The housemen who hold the sealed envelopes up to the light to select appropriate management for the patient, or the patient who rapidly appreciates any meaningful differences in the active preparation, are not blind in these trials. Only the designer is really blind—to the mangled English of the word "randomised" and to the fact that allocation at random is less efficient statistically than "alternate case" design.

If very large numbers of cases are required for a controlled study then either the question asked at the start is inappropriate or the answer is not worth having at the end.

The importance of the difference being tested is inversely related to its ethical validity. Tunnel vision with respect to ethics is illustrated by the patient information pamphlet on the Medical Research Council's chorion villus biopsy versus amniocentesis trial. To describe a 19 to 20 week legal abortion for an abnormal fetus as "a bit more difficult" than a similar procedure at 12 weeks is more than "economical with the truth." The patients were not gullible and there were no recruits to the "willing to be randomised" group. It is regrettable that the results of the trial will now be based on a biased selection of women of too low intelligence to understand the women's magazines.

There is light on the horizon. The recent introduction of Cox (staged logistic) multiple regression analysis¹ and path analysis² into obstetric research has provided powerful tools which can be used to obtain important results from traditional retrospective studies or open clinical trials. These analyses isolate meaningful and causal associations with no vital necessity for controls or putting patients into artificial slots which may not be to their advantage. Perhaps it will not be too long before their application will send the banner of "double blind controlled trials for obstetric research" back to the home of lost causes.

DENIS F HAWKINS

Royal Postgraduate Medical School,
Institute of Obstetrics and Gynaecology,
Hammersmith Hospital,
London W12 0HS

- 1 Nelson KB, Ellenberg JH. Antecedents of cerebral palsy. Multivariate analysis of risk. *N Engl J Med* 1986;315:81-6.
- 2 Rogers MS, Chang AMZ. Perinatal asphyxia: the use of path analysis in its explanation. *J Obstet Gynaecol* 1987;8:29-35.

Leucocyte sodium pump activity after meals or insulin

SIR,—Dr Leung L Ng and colleagues (28 November, p 1369) suggest that the total activity of leucocyte sodium pumps is reflected by the ouabain sensitive sodium efflux rate and that a defect in postprandial activation of the pump in obese people may ultimately lead to positive energy balance.

Their values of ouabain sensitive sodium efflux rate are derived from the product of their measurements of ouabain sensitive sodium efflux rate constant (k_0), and white cell sodium concentration (Na_{WBC}). For this calculation to be valid Na_{WBC} and k_0 should be measured under similar conditions. If this is not possible intracellular sodium content and flux should be shown to be the same in the differing conditions. In their experiments Na_{WBC} was measured in cells which had been incubated for 30 minutes to allow recovery from the isolation procedure, but k_0 was measured over 20 minutes immediately after two centrifugations and a wash in tissue culture fluid.

In our work with leucocytes we have been impressed by the extreme sensitivity of the cells to handling and the isolation procedure. In particular, in leucocytes from five normal subjects we

measured Na_{WBC} serially from the time of isolation and found in every case that the sodium content in the first few minutes after isolation was about twice as high as the final, stable value reached after 20 to 45 minutes. From our experience we would expect that the washing procedure used to remove ^{22}Na would raise Na_{WBC} , and when we subjected cells which had been incubating for 60 minutes to a procedure like that used by Dr Ng and colleagues we found a 30% increase in Na_{WBC} . Although their method has been widely used since it was described by Hilton and Patrick in 1973,¹ we are unaware of published evidence that either sodium content or sodium efflux rate is constant under the conditions used to measure k_0 . We therefore believe that sodium efflux rate should not be calculated in this way. The extremely high standard deviations for Na_{WBC} in their groups add to our concern about the validity of the calculated ouabain sensitive sodium efflux rates on which their conclusions rely.

JOHN MAIN
T H THOMAS
R WILKINSON

Freeman Hospital,
Newcastle upon Tyne NE7 7DN

- 1 Hilton PJ, Patrick J. Sodium and potassium flux rates in human leucocytes in an artificial extracellular fluid. *Clin Sci* 1973;44: 439-45.

Child abuse and osteogenesis imperfecta

SIR,—The claim by Drs Colin R Paterson and Susan J McAllion to have seen 13 cases of type IVA osteogenesis imperfecta misdiagnosed as child abuse (12 December, p 1561) would carry more conviction if they had published them in detail in a form that would enable others to make an independent judgment of the correctness of their opinion. In a recent case, with which I was concerned, Dr Paterson failed to convince a court that an abused child had osteogenesis imperfecta. Dr Paterson needs to explain how he diagnoses osteogenesis imperfecta without a family history, no radiological features, and no repeated fractures. In this case he based it on absence of bruises, a single fracture in a cousin, and joint hyperflexibility in both parents—a curious finding in an autosomal dominant condition.

