming a plasma volume of, say, 3 l. This concentration is of the order found in the adrenal venous effluent in stress or after corticotrophin administration.⁴

Thus the hypertensive episodes may be due to the direct action of hydrocortisone on the adrenal medulla and phaeochromocytoma tissue. High circulating levels of prednisone are also likely to potentiate the release of catecholamines from chromaffin tissue. Furthermore, in dogs we found that corticotrophin administration results in the release of adrenal catecholamines⁵ and hypertensive crises have been described following corticotrophin administration to patients with phaeochromocytoma.^{1,6,7}

We suggest that high doses of corticosteroids may have a significant direct action on chromaffin tissue and wonder what role the intra-adrenal and peripheral interactions between corticosteroids and catecholamines play in massive dose corticosteroid therapy for shock.

Finally, we repeat that the administration of either corticosteroids or corticotrophin may be hazardous in patients with phaeochromocytoma.⁸

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¹ Cowley, D J, Montgomery, D A D, and Welbourn, R B, *British Journal of Surgery*, 1970, 57, 832.

² Ramey, E R, and Goldstein, M S, *Physiological Reviews*, 1957, 37, 155.

³ Critchley, J A J H, *et al*, *Journal of Physiology*, 1974, 254, 30P.

⁴ Marotta, S F, *Proceedings of the Society of Experimental Biology and Medicine*, 1972, 141, 923.

⁵ Critchley, J A J H, and Ungar, A, *Journal of Physiology*, 1974, 239, 16P.

⁶ Welbourn, R B, personal communication.

⁷ Moorhead, E L, *et al*, *Journal of the American Medical Association*, 1966, 196, 1107.

⁸ Critchley, J A J H, West, C P, and Waite, J, *Lancet*, 1974, 2, 782.

Student health

SIR,—I would like to make a few comments on the letter from Mr D R Forsyth (25 December, p 1560).

Manchester University Student Health Service tries to offer a service to suit the individual student. Some students do in fact like to be seen by prearranged appointment. However, there is always at least one doctor available to see patients who walk in. Similarly, the counsellors see students either by walk-in or appointment. Nurses are always available and can and do refer patients to the doctor directly. The reception staff make considerable effort to ensure that the patient attends at the centre to fit in with university commitments. The system is kept as flexible as possible.

Unfortunately we are not allowed to provide general practitioner services as part of the NHS. Hence the number of doctors is limited as the service is funded almost entirely by the university. There are four medical officers at the centre, although the accepted ratio is 1500 to 2000 patients per doctor, so there should be 12 doctors. Attendances at the student health centre have increased from 26 000 to 34 000 and now some 40 000 over the last three years.

We hope that in Manchester the student has no dilemma about a choice to be made between health and education.

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Erythromycin-resistant *Clostridium welchii*

SIR,—I wish to report the isolation of a strain of *Clostridium welchii* resistant to erythromycin. The minimum inhibitory concentration (MIC) in broth is 512 mg/l: sensitive strains, tested in parallel, were inhibited by 2 mg/l. The strain was also resistant to tetracycline and the patient was hypersensitive to penicillin.

Tetracycline resistance in *C. welchii* is now well recognised, but I have seen no report of resistance to erythromycin in the UK, and this antibiotic has been recommended^{1,2} for the prophylactic treatment of patients hypersensitive to penicillin who are undergoing certain operations prone to the complication

of gas gangrene.³ In Sweden Dornbusch *et al*⁴ found 247 of 252 strains were inhibited by 1 mg (or less)/l; the remaining five were less sensitive, MICs ranging from 2 to 64 mg/l.

Garrod *et al*¹ quote 2 mg/l as the usual MIC. Sapico *et al*⁵ found the MIC of most strains to be 3.1 mg/l and regarded them as of intermediate sensitivity. Whether the MIC of erythromycin for normal strains of *C welchii* is 1, 2, or 3.1 mg/l, a consideration of the likely blood levels of erythromycin given orally does not inspire much confidence in this antibiotic for the prophylaxis of *C welchii* infection, and for strains with unequivocal resistance, such as the one reported here, erythromycin would clearly be ineffective.

Eykyn and Phillips⁶ have recently suggested metronidazole as a possible alternative to penicillin for the treatment and prevention of gas gangrene; it certainly seems preferable to erythromycin when the blood levels of the two drugs are compared with their MICs for *C welchii*.

For prophylactic treatment of the patient undergoing a mid-thigh amputation or the insertion of a hip prosthesis penicillin will be the best-guess antibiotic. Should the patient be hypersensitive to penicillin it might be advisable to choose an alternative antibiotic not by guesswork but by preoperative sensitivity testing of the *C welchii* isolated from his faeces, since these are the organisms from which he is at risk.

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¹ Garrod, L P, Lambert, H P, and O'Grady, F, *Antibiotic and Chemotherapy*. Edinburgh and London, Churchill Livingstone, 1973.

² Brumfit, W, and Hamilton-Miller, J M T, *Journal of Antibiotic and Chemotherapy*, 1975, 1, 163.

³ Parker, M T, *British Medical Journal*, 1969, 3, 671.

⁴ Dornbusch, K, Nord, C-E, and Dahlbäck, A, *Scandinavian Journal of Infectious Diseases*, 1975, 7, 121.

⁵ Sapico, F L, *et al*, *Antimicrobial Agents and Chemotherapy*, 1972, 2, 320.

⁶ Eykyn, S J, and Phillips, I, *British Medical Journal*, 1976, 1, 1418.

