vascular surgery, if only to reduce the number of confounding variables in studies that may have a considerable impact on the management of cerebrovascular disease in Britain. Rather different conclusions about the extracranial-intracranial bypass study can be reached, however, by studying the articles that Professor Dudley cites.

His use of the term "purportedly randomised" seems to imply that randomisation of the patients in the trial, whose outcome generated the results published by the study group, might not actually have taken place. This issue, which is distinct from that of "generalisability," has not, to my knowledge, been raised by any other commentator, and no evidence is provided to support such doubts. The basis for the conclusion that 50-70% of eligible patients were not randomised in the trial is also difficult to discern. Professor Dudley quotes Sundt's figures that 1695 out of 2772 (61%) "eligible" patients were operated on outside the trial,¹ yet this includes 681 patients from European centres whom Sundt was unable to verify as being eligible for entry. We must remember that at least some of these data were collected retrospectively and that the analysis also excluded Canadian centres, where randomisation was assumed to be complete and which contributed 14% of all patients in the trial. At the other extreme, the figures from the Committee of the American Association of Neurological Surgeons, prepared with the help of the prospectively collected records of the trial centre, suggest that only 570 out of 1947 (29%) eligible patients were operated on outside the trial.² Furthermore, to suggest that the investigators have been "uncompromising and rigid" while seeming to pay little attention to their detailed reply to previous critics³ seems ungenerous. Certainly, current research using positron emission tomography and carbon monoxide reactivity may define a small subgroup in whom extracranial-intracranial bypass might prove beneficial,² but the message from the trial is quite clear: the onus is on these workers to prove such benefit and until then the operation should not be recommended to patients. There is nothing elegant or rational about the patient who has a stroke while having an operation that was not going to confer any benefit anyway.

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SIR,—As a doctor "looking after patients comparable with those designated eligible in the trial," I find it difficult to accept Professor H A F Dudley's second conclusion (13 June, p 150) about the extracranial-intracranial bypass study¹: that we will still have to decide about treatment on an ad hominem basis. I would also question his suggestion that were a new trial to be organised different endpoints should be considered; stroke or stroke related death remains the only logical endpoint to document in the evaluation of a procedure designed to "improve" the cerebral circulation. Transient ischaemic attacks are notoriously difficult to classify; nevertheless, it is interesting that the percentage reduction (about 80%) was similar at one year in patients randomised for treatment of transient ischaemic attacks, whether they were treated surgically (n=207) or medically (n=175).

Sundt has performed a valuable service in show-

ing that centres were apparently not prepared to randomise all subjects deemed eligible for the trial.² It seems that 570 subjects who fulfilled the entry criteria were excluded, usually as a result of a failure to obtain informed consent.³ But 1377 were randomised (714 to the medical group and 663 to the surgical groups), creating comparable groups with symptoms and arterial disease of the type we see in clinical practice. Extracranial-intracranial bypass failed to produce a positive result in the group as a whole, and subgroup analysis showed that it proved significantly inferior in patients with internal carotid artery occlusion and continuing ischaemic symptoms. This was particularly disappointing because various physiological studies had suggested that collateral augmentation might prove beneficial in at least some of these patients who are haemodynamically compromised.^{4,5}

Prospective clinical trials may not be ideal for evaluating new surgical techniques, but we have no alternative. Their success clearly depends on the scientific integrity of participating centres, and Sundt would provide an additional service if he could find out why referring centres deviated from this ideal. If they know who should be operated on they should tell the rest of us so that we can evaluate their certainty in a new trial. At the moment, extracranial-intracranial bypass remains an elegant procedure without a clinical indication.

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Endoscopic coagulation of upper gastrointestinal haemorrhage, one; randomised clinical trials, two

SIR,—Like Professors H A F Dudley and I Taylor, I have also been intrigued by the controversy over extracranial-intracranial bypass surgery and by what I judge to be the desperate last ditch attempts of those with a vested interest in perpetuating these interventions to stay in the game (13 June, p 150; 27 June, p 1686). I believe that my two distinguished colleagues have made the same mistake by confusing bias with generalisability and pragmatic with explanatory trials. Randomisation, by definition, excludes systematic bias in the calculation of the results, but, of course, these results apply only to the population studied. If the population is a small, superselected group of patients then results cannot be generalised to all patients with that disease. At the same time, if you are prepared to believe results only from a single centre of excellence which accepts only patients with tight entry criteria randomised to procedures with tightly descriptive performance criteria then, whatever your results, you inevitably limit their generalisability (catch 22).

