Sir,—Thank you for allowing us to comment on the letter from Drs Goodman and Black.

In our recent paper we did not comment on our refusal rate because we did not find this a problem. Only one patient refused to take part in the study; in fact the first patient we asked to participate. Over four trials involving propofol (three published so far) with a total of 180 patients, only six patients have refused to participate, five of whom were in our latest, as yet unpublished trial,—several refusing because they did not wish a spinal anaesthetic.

We can offer a few possible reasons for our low refusal rate. First, our studies have involved no major changes in our usual anaesthetic techniques. Over 50% of patients in the Orthopaedic Department are anaesthetized using regional anaesthetic techniques; surgeons, nursing staff and patients expect this. Second, both of us are regular anaesthetists in the Department and are well known to ward nursing staff, and patients who are frequently returning for repeat operations. We see patients in the afternoon before operation, not the morning of operation, when they will inevitably be more anxious. Third, the propofol trials have been continuing in the Department for several years, and are accepted by surgeons, nurses and patients alike. Last, there is a strong local tradition of participation in clinical trials, and of patients wishing to help the advancement of anaesthetic techniques; surgeons, nursing staff and patients both look forward to and expect participation.

Nevertheless, in our latest trial, it may be that we are beginning to see an increase in resistance among patients to participate in investigations involving new drugs.

I. S. GRANT
N. MACKENZIE
Dundee

DOES ANAESTHESIA AFFECT FREE-FLAP SURVIVAL?

Sir,—The recent article by Dr Macdonald (1985) nicely illustrates the physiological principles which should be applied in the management of anaesthesia for microvascular surgery. Controlled clinical studies of the effects of drugs used in anaesthesia under these circumstances are lacking. The few clinical reports of anaesthetic management of free-flap surgery rely more on anecdote than on scientific evaluation (Robins, 1983), and no assessment has been made of those pharmacological manoeuvres which may affect the flap. For instance, if systemic or regional vasodilatation is used, can a steal phenomenon occur? If so, is it beneficial or detrimental to the flap? Blood flow is improved by dilution (Earle, Fratranne and Nunez, 1974), but no proof exists that it is enhanced by dextran, gelatin, or hydroxylethylated starch solution in microvascular surgery. No measurements of flow, perfusion or effect on outcome have been reported.

Dr Macdonald reports that the average time of surgery is about 8 h, but he places little emphasis on the use of warming blankets and heated humidifiers to maintain temperature, and the other methods listed are usually ineffective.

A particular omission from his report is the problem of maintaining close observation of the status of the patient over these prolonged periods. Regular relief should be provided, both to refresh the anaesthetist and to allow the relieving anaesthetist to bring a new appraisal of the situation (Cooper et al., 1978; Robins, 1983).

The only measurement of successful anaesthesia, to date, has been flap survival, which may not be certain for several days after operation. Many operative and postoperative factors can affect flap survival, from surgical technique to application of constrictive dressings. Is the anaesthetic of greater relevance than the surgical technique in predicting flap survival? If the usual principles of avoidance of hypothermia, hypoxia, hypocapnia or hypotension are followed, a straightforward anaesthetic technique would probably suffice, until better evidence for improvement in free-flap survival is presented.

REFERENCES

Sir,—Thank you for letting me see Dr Rylah's letter. I am sure we have much to learn from controlled clinical studies in these cases, although one can anticipate practical and ethical difficulties in mounting such studies in patients.

Regarding temperature maintenance, Morris and Kumar (1972) found the use of a warming blanket ineffective, and I have found it unnecessary. Covering the patient with plastic or foil sheeting, using a condenser-humidifier in the anaesthetic circuit and warming the infusion fluids in 11 consecutive patients has led to a slight increase in nasopharyngeal temperature (0.3-1.8 °C) in six patients, no change in two and a slight decrease (0.3-1.3 °C) in three (fig. 1). These simple measures are adequate for the circumstances in which I work, and avoid any danger from burning or electrical hazards.