Safety of children in cars

SIR,—Your leading article on this subject (1 January, p 2) surprised me greatly by making no mention of the desirability of placing young children in the rear seat of a car during all journeys whether they are restrained by a seat, by a harness, or not at all. Has the Transport and Road Research Laboratory nothing to say about the special hazards for children of sitting in the "death seat" next to the driver?

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*A leading article a year ago (24 January 1976, p 180) was entirely devoted to the dangers of front-seat riding for children.—Ed, *BMJ*.

Dysphagia

SIR,—Dr Michael Atkinson (8 January, p 91) endeavours to cover the whole of this vast subject and as a result there is obviously a lack of completeness. However, I think I must comment on two of the statements that he makes.

Dealing with peptic oesophageal stricture the author states that surgical measures

to control reflux should be considered in younger patients. In fact it is often the very elderly patient who presents the greatest difficulty and in whom dilatation is most unsatisfactory. Surgery on the hiatus hernia with an attack on the stricture or bypass operation often offers the only hope of a reasonable existence. A rather optimistic approach to this subject may be justified to the patient as a form of encouragement, but is certainly not justified in dealing with a lesion which may be extremely difficult to treat.

Secondly, in dealing with neoplastic dysphagia Dr Atkinson writes that if resection is contraindicated palliative intubation offers the only means of relief. This is quite untrue. A bypass operation, bringing the stomach under the skin on the chest wall and anastomosing it to the divided oesophagus in the region of the clavicle, avoids opening the chest and the risk of mediastinitis should it leak. This gives infinitely better swallowing than an intra-oesophageal tube and, even in the very elderly, has no greater mortality. Even in a case of broncho-oesophageal fistula due to a growth this operation with the modification of drainage of the lower oesophageal stump, otherwise unnecessary, will allow the unfortunate patient comfort in his last days.

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Effect of Intralipid on colour of blood

SIR,—A chance observation on the colour of a blood sample led to the conclusion that infusion of Intralipid 20% (an emulsion of fats for parenteral feeding) may cause blood to appear much better oxygenated than is the case.

A child of 8 years, having had major cardiac surgery, was undergoing a prolonged and complicated recovery period during which artificial ventilation and intravenous feeding were required. A blood sample drawn from an indwelling radial artery cannula was noted to be of a gratifying bright red colour, but on analysis by a Radiometer ABL 1 automatic blood gas measuring instrument the partial pressure of oxygen was only 8.2 kPa (62 mm Hg) and the oxygen saturation of the haemoglobin was only in the high 80s. Since the tendency to believe one's eyes and disbelieve the machine (especially if rather complicated) is a strong one we assumed that the Intralipid 20% infusion which was running into the child at the time of sampling had in some way deranged the ABL 1—we knew that such infusions disabled certain of the estimations performed in our main hospital laboratory.

The other explanation was that the machine was right and that the colour range was due to the Intralipid 20%. This was easily tested by mixing a normal venous blood specimen with small amounts

of Intralipid 20%, and noting the colour change in successively stronger mixtures as compared with the results from the ABL 1. We measured colour (as % oxygen saturation) with an American Optical reflectance oscimeter. The colour change was obvious to the naked eye, although mixing in a glass syringe was difficult since the fat globules tended to rise and separate. The results are shown in the accompanying table.

The child was not being infused at an excessive rate, but it is possible that the normal mechanisms for handling Intralipid infusion were not intact in view of the severity of the child's condition.

We have no knowledge of the rate of onset of this phenomenon at different infusion rates or of its half lives when infusions of different rates and durations are stopped. It is possible that the in-vivo observation reflected more than mere mixing (perhaps plasma protein-microglobule complex formation) and that the in-vitro demonstration was purely fortuitous: the patient's blood showed little tendency toward globule separation whereas the in-vitro experiment was plagued by it. Perhaps globules of different size are removed from the blood at different rates.

Various possibilities present themselves for further study, but in view of the hazard which may arise from such misleading appearances it seemed appropriate to point out that a bright red blood sample from a patient with an Intralipid infusion running is not necessarily of arterial origin (where doubt exists), that it is probably not as well saturated with oxygen as it appears to be, and that the difference may be large.

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The reprint game

SIR,—Referring to Dr John W Todd's letter (22 January, p 231), my experiences are exactly the same and I am equally exasperated. One correspondent even requested a whole chapter from a textbook. Most of them write from institutes which are certainly equipped with photocopiers. Their only excuse—which, however, none of them has voiced so far—might be that photocopies of illustrations are always extremely bad and indeed quite useless. A recent paper, written with a co-author, produced about 200 requests, mostly from the USA. Not one of them offered to refund postage or the not inconsiderable cost of the reprints themselves. The "reprint game" has developed into a "reprint racket."

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Effect of Intralipid on apparent oxygen saturation of blood as measured by reflective oscimetry (ABL 1)

	Percentage by volume of Intralipid 20% mixed with venous blood			
	0	5	10	15
Haemoglobin (g/dl) (by ABL 1)	12.9	13.7	15.1	16.3*
pH	7.277	7.295	7.291	7.288
P _{CO} ₂ (kPa)	7.26	7.39	7.22	7.22
P _O ₂ (kPa)	2.93	2.89	3.02	2.97
Base excess (mmol/l)	-2.4	-0.8	-1.8	-2.0
Standard bicarbonate (mmol/l)	20.9	22.1	21.2	20.9
Oxygen saturation (%) (derived by ABL 1)	29.7	29.7	31.9	31
Oxygen saturation (%) (measured by AO)	23†	28	37	45

Conversion: SI to traditional units—P_{CO}₂ and P_O₂: 1 kPa ≈ 7.5 mm Hg.

*Note rising haemoglobin values due to increasing turbidity of sample.

†This particular AO machine is known to read low at low saturations.