By coincidence, these points were beautifully highlighted in a recent issue of the *New England Journal of Medicine*, which was partly devoted to studies of endoscopic coagulation for patients with upper gastrointestinal bleeding. The first paper described the results of a randomised trial conducted

by a single operator in Los Angeles, using multipolar electrocoagulation for actively bleeding lesions in the stomach, duodenum, and oesophagogastric junction.¹ Of 329 patients admitted with upper gastrointestinal bleeding, only 44 (13%) were randomised. A few were excluded because they failed to provide consent, but most were excluded because they were not actively bleeding at the time of endoscopy or were bleeding from sites excluded within the tightly descriptive protocol. Although 13% died in the control arm and none in the active arm, this difference was not significant. There was, however, a highly significant reduction in the number of patients requiring emergency surgical intervention (57% v 14%) and in the mean length of hospital stay (7 days v 4 days).

In the companion paper from Dallas five operators and their senior residents conducted a randomised controlled trial of laser photocoagulation for patients presenting in the same way.² Of 1062 potential patients, 571 were excluded, mainly because they refused consent to the trial, but, in addition, a large number were judged too "unstable" to be moved from the intensive care unit to the equipment; 317 patients who underwent endoscopy were not randomised, mainly because the lesions visualised failed to meet the entry criteria. This left 174 patients (16% of the original total) who were randomised. There were no deaths in either group and there were no significant differences in the rebleeding rate or the need for urgent surgery. Although not significant, the mean duration of hospital stay was three days longer in the photocoagulation group than the control group.

What are the possible explanations for these differences in outcome? Is electrocoagulation good for you, whereas photocoagulation does not work? Was the single operator in Los Angeles more skilful than the five operators and their residents in Dallas, or are randomised controlled trials a waste of time and we should really rely on a priori reasoning and the "individualisation of treatment?"

Personally, I believe that the problem lies elsewhere. There has been a profusion of small descriptive trials relating to the management of upper gastrointestinal haemorrhage by endoscopic coagulation (14 are listed among the reference sections of the two papers cited above). Taken alone, each suffers from random bias as a result of small numbers, which could easily lead to a maldistribution of both known and unknown prognostic variables. Taken alone, each lacks statistical power. For example, if mortality from upper gastrointestinal haemorrhage is 10% then a randomised controlled trial of 10 000 would be required to detect a 20% reduction in deaths from this cause.³ In spite of this, if a formal statistical overview of all these trials were conducted then some approximation to the truth concerning these complex procedures might be achieved. However, if these treatments are practicable in only 13-16% of all cases of gastrointestinal haemorrhage then they are not strictly relevant in the real world, particularly when an argon laser unit costs \$80 000.

I conclude, therefore, that there are some expensive and complex technologies which, by their very nature, do not lend themselves to scientific evaluation. For this reason they have as much justification in their use as osteopathy or homoeopathy for the same disease processes. Professor Taylor, quite rightly, draws our attention to the ethical dilemmas and pitfalls when an individual clinician forfeits a certain degree of clinical independence. I also happen to believe that there is a serious ethical dilemma in the type of clinical independence which allows the freedom to indulge in expensive, unproved, and hazardous remedies.

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Intensive care: a specialty or a branch of anaesthetics?

SIR,—I have read the recommendations of the interfaculty collegiate liaison group on intensive therapy¹ and have followed the correspondence in the *BMJ* (25 April, p 1095; 30 May, p 1415) and *Anaesthesia*.²

From the standpoint of a consultant anaesthetist in a district general hospital with a four sessional weekly commitment to eight intensive care beds, I have several observations to make. I have, incidentally, fulfilled the recommendations of the liaison group in terms of training.

The constitution of the liaison group does not reflect the lifestyle of intensivists who work in district general hospitals. Most doctors who train for consultant posts in intensive care will work in district general hospitals and their views should be better represented in the group.

The general aim to provide modular training for doctors of any specialty in intensive care is admirable. The problems of the divisive and competitive training arrangements of the USA and Australia must be avoided. Although the liaison group goes a long way to meet this end, staging training at senior registrar level may defeat its aim. The main obstacle to a modular training scheme accessible to all specialties is the problem of transition from one specialty to another. The liaison group intensifies this by pitching the grade at senior registrar level. The programme would be better suited to registrars, who would enjoy and benefit from the variety, are adaptable, and have not finalised their career commitments. There would be valuable spin offs in other spheres of medicine common to all, such as resuscitation, which is practised appallingly by nearly all except anaesthetists.

Stoddart is correct in saying that anaesthetists are at present more suited to running intensive care units than physicians or surgeons, especially in district general hospitals.² This does not detract from the outstanding contributions made by those from other specialties. Many anaesthetists have copious medical experience to reinforce their specialist knowledge of anaesthesia, physiology, and pharmacology and have been aware for many years of the restrictions of specialisation and the acrimony that can arise from the self centred view. They are well suited to intensive care as either "brokers" or "shareholders" to use Dudley's analogy.³ Career physicians and surgeons would derive much from experience in anaesthesia but may be discouraged from doing so because there is no prestigious diploma to be had after a year in anaesthesia, whereas the full MRCP may be obtained by those with the determination after a year in medicine.