Dr Paterson seems to be in two minds in ascribing "unexplained" fractures in young babies to either osteogenesis imperfecta or copper deficiency. In the recent case of Lees,¹ Dr Paterson first gave evidence at the trial for the defence diagnosing osteogenesis imperfecta. Later after further research he changed his diagnosis to copper deficiency. On appeal, when the accused sought a new trial, the Lord Chief Justice expressed regret that Dr Paterson had not done his research before giving evidence initially. Lord Lane said that no doubt the result of the trial was a disappointment to Dr Paterson and he was moved thereby to carry out extensive research into the literature of copper deficiency. The court stated it was unimpressed by much of what Dr Paterson had said and rejected his evidence as a basis for a retrial.

This rejection was echoed in a recent wardship case, where the judge declined to accept Dr Paterson's evidence. On that occasion the court found that Dr Paterson was mistaken in diagnosing anaemia, having relied on erroneous American tables for haemoglobin concentrations, and rejected Dr Paterson's evidence that he had measured the anterior fontanelle of the child at 4.8 cm across. Dr Paterson's approach seems to be to find evidence of collagen defect such as hyperextensibility of the joints in a parent or relative on the basis of clinically controversial procedures and use this as a

peg on which to hang the diagnosis of either copper deficiency or osteogenesis imperfecta. Such procedures are not entirely satisfactory. It seems that Dr Paterson now seems to believe that of his two suits osteogenesis imperfecta type IVa is probably the stronger. On the evidence he has produced so far it is not strong enough.

L S TAITZ

Department of Paediatrics,
Children's Hospital,
Sheffield

- 1 Regina v Lees and Lees: Court of Criminal Appeal. February 1987.

SIR,—While sharing the anxieties of Drs Colin R Paterson and Susan J McAllion (12 December, p 1561) that children with osteogenesis imperfecta may be misdiagnosed as victims of non-accidental injury, we are equally concerned that children who are abused may be incorrectly diagnosed as suffering from osteogenesis imperfecta, cutis laxa, copper deficiency, or other metabolic bone diseases which have been used as "defence" submissions in care or criminal proceedings.

In particular, we feel that adequate substantiation of the diagnosis of osteogenesis imperfecta in patients with type IVA disease, who had the highest level of suspicion of non-accidental injury, has not been made. In a recent paper by Dr Paterson of the cohort of 78 patients with type IVA osteogenesis imperfecta the authors examined radiographs of only 17 patients, among whom only 12 sets of skull radiographs were available. The observed incidence of skull fractures of 28% in mild osteogenesis imperfecta is difficult to accept. Similarly, patient delineation by questionnaire is subject to vagaries of recall and open to errors of fact.

Until definitive diagnosis, perhaps by better biochemical analysis of collagen or by gene analysis, is available, there must be continuing doubt about the accuracy of the diagnosis of some cases of type IVA disease as described by Dr Paterson and his colleagues.

HELEN CARTY

Alder Hey Children's Hospital,
Liverpool L12 2AP

DONALD G SHAW

The Hospital for Sick Children,
Great Ormond Street,
London WC1

- 1 Paterson CR, McAllion SJ, Shaw JW. Clinical and radiological features of osteogenesis imperfecta type IVA. *Acta Paediatr Scand* 1987;76:548-52.

Free radicals and Dupuytren's contracture

SIR,—The observation of Dr G A C Murrell and others (28 November, p 1373) that xanthine oxidase activity was present in the palmar fascia of patients with Dupuytren's contracture might also be extended to the tendon sheath problems seen with inflammatory synovitis.

The tendon sheath is lined with a synovial intima. We have found that the synovial lining of both normal and rheumatoid joints also contains xanthine oxidase activity¹ and have therefore suggested that the inflamed joint may be the target of damage by free radicals promoted by this enzyme.^{2,3} We have provided direct evidence that the mobile inflamed joint is subject to hypoxic reperfusion injury.⁴ A similar sequence of events might explain the pathological changes observed in rheumatoid tendons as the inflamed synovial lining is likely to become ischaemic on movement, allowing the build up of hypoxanthine and xanthine. The ischaemic process would allow the conversion of normal xanthine dehydrogenase to an oxidase

capable of producing both superoxide and hydrogen peroxide with the reintroduction of the blood supply.⁵ Dr Murrel and his colleagues have found that the xanthine oxidase inhibitor allopurinol is of benefit in Depuytren's contracture.⁶ Although this trial was uncontrolled we have been unable to find reports of spontaneous resolution in published reports. It would be of interest to establish whether allopurinol suppresses the destructive consequences of inflammatory tenosynovitis associated with rheumatoid disease.

