

were taken from this mixture at nine intervals for up to 128 min. Each sample was immediately acidified, stored at -20°C and subsequently transferred to Groningen for analysis. All samples revealed vecuronium without any of its breakdown products.

Unlike the 3-hydroxy metabolite, neither of the two other metabolites of vecuronium (17-hydroxy and 3,17-dihydroxy vecuronium) have been detected previously in biological material [2]. The 17-hydroxy vecuronium in this patient's blood may suggest an alternative metabolic pathway. However, this statement must be taken with caution, as her original samples were not acidified, and a sample of blood had not been collected before she received vecuronium. Finally, the sensitivity and selectivity of the analytical methods may have been at least partly responsible for 17-hydroxy vecuronium not having been demonstrated earlier in human material.

It is, nevertheless, of interest that 1 yr earlier, the same patient had required a general anaesthetic. According to the anaesthetic chart, she had been given vecuronium 4 mg and, about 5 min later, pancuronium 4 mg. Although there was no comment on the record as to why the two agents were administered in such short order, it is very likely that on that occasion also, no effect was seen with vecuronium. Final confirmation of her resistance to vecuronium and the detection of 17-hydroxy metabolite obviously can only be obtained if this particular patient requires a general anaesthetic again.

Anaesthetists confronted with apparent resistance to vecuronium which cannot be explained on more classical grounds should ask for plasma vecuronium analysis for the patient in question.

D. A. COZANITIS
Helsinki

1. Hunter JM. Resistance to non-depolarizing neuromuscular blocking agents. *British Journal of Anaesthesia* 1991; 67: 511-514.
2. Marshall IG, Gibb AJ, Durant NN. Neuromuscular and vagal blocking actions of pancuronium bromide, its metabolites and vecuronium bromide (Org NC 45) and its potential metabolites in the anaesthetized cat. *British Journal of Anaesthesia* 1983; 55: 703-714.

REPEATED RESISTANCE TO NON-DEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS IN A PATIENT WITH MULTIPLE MYELOMA

Sir,—We read with interest the article by Tatman, Wrigley and Jones [1] and the accompanying editorial by Hunter [2] on the subject of resistance to non-depolarizing neuromuscular blocking agents, and now report a similar case.

A 62-year-old man with a 7-yr history of multiple myeloma, persistent haematuria, thrombocytopenia and clot retention was referred for cystoscopy and evacuation of clot under general anaesthesia. Current medication included ranitidine, nifedipine, acyclovir, fluconazole and cotrimoxazole. Anaesthesia was induced with thiopentone 350 mg, fentanyl 100 μg and vecuronium 7 mg. Three minutes later, the patient started coughing on attempted laryngoscopy. The anaesthetist resumed manual ventilation with 70% nitrous oxide in oxygen supplemented by 1% isoflurane. Second doses of vecuronium 3 mg and thiopentone 150 mg were administered and laryngoscopy was performed after an additional 3 min. Tracheal intubation was accomplished, although it was noted that the cords were still not fully relaxed. During anaesthesia, further boluses of vecuronium 2 mg were necessary

at 10-min intervals to suppress ventilatory efforts. A total of vecuronium 18 mg was given over a period of 90 min. Neuromuscular block was not monitored.

The following morning, the patient presented again with persistent clot retention, and a rapid sequence induction was carried out using thiopentone 250 mg, fentanyl 100 μg and suxamethonium 100 mg. Tracheal intubation was uneventful at 1 min. Neuromuscular block was maintained with atracurium 40 mg, but breathing started 15 min later, and another dose of atracurium 10 mg was administered. Neuromuscular monitoring was commenced, and after the second dose of atracurium all four twitches of the train-of-four were present. Another dose of atracurium 20 mg was needed to ablate the third and fourth twitch responses. During the 1-h procedure, atracurium 80 mg in total was needed to maintain relaxation. At the end of surgery, all four twitches of the train-of-four were present.

Protein electrophoresis performed later revealed results which were consistent with myeloma (normal values in parentheses): IgG 42.6 g litre $^{-1}$ (5.3-16.5 g litre $^{-1}$), IgA 0.24 g litre $^{-1}$ (0.80-4.00 g litre $^{-1}$), IgM 0.5 g litre $^{-1}$ (0.5-2.0 g litre $^{-1}$), paraproteins 36.2 g litre $^{-1}$ (normally absent); beta-2-microglobulin 7.6 mg litre $^{-1}$ (0.0-2.6 mg litre $^{-1}$); albumin 32 g litre $^{-1}$ (35-50 g litre $^{-1}$); alpha₁ acid glycoprotein (AAG) 0.8 g litre $^{-1}$ (0.6-1.2 g litre $^{-1}$). Serum electrolyte concentrations before the second anaesthetic were: sodium 133 mmol litre $^{-1}$, potassium 3.4 mmol litre $^{-1}$, creatinine 148 μmol litre $^{-1}$, calcium 1.8 mmol litre $^{-1}$ (2.15-2.55 mmol litre $^{-1}$).

Little is known about altered drug responses in patients with paraproteinaemia secondary to multiple myeloma. It has been speculated that the presence of abnormal circulating immunoglobulins and decreased plasma albumin concentrations could result in altered responses to drugs normally bound to protein [3], although a standard text does not mention that paraproteinaemia presents a significant anaesthetic problem [4]. The extent of plasma protein binding of both vecuronium and atracurium is similar, but different authors have expressed varying views on which plasma proteins are implicated [2].

It is expected that neuromuscular blocking agents would bind mainly to AAG. This is thought to be the basis of the resistance to atracurium in the case reported by Tatman, Wrigley and Jones. However, in this patient, AAG was normal and serum albumin reduced slightly, which may potentiate block. Although other factors such as drug interactions may be involved, it is likely that the altered response to neuromuscular blocking drugs is caused by increased binding to paraproteins, including possibly IgG or beta-2-microglobulin. It is important to note that there was no apparent change in the response to suxamethonium.

We would welcome further comments on the subject of altered pharmacodynamics in patients with multiple myeloma.

C. IP YAM
P. WOOD
Liverpool

1. Tatman AJ, Wrigley SR, Jones RM. Resistance to atracurium in a patient with an increase in plasma alpha₁ globulins. *British Journal of Anaesthesia* 1991; 67: 623-625.
2. Hunter JM. Resistance to non-depolarizing neuromuscular blocking agents. *British Journal of Anaesthesia* 1991; 67: 511-514.
3. Stoelting RK, Dierdorf SF, McCammon RL. In: *Anaesthesia and Co-existing Disease*, 2nd Edn. Edinburgh: Churchill Livingstone, 1988; 711.
4. Mason RA. In: *Anaesthetic Databook. A Clinical Practice Compendium*. Edinburgh: Churchill Livingstone, 1989; 202.