"Maintaining close observation of the status of the patient" is, of course, important, and, as Dr Rylah points out, it has been emphasized in other publications. The administrative implications were discussed by Dr Peter Baskett at the recent Faculty of Anaesthetists symposium in London. I did not consider that it came within the scope of my title—unless we also take into consideration the physiological functioning of the anaesthetist.
The answer to the question "Is the anaesthetic of greater relevance than the surgical technique?" is a resounding "No!". No amount of care in the conduct of the anaesthetic will compensate for poor surgical technique, but I would suggest that a bad anaesthetic can render fruitless the most meticulous surgery.

D. J. F. Macdonald
Glasgow

REFERENCE

EXCRETION OF LAUDANOSINE IN MAN
Sir,—The work of Dr Fahey and colleagues (1985) addresses an important issue concerning the fate of one of the metabolic products of atracurium. Although the authors set out to determine "... the influence of renal failure on the excretion of laudanosine in patients receiving atracurium...", the authors provide data only on the plasma concentrations of laudanosine in patients with renal failure and in patients with normal renal function. The fact that there was a difference in the plasma concentrations of laudanosine between the two groups of patients—starting 90 min after the administration of atracurium—is not tantamount to the demonstration of different excretion rates of laudanosine in the two groups. First, did the plasma concentrations of laudanosine decrease in either group during this time? Second, assuming that there was a net disappearance of laudanosine from plasma, was the rate of disappearance different between the two groups? Third, if different rates of disappearance were demonstrated, it would have been of interest to learn about the amounts of laudanosine eliminated via the renal vs. non-renal routes. Fourth, do the data imply a larger volume of distribution of laudanosine in normal patients or larger amounts of laudanosine generated in the renal patients? Last, from the presented data, what do the authors deduce about the excretion of laudanosine in man and about the influence of renal failure on it?

This very interesting work poses yet another, incidental, question not directly related to the primary goal of the study. Plasma concentrations of laudanosine were found to be greatest soon after the administration of atracurium (2, 4 and 6 min). Assuming that laudanosine is formed from atracurium in vivo, one would expect to find increasing—rather than decreasing—plasma concentrations of laudanosine soon after the administration of atracurium. Was the injected solution analysed for laudanosine and was any detected? If no laudanosine was injected with atracurium, is there a kinetic explanation for these interesting data?

V. Nigrovic
Toledo

REFERENCE

BRITISH JOURNAL OF ANAESTHESIA

Sir,—Dr Nigrovic presents some interesting questions about our work. At the outset, it should be made clear that we examined laudanosine concentrations in normal and renal failure patients as a pilot study to determine if there were any differences between the two patient groups. We did indeed demonstrate that there was a difference in plasma concentrations of laudanosine 90 min after the initial dose of atracurium, but it was not our intention to examine rates of disappearance of laudanosine from plasma, nor to quantitate laudanosine excretion through renal and non-renal routes. Other investigators have attempted to estimate such kinetic parameters as elimination half-life and renal clearance of laudanosine in patients receiving atracurium, but by their own admission, these values are crude estimates at best (Ward et al., 1985). So, in answer to Dr Nigrovic’s question, we believe our data suggest that the kidney plays a major role in the excretion of laudanosine in patients receiving atracurium. Finally, as a pilot study, our results suggest further research is needed to define the role of the kidney in laudanosine excretion.

Perhaps the most interesting of Dr Nigrovic’s questions concerns the extremely rapid attainment of peak laudanosine concentrations after a bolus of atracurium. We did analyse several vials of atracurium used in our study for laudanosine and found only trace amounts of laudanosine. One explanation for rapid peaking of plasma laudanosine concentrations may be that Hofmann elimination of atracurium is most active when there are large amounts of atracurium present in the circulating blood volume shortly after bolus administration. Hofmann elimination would rapidly produce two molecules of laudanosine per molecule of atracurium and thus result in a "bolus" of laudanosine into the circulating blood volume. After this initial 1–2 min period, redistribution and metabolic organ clearance of atracurium and laudanosine would produce the decrease in laudanosine concentrations seen thereafter.

M. R. Fahey
San Francisco

REFERENCE

ELIMINATION OF ATRACURIUM IN MAN Vs. RAT
Sir,—Atracurium is a relatively short-acting non-depolarizing neuromuscular blocking drug which is rapidly inactivated by Hofmann elimination, and by ester hydrolysis independent of