J M OUTHWAITE
P MERRY
R E ALLEN
D R BLAKE

Bone and Joint Research Unit,
The London Hospital,
London E1 1AD

- 1 Allen RE, Outhwaite JM, Morris CJ, Blake DR. Xanthine oxidoreductase is present in human synovium. *Ann Rheum Dis* 1987;46:843-5.
- 2 Woodruff T, Blake DR, Freeman J, et al. Is chronic synovitis an example of reperfusion injury? *Ann Rheum Dis* 1986;45:608-11.
- 3 Andrews FJ, Blake DR, Freeman J, et al. Free radicals and reperfusion injury in the inflamed joint. In: Swaak AJG, Koster JF, eds. *Free radicals and arthritic diseases*. Rijswijk, Netherlands: Eurage, 1986. (Topics in aging research in Europe, vol 11.)
- 4 Outhwaite JM, Allen RE, Lunec J, et al. The effect of joint movement on an index of free radical damage. *Br J Rheumatol* 1987;26(Suppl 2, No 123):70.
- 5 McCord JM. Oxygen derived free radicals in post ischaemic tissue injury. *N Engl J Med* 1985;312:159-63.
- 6 Murrel GAC, Murrel TGC, Pilowsky EA. Hypothesis on the resolution of Dupuytren's contracture with allopurinol. *Speculations in Science and Technology* 1987;10:107-12.

The natural course of gold nephropathy

SIR,—We would like to clarify the points raised by Drs John A Hunter and Hilary A Capell (21 November, p 1350) concerning our study of the natural course of gold nephropathy (26 September, p 745). The criterion for nephrological referral was persistent proteinuria in excess of 0.3 g/l (in the absence of urinary infection) that developed during gold treatment. Twenty two patients fulfilled this criterion, and in only one patient, who was shown to have amyloid, was a disease other than gold nephropathy shown by renal biopsy.

We strongly recommend that all patients with rheumatoid arthritis and proteinuria should be investigated fully and that renal biopsy should be carried out, if indicated, to provide a precise diagnosis permitting appropriate treatment and accurate prognosis. In more than 90% of patients who develop proteinuria during gold treatment, however, the drug is the cause of the proteinuria, which resolves when treatment is stopped. In these particular patients and circumstances, provided that the results of relevant tests for causes of proteinuria other than gold nephropathy are negative, the proteinuria resolves within one to two years of gold treatment being stopped, and renal function does not deteriorate, renal biopsy seldom contributes to the management of the patients and is unnecessary in routine clinical practice.

We agree that effective treatment for the rheumatoid arthritis needs to be continued but suggest that, to avoid confusion, a drug which does not cause proteinuria should be given until the gold induced proteinuria has resolved. Thereafter penicillamine, particularly in low dosage, is a suitable treatment. The prescriber should, however, be aware of the increased incidence of proteinuria during penicillamine treatment in patients with rheumatoid arthritis who have a history of gold induced proteinuria.¹

With regard to the role of corticosteroid treatment, our results indicate that gold nephropathy resolves without such treatment and we

were able to manage several patients with severe proteinuria (15-31 g/day) with dietary and diuretic treatment. Continuing proteinuria of this severity, however, particularly when associated with profound hypoalbuminaemia, deteriorating renal function, and threatened acute renal failure, might be an indication for short term high dose corticosteroid treatment either alone or in combination with other immunosuppressive agents, and I am pleased to supply the reference for this.²

CLIVE L HALL

Royal United Hospital,
Bath BA1 3NG

- 1 Hall CL. Gold and D-penicillamine induced renal glomerular disease. In: Bacon PA, Hadler NM eds. *The kidney in rheumatic disease*. London: Butterworths, 1982:246-66.
- 2 Ponticelli C, Zucchelli P, Imbasciati E, et al. Controlled trial of methyl prednisolone and chlorambucil in idiopathic membranous nephropathy. *N Engl J Med* 1984;310:946-50.

Contraceptive services for ethnic minorities

SIR,—We disagree with Dr Jon Fuller's suggestion that "in an ideal world people would receive contraceptive advice..." (28 November, p 1365). In contraception one does not give advice: one listens to the patients' needs, likes, fears, and worries and helps them to come to a decision on the best method of contraception for them. Any other course is at worst patronising, at best useless.