Running a DGH intensive care unit is physically and mentally demanding and the specialist back up of the teaching hospital may not be there—neither may the junior staff.⁴ Although I must count myself fortunate in having access to all the necessary specialties and to a dedicated registrar grade intensivist, I still have to roll up my sleeves and get to work. The input of many clinicians into the management of a patient has to be coordinated, the practical aspects of the work completed, and summaries written. The practical as well as the intellectual skills that make intensive care successful have to be learnt. Unfortunately it is learnt by

an apprenticeship, time consuming and often antisocial in terms of domestic commitments. Senior registrars are in their 30s by the time they complete their higher professional training. They have wives and families who would love to see them. They should be learning management skills, not the practical skills, at this stage. This type of training is surely more appropriate to registrar grades and would be more attractive to differing specialties at that level.

There is undoubtedly scope for training in intensive care at senior registrar grade but it should provide opportunities for research and development of the specialty.⁵ But the basic skills and groundwork are best learnt at registrar grade. Here, cross fertilisation of ideas and cooperation of the specialties in the intensive care unit can be achieved. This in itself would make the unit a less forbidding place for junior staff than it is at present.

The aim of the liaison group is to improve the care of critically ill patients in Britain. We must be sure that the training scheme adopted achieves these aims rather than simply trains people.

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Child abuse or copper deficiency?

SIR,—I was glad to see the beginnings of a debate on the possible risk of confusion between infantile copper deficiency and child abuse, as highlighted by Dr Stephen Chapman (30 May, p 1370). Over the past 10 years I have seen, both in England and abroad, 35 infants who seemed to have had a temporary, severe osteogenesis imperfecta-like disorder. In most cases the initial diagnosis was child abuse, but in three the initial diagnosis was osteogenesis imperfecta because the fractures occurred in hospital. In each case where the patients were thought to be victims of child abuse there was remarkably little clinical evidence of the trauma that would have been needed had the bones been normal. In five of these cases further fractures, generally rib fractures, occurred in hospital. In almost all cases most of the fractures were found by radiology and had not been suspected clinically.

Bone density was usually normal, as far as may be judged by ordinary radiographs (this assessment, however, must be taken with caution¹). The combination of reduced bone strength and maintained mineral content makes it likely that the disorder, like osteogenesis imperfecta and experimental lathyrism,^{2,3} represents a collagen defect. Apart from long bone and rib fractures, many patients had metaphyseal fractures or fracture like appearances. Many patients also had extraskelatal abnormalities, such as petechiae, hernias, anaemia (generally microcytic), or neutropenia. Some had gastrointestinal symptoms, such as vomiting (often projectile) or intermittent diarrhoea. These features suggest that the most probable cause of such a temporary collagen defect is copper deficiency, which may be transient but leaves behind bone of abnormal strength for some months. It is striking that in all but two cases the fractures were discovered within the first six months of life.

What could cause such a deficiency? Risk factors seem to include preterm birth and multiple pregnancy (11 of my cases were twins), both of which are recognised risk factors in reports of copper deficiency. Preterm infants often have a transient copper deficiency in early infancy.⁴ The disorder occurred in only one breast fed infant, and formula feeds may play a part in its development.

Most of these cases were investigated many months after the fractures had occurred, and in only one case was a low serum copper concentration found, at 6 weeks of age. In any case, serum copper concentration may be a poor measure of tissue copper stores.⁵ Whether all the cases of this syndrome represent copper deficiency or result from some other temporary defect of collagen maturation requires further investigation. In the mean time we need to be cautious in identifying child abuse without any corroborative social evidence, as this disorder, like osteogenesis imperfecta and rickets,^{6,7} may be mistaken for child abuse, with devastating effects on a family.

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AUTHOR'S REPLY,—I am glad to see that Dr Paterson welcomes the beginnings of a debate in the medical press, as up to this time the possible role of copper deficiency as a cause of fractures in cases of suspected child abuse has been raised by him only in the courts. Dr Paterson now believes that he has personally seen 35 cases with fractures. This is a remarkable number in view of the fact that the total number of reported cases in the world is only about 15.

Dr Paterson cannot reconcile the absence of external signs of trauma with normal bones. All of us who deal with acute trauma in normal children, however, realise that this does occur. The incidence of occult fractures in non-accidental injury is high, and there are several reasons for this. Many are due to twisting or pulling forces applied at a site remote from the actual fracture, and if the periosteum remains intact there will be no bleeding from the fractured bone into the soft tissues. The fracture may be old, and thus the external signs (if there were any) would have resolved. Local soft tissue injury may be reduced if the child is injured when clothed. If there is a collagen disorder that increases fragility of the blood vessels then bruising, even without fractures, should be even more common.

If, then, the conclusion of reduced bone strength is untenable normal bone density is further evidence that is much more likely to equate with normal bones than with a collagen defect. All the patients in published cases of copper deficiency with fractures have had obviously osteoporotic bones, and in many this has been severe. Fractures have probably been secondary to osteoporosis. A failure to appreciate that intra-articular metaphyseal fractures may heal without callus formation leads Dr Paterson to deny that they are fractures