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CORRESPONDENCE

- *All letters must be typed with double spacing and signed by all authors.*
- *No letter should be more than 400 words.*
- *For letters on scientific subjects we normally reserve our correspondence columns for those relating to issues discussed recently (within six weeks) in the BMJ.*
- *We do not routinely acknowledge letters. Please send a stamped addressed envelope if you would like an acknowledgment.*
- *Because we receive many more letters than we can publish we may shorten those we do print, particularly when we receive several on the same subject.*

Extracranial-intracranial bypass, one; clinical trials, nil

SIR,—Many of us outside the specialty of cerebrovascular surgery have nevertheless followed the correspondence relating to the international extracranial-intracranial bypass trial with interest.[1,2] The interpretation of the trial made by Professor H A F Dudley (13 June, p 1501) raises many questions of concern to all those involved in randomised trials in which one "arm" is a surgical procedure.

Trials of technical innovations in a single centre with interested parties are difficult enough to perform; trials including many centres inevitably encounter problems related to quality control and protocol violations. Once a trial becomes truly multicentre and international, however, gathering accurate data is likely to be fraught with difficulties.

It is intriguing to consider why some eligible patients are selected for randomisation while others who are equally eligible are not. In addition, what reasons are there for a randomised patient not receiving the allocated treatment? Discrepancies of this type obviously throw doubt on the validity of any data obtained. From experience of randomised surgical trials for over 10 years, I would suggest that the two chief reasons for trial idiosyncrasy are, firstly, problems with informed consent and, secondly, a lack of time and commitment on the part of the participating surgeon.

Both these reasons are understandable. It can be extremely difficult (and time consuming) to explain to a patient that he has a potentially crippling or fatal disease that is suitable for randomisation but that whereas one treatment arm is active, the other consists of a "wait and see" policy. Equally, once a patient is included in a trial entailing long term careful follow up and investigation the extra time needed and resulting paperwork may be considerable.

There is no doubt that surgeons are often willing, for the very best of motives, to participate in therapeutic trials. Such enthusiasm, however, may backfire if the protocol is not scrupulously adhered to. In my view, when a surgeon agrees to participate in a randomised clinical trial he should be made fully aware of all the potential difficulties, ethical considerations, time, and attention to detail that such a commitment entails. Strict adherence to the protocol is essential, and the surgeon must accept that his clinical freedom will be inhibited. If a patient admitted under his care is eligible for randomisation then that patient must be included in the study. If the patient does not give informed consent to randomisation then, whatever treatment is provided, the patient's progress should nevertheless be monitored in exactly the same way as it would have been had he been allocated to the randomised treatment.

Accordingly, if a surgeon is invited to participate in a controlled randomised trial he should consider carefully the overall implications before agreeing. Should he decide to participate in this long term and time consuming exercise, with all its ethical dilemmas and pitfalls, then he immediately forfeits a certain degree of clinical independence. Failure to adhere to the protocol, with non-randomisation of eligible patients or randomisation of ineligible patients, can have serious long term consequences, as illustrated so dramatically in the extracranial-intracranial study.

The truth, as Popper pointed out, is never manifest, and therefore we must make do with science. It is most important that the scientific status of any therapeutic procedure is established, and in clinical medicine this demands a careful and disciplined approach to clinical trials.

I TAYLOR

Faculty of Medicine,
Southampton General Hospital,
Southampton SO1 6HU

1 Extracranial-intracranial Bypass Study Group. Failure of extracranial-intracranial bypass to reduce the risk of ischaemic stroke. Results of an international study. *N Engl J Med* 1985;313:1191-200.
2 Sundt T. Was the international randomised trial of extracranial-intracranial arterial bypass representative of population at risk? *N Engl J Med* 1987;316:814-6.

The search for a hormonal switch for obesity

SIR,—We think that there is a good case for adding two regulatory peptides to the already long list cited by Drs C Dieguez and M F Scanlon in their interesting leading article on possible endocrine causes of obesity (30 May, p 1371). These are neuropeptide Y and galanin, both of which have been convincingly shown to be among the most powerful known central stimulants of appetite in rodents.

Neuropeptide Y (the most abundant neuropeptide in the brain) is found in high concentrations in the hypothalamic nuclei,[1] including the para-