The implication in his article is that language is the basis of his definition of "ethnic minority." Our experience over the past 20 years in clinic and domiciliary contraceptive services in Sheffield leads us to different conclusions about patients whose first language is not English. The most important issue to such patients is exactly the same as to a native English speaker: to achieve as direct contact as possible with the doctor in whom they have confidence. A consultation in very rudimentary English (and it is surprising how far a very few words will sometimes stretch) is usually preferred to a discussion through an interpreter. It is not uncommon for patients to express a preference for a consultation with an English doctor, in English, over a consultation with a doctor of their own race.

The proposal to use "patients' advocates" seems potentially disastrous. Such an expert, informed, fluent, and therefore inevitably dominant person would erect an impenetrable barrier between doctor and patient and often would present to the doctor his or her own "interpretation" of the wishes of the patient. At our largest clinic 20% of patients are Roman Catholics. Had their interests been represented by someone who interpreted "the patients' needs and beliefs and provided an insight into the current beliefs of that community" we suggest that many thousands of patients would have been very dissatisfied with the service that we would have provided under the mistaken belief that it was what the patient wanted.

J TATTERSALL
JENNIFER WORDSWORTH

Central Health Clinic,
Sheffield S1 2PJ

Treatment of cardiac arrest by ambulance staff

SIR,—We support the view expressed by Dr J A Rowley and others (28 November, p 1387) regarding advanced cardiac training for ambulance staff. The major determinant of survival from out of hospital cardiac arrest is prompt defibrillation.^{1,2} There would therefore be greater life saving

potential from making defibrillators widely available than from the more extensive training of a smaller number of ambulance crews.

The training programme described, however, required 96 hours.³ This may still be too lengthy a commitment for some ambulance services if many staff are to be trained. Hospital attachment, monitoring of individual rescuer's performance, and refresher training add constraints to developing and maintaining prehospital definitive cardiac care programmes.

Since October 1986 we have been coordinating a trial using semiautomatic advisory defibrillators in south east London. Two hundred ambulance staff underwent a six hour training programme and all completed the course satisfactorily. Preliminary analysis of our results indicates that the machine is sensitive and specific for ventricular fibrillation and that ambulance crews are using the defibrillator correctly according to the protocol. Hospital attachment, delays in recognising arrhythmias, and retraining are not problems. Previous work comparing automatic external defibrillators with conventional manual defibrillators has shown that they are equally effective at terminating ventricular fibrillation.⁴

This training could be easily included in basic ambulance training, thereby maximising the provision of prehospital defibrillation and avoiding delays associated with more expensive and extensive cardiac training.

GERALDINE WALTERS
EDWARD GLUCKSMAN

Accident and Emergency Department,
King's College Hospital,
London SE5 9RS

- 1 Weaver WD, Cobb LA, Hallstrom AP, Fahrenbruch C, Copass MK, Ray R. Factors influencing survival after out-of-hospital cardiac arrest. *J Am Coll Cardiol* 1986;7:752-7.
- 2 Eisenberg M, Bergner L, Hallstrom AP. Paramedic programmes and out-of-hospital cardiac arrest: II. Impact on community mortality. *Am J Publ H* 1979;69:39-42.
- 3 Rowley JM, Garner C, Handy M, Hampton JR. Simple training programme for ambulance personnel in the management of cardiac arrest in the community. *Br Med J* 1985;291:1099-101.
- 4 Stults KR, Brown DD, Kerber RE. Efficacy of an automated external defibrillator in the management of cardiac arrest: validation of the diagnostic algorithm and initial clinical experience in a rural environment. *Circulation* 1986;73:701-9.

Sequential hormonochemotherapy in advanced breast cancer

SIR,—The excellent response rate to cyclical sequential hormonochemotherapy in metastatic breast cancer reported by Mrs Ghilchik and associates (7 November, p 1172) is exciting.

The article does not specify, however, whether these patients had received any previous hormonal treatment or chemotherapy, either as adjuvant treatment or for earlier relapses. No data on the oestrogen or progesterone receptor states of their tumours is given, but we may assume that since all but two were postmenopausal, with a mean age of 63 years, most were oestrogen receptor positive.¹

In a small series of patients such as this it is not possible to show that sequential combination therapy has significantly improved the response rate over either hormonal treatment or chemotherapy alone. Hormonal treatment may give up to a 70% overall response rate in patients who are both oestrogen and progesterone receptor positive.² Cyclophosphamide-methotrexate-fluorouracil chemotherapy regimens will give response rates of 50 to 80% in non-pretreated patients, which has been reproducible across several series.³

It is not possible, therefore, to discern from the results of this study whether the combination was truly better than either of these two treatment