problems from this study are not going to be as great as was originally anticipated.

I return to my basic thesis that any patient on routine aspirin or NSAID medication [1] should have a bleeding time performed before an extradural is sited. If the bleeding time is prolonged beyond 10 min, then the anaesthetist must balance the advantages and disadvantages of siting the extradural in that particular patient.

R. MACDONALD
Leeds


ATRACURIUM AND HISTAMINE

Sir,—I was interested to read the paper by Adt, Baumert and Reimann on the role of histamine in the cardiovascular effects of atracurium [1], in which work by myself and colleagues was quoted extensively [2, 3]. I would like to congratulate them on a well executed and researched project. The obvious question is, of course, how much one may infer about the true haemodynamic side effects of a drug when patients recruited to the study have been prescreened for preoperative cardiovascular medications? These drugs may well obtrude or exaggerate any haemodynamic event after i.v. administration of a large bolus dose of atracurium. I think the authors need to look in more detail at the individual patient responses and the preoperative medication. It is interesting, however, to observe the data on cardiac index and systemic vascular resistance.

R. P. F. SCOTT
Salisbury


Sir,—Thank you for the opportunity of replying to Dr Scott’s comments. Conditions for clinical studies are optimal when healthy individuals are investigated and all interfering medication is excluded. We represent a clinic for cardiac disease where all patients require medication before anaesthesia, and we are especially interested in obtaining data from these patients. However, while there is compelling evidence (see below) that such patients react sensitively to intraoperative histamine release, effective intraoperative protection can be achieved by means of H₁- and H₂-receptor antagonists.

We have shown that a transient increase in plasma histamine concentration occurs after i.v. heparin, which could account for a cardiovascular reaction [1, 2]. In differing patients, different plasma histamine concentrations can occur, for which different preoperative medications may be partly responsible. However, there is no clear relationship between medication and cardiovascular reaction pattern; for example, patients with and without beta receptor blockers did not develop tachycardia, and the decrease in mean arterial pressure after histamine release was independent of antihypertensive premedication. Lorenz and Doenicke have demonstrated that, in approximately 3% of all patients undergoing surgery, serious to life-threatening plasma histamine concentrations occur—for example after administration of antibiotics—whereas the incidence of all types of histamine reactions may be as great as 20-30%. We believe that the variety of drugs administered during surgery is the cause of in calculable histamine release and that preoperative medication is of less importance for cardiovascular sequelae.

During coronary artery surgery there is a tendency to interpret intraoperative arrhythmias as cardiac ischaemia. However, Levi’s group have achieved very impressive results in animal studies, showing that cardiac anaphylaxis is an independent pathological phenomenon in which histamine often plays a lethal role [4, 5]. Similarly, preliminary results of an in vitro study of mast cells from human hearts show that these mast cells do, in fact, release histamine when perfused with drugs that are clinically suspected to be histamine liberators. These results underline that the influence of histamine on the heart is of a clinical importance which has not yet been completely investigated.

It is our philosophy to protect patients with a deficient cardiovascular system against histamine-indicated reactions, occurring during anaesthesia, by means of prophylactic administration of H₁- and H₂-receptor antagonists. The aim of the study under discussion was, first, to establish the amount of histamine released and the cardiovascular reaction induced by a clinical dose of atracurium and, second, to investigate if muscle relaxation induced in these patients can be achieved safely following the above-mentioned “prophylaxis”. In our opinion, both questions have been answered adequately.

M. ADT
Berlin


PROBABLE RESISTANCE TO VECURONIUM INVOLVING THE 17-HYDROXY METABOLITE

Sir,—The editorial by Hunter [1] has prompted this report of a case of probable resistance to vecuronium accompanied by the detection of its 17-hydroxy metabolite. A 26-yr-old waitress (weight 62 kg), being otherwise healthy, was to undergo knee surgery. She was not currently receiving medication and did not abuse alcohol or other chemical substances. Premedication comprised diazepam 5 mg orally and pethidine 50 i.m. After administration of glycopyrronium 0.2 mg and vecuronium 1 mg, anaesthesia was induced i.v. with thiopentone 250 mg and the trachea was intubated with the aid of suxamethonium 100 mg. The patient’s lungs were then ventilated manually with nitrous oxide and 1% enflurane in oxygen. Vecuronium 4 mg was injected, but without effect: the peripheral neurostimulator showed no fade on train-of-four stimulation. I therefore injected 1 mg of vecuronium 3 mg which provided neuromuscular block sufficient for the 45-min surgery. The residual block was antagonized with neostigmine-glycopyrronium and the postoperative course was uneventful.

The blood samples, and amoules of vecuronium belonging to the same batch as that given, were analysed at the University Hospital, Groningen. The serum and plasma samples, respectively, contained 17-hydroxy vecuronium 304 and 305 ng ml⁻¹ and vecuronium 35 and 65 ng ml⁻¹. The amoules were found to contain only vecuronium, ruling out the possibility that the patient received any drug other than that stipulated.

In an effort to confirm the finding, the patient agreed to donate blood for an in vitro experiment. A solution of vecuronium 2-2.5 µg ml⁻¹ was added to the patient’s plasma and 2-ml samples...