concentrations. intubation need not necessarily result in hypertension and which reduce the tachycardia and hypertensive responses asso-

\textit{...} and Wilson tests, the thyromental distance is quoted still as a predictor of difficult or impossibly laryngoscopy. The paper by Mathew, Hanna and Aldrete [3] was a retrospective study of 22 easy and 22 difficult intubations in 44 patients and showed correlation between thyromental distance less than 6 cm, Mallampati class 11 or IV and difficulty in intubation.

A prospective study of 250 patients in Singapore [4] has shown a spread of thyromental distance from 3.5 to 9 cm, with patients either side of the 6-cm distance in easy and difficult laryngoscopies groups. It was found that a thyromental distance of less than 6 cm correctly predicted 61% of difficult laryngoscopies, but just 25% of easy laryngoscopies. Only 10% of predicted difficult laryngo-

\textit{...} in the majority of patients, we would suggest concentration greater than the reported toxic plasma concen-

\textit{...} in normal saline. Bedford and Feinstein [1] have reported that peak

\textit{...} mm Hg and observed

\textit{...} arte-

\textit{...} coron-

\textit{...} patients, although they observed no significant effect on heart rate responses. These results are consistent with previous investigations [2, 3] showing little effect of either verapamil or sodium nitroprusside on heart rate increases after tracheal intubation. My previous study [2] in hypertensive patients showed that mean arterial pressure increased from baseline after tracheal intubation by 18 (9)% (mean (sd)) when verapamil 0.5 mg kg\textsuperscript{-1} was given i.v. 1 min before laryngoscopy and tracheal intubation, and by 53 (14)% after normal saline (P < 0.001). This result supports their assumption that pretreatment with i.v. verapamil may be useful in hypertensive patients undergoing tracheal intubation. Furthermore, I agree that failure of verapamil to attenuate tachycardia associated with tracheal intubation limits its usefulness in patients with ischaemic heart disease, as it is generally supposed that such patients tolerate hypertension better, and tolerate hypotension and tachycardia poorly; Lieberman and colleagues [4] have noted that myocardial ischaemia accompanied significant increases in heart rate and decreases in arterial and coronary perfusion pressure in patients undergoing coronary artery revascularization with halothane anaesthesia.
transient ST-T segment depression in two of 12 hypertensive patients. As hypertensive patients sustain a progressive increase in mortality and morbidity from coronary artery disease [2], hyperdynamic responses leading possibly to myocardial ischaemia should be treated in these patients. We thank Dr Nishikawa for calling attention to the results of his study indicating the usefulness of verapamil in hypertensive patients.

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FADE DURING RECOVERY FROM VECURONIUM

Sir,—Fletcher and colleagues [1] have repeated the observations of Bowman [2], Pearce, Casson and Jones [3] and others in demonstrating that greater train-of-four fade occurs during offset of the action of vecuronium than during onset. They suggest that fade results from block of prejunctional receptors at the neuromuscular junction, and that vecuronium is able to enter and leave the region of the prejunctional receptor only slowly, resulting in a slower onset and offset of prejunctional effects. Bowman and Webb [4] showed that tetanic fade in the cat soleus muscle was more pronounced when neuromuscular block had been produced by bolus i.v. injection of tubocurarine, than after the same dose of block produced by a much smaller i.a. injection. Bowman [2] postulated that "a slower rate of binding to the 'fade sites' would explain the observations that peak tension depression and fade develop and recover with different time courses." He argued that a slower rate of binding "would also explain the absence of tetanic fade when twitch depression is produced by intra-arterial rather than intravenous injection of tubocurarine, since the relatively small bolus dose administered intra-arterially would pass through the muscle and be diluted in the general circulation before there was time for binding to the fade sites to occur".

We have observed a marked difference between tetanic fade during recovery from vecuronium block in the isolated forearm and from systemic i.v. injection. In the isolated forearm technique, a small dose of vecuronium (0.3 mg diluted in saline 20 ml) is injected into a forearm isolated from the general circulation by an arterial tourniquet. This dose rapidly produces >90 % twitch depression of the adductor pollicis muscle, following which the cuff is released (3 min after injection). When twitch height has recovered to approximately 50 %, a 50-Hz tetanic stimulation for 5 s produces no perceptible fade. At a similar point of recovery following an ED₉₀ systemic dose, however, there is marked fade in response to tetanic stimulation (fig. 1).

The authors of the recent article suggest that the difference in fade between onset and offset was caused by slow drug transfer both to and from the prejunctional receptor region. Whilst this explains the observations after systemic drug administration, it does not explain the difference seen in the isolated forearm. If fade during offset was caused by slow local movement of vecuronium away from the prejunctional region, then it should be present to the same degree in the previously isolated forearm which reaches a given twitch height earlier than after a systemic ED₉₀ dose.

It is possible that less prejunctional block could occur during onset of vecuronium block in the isolated forearm for the reason postulated by Bowman regarding i.a. injection—that is, that there is less time for binding to "fade sites" before the tourniquet is released, and drug is washed out into the general circulation. However, recovery in the previously isolated forearm, although more rapid than after a systemic dose, takes 15-30 min. This implies that there is a significant biophase concentration in the neuromuscular junction during the recovery period, which produces single twitch depression. Given this time span, this would be expected to allow time for access of drug to the prejunctional region.

Whilst drug biophase concentration is modelled to mirror closely the slowly declining plasma concentration during the beta phase of recovery after a systemic bolus, a considerable concentration gradient exists between plasma and the biophase of a recovering previously isolated forearm, and between plasma and biophase during recovery from i.a. injection. We believe that the reduction of tetanic fade seen during offset of neuromuscular block in the isolated forearm and after i.a. injection is linked to that concentration gradient. If there is a difference in pharmacodynamic characteristics between pre- and postjunctional receptors, redistribution of drug between binding sites within the neuromuscular junction may have an important influence on receptor occupancy in these situations, leading to differences in relative degrees of pre- and postjunctional effects.

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Fig. 1. Maximal twitches of the adductor pollicis muscles evoked by stimulation of the ulnar nerve at 0.1 Hz. During recovery a tetanus (50 Hz for 5 s) was interposed. The upper record shows the response to vecuronium 0.3 mg injected into an isolated arm. After release of the tourniquet, at 50 % recovery from 95 % block there is little tetanic fade and relatively little post-tetanic facilitation. The lower record shows 90 % block produced by cumulative i.v. vecuronium (total dose 1.5 mg). At 50 % recovery there is marked tetanic fade and greater post-tetanic facilitation.