Sir,—We are grateful for the remarks of Professor Mapleson. There is no dispute between Professor Mapleson and ourselves, only a difference in approach. We both accept that the body is composed of many compartments.

If Professor Mapleson wants to have equations applicable over a wide range of circumstances, the use of a theoretical multi-compartment model is necessary. The circumstances should be specified quantitatively and qualitatively, otherwise they cannot be introduced into the model. However, in an individual practical instance, there is usually no information about the circumstances, or about the size and the exact number of body compartments. If we take into account the standard error of measurement we find only two compartments although it is likely that there are more.

Thus, the theory starts from a hypothetical, multi-compartment system, but in practice we find an unknown, two-compartment system. The theory is probably correct in practice, what can we do with the knowledge obtained from multi-compartment systems?

It was our purpose to draw attention to these questions.

H. H. Beneken Kolmer
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THE UPTAKE OF HALOTHANE

Sir.—Dr Beneken Kolmer and colleagues (1975) simplify multi-compartment analysis for halothane to a two-compartment system. Unfortunately, this is erroneous. The uptake of nitrous oxide was found by Severinghaus (1954) to obey the equation: uptake = 1000e^{-0.8} ml/min, which is not an exponential, but a power function. Lowe (1972) ascertained that the same power function applied to all inhalation anaesthetics, including halothane.

I used Dr Lowe's data (1972) to calculate time constants, and this cannot be simplified as a single exponential uptake with a knee characteristic of the two-compartment system postulated by Beneken Kolmer. Thus, in a 100-kg patient, the blood-flow of brain can be assumed to be 1 litre/min, the brain–blood partition coefficient (\(\lambda\)) is 2.3 (Lowe, 1972) and brain volume is 2.1 litre. The time constant of this system can be calculated as:

\[ \lambda \times \frac{V}{Q} = 2.3 \times 2.1 = 4.83 \text{ min} \]

For liver, blood-flow is 2.0 litre/min, the partition coefficient of halothane was found to be 1.9, the volume may be assumed to be 5.7 litre, and the time-constant is therefore 5.25 min. Similarly, the kidney has a blood-flow of 1.8 litre/min, takes up 1.3 times as much halothane as blood (\(\lambda = 1.3\)), has a volume of 0.6 litre, and a time-constant \(\lambda \times \frac{V}{Q} = 0.43\) min. Poorly perfused tissue, such as muscle, may be assumed to have a blood-flow of 0.7 litre/min, \(\lambda = 2.0\) (Lowe, 1972) volume is 27.0 litre and the time constant is therefore 76.5 min.

Finally, fat, with a blood-flow of 0.4 litre/min, was found by Lowe (1972) to have a tissue–blood partition coefficient of 75. With an assumed volume of 15 litre the time constant is therefore 2812 min.

It is not surprising that the whole-body uptake for halothane is a sum of many exponentials—too many for the most astute mathematician to calculate mentally. As Turbellier and colleagues (1974) confirmed, if Beneken Kolmer would study uptake of halothane from the closed system, he will be rewarded by a most remarkable and absolutely predictable uptake of both nitrous oxide and halothane as a power function of the square-root of time.

JACOBUS W. MOSTERT
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REFERENCES


REACTION TO ALTHESIN

Sir.—I am grateful to Dr Sutton for his comments (Sutton, 1976) on my report (Steel, 1976).

As a result of shortage of editorial space the original and detailed report as submitted initially was redrafted in a very condensed form. Regrettably, the full description of the siting of the two indwelling cannulae was amongst the victims of this axe of abbreviation. In accord with anaesthetists who insist that there are two i.v. cannulae in situ during thoracic surgery, I believe the same practice is equally desirable in all cases of major surgery performed under extradural nerve block.

In my practice, the i.v. infusion is set up via a cannula of large diameter in one arm, whilst a small-diameter Venflon or Butterfly is inserted in the other arm. Except in an emergency, additional i.v. drugs are injected through the latter, since a multiplicity of foreign fluids injected into a drip is one of the factors responsible for subsequent problems with infusions. The patient referred to had a dextrose and saline infusion in her left fore-arm and Althesin was injected via a Venflon in the dorsum of the right hand. When cardiac arrest occurred, sodium bicarbonate was injected through the cannula in the left arm with the dextrose/saline infusing at maximum speed to flush the drug into the circulation. No drug other than the initial injection of Althesin was injected at any time through the Venflon on the right side; nor was there any perivenuous injection or extravasation on either side. The local reaction which occurred was similar to that in the third case described by Avery and Evans (1973), although in that instance alcuronium was given at the same site as the Althesin.

 Whilst I agree that the optimum dose of an i.v. anaesthetic agent should be the minimum effective amount, practising anaesthetists know well that in both the chronic alcoholic and the highly nervous person the minimum effective dose is frequently well above normal. Dr Sutton has missed my stating that the patient was in the second category and that the reduction in arterial pressure following the extradural

CORRESPONDENCE
injection was minimal; a phenomenon which I have observed previously in the highly nervous patient.

This patient's notes show that a most experienced colleague of mine found it necessary to give 6 ml of Althesin, diazepam 5 mg, nitrous oxide–oxygen and trichlorethylene together with two further small increments of Althesin for a previous stretching of the bladder. Obviously, I am content to abide by the judgement of a colleague with personal experience of this patient, and feel that while Dr Sutton's remarks on dosage may be applicable in general they are not relevant to this particular and abnormal patient.

I am aware that it is a disappointment when the undesirable side-effects of a new anaesthetic induction agent start to become manifest and I also have had to cry "Peccavi!" under such circumstances (Steel, 1968). No apologia, however, can deny that the occurrence of an anaphylactic-like reaction to Althesin with bronchospasm has been amply documented and that at least one hospital has withdrawn it from routine use (Watt, 1975).

G. C. Steel
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REFERENCES

THE HYDROLYSIS OF SUXAMETHONIUM IN BLOOD

Sir,—We read with interest the paper by Dr Holst-Larsen (1976). Using a similar, but independently conceived technique, we have found results which complement his findings.

Our subjects were fit, adult, non-pregnant patients scheduled for gynaecological procedures. The patients were premedicated with lorazepam 2.5 mg and immediately before the induction of anaesthesia, a tourniquet was placed around the right arm and inflated to a pressure greater than 200 mm Hg. Thiopentone 350–400 mg was given through an indwelling cannula in the left hand and anaesthesia was maintained with nitrous oxide and oxygen (4 litre/2 litre) with very low concentrations of halothane. Approximately 30 s after thiopentone was injected, suxamethonium 1 mg/kg was given via the same indwelling cannula. Unlike Dr Holst-Larsen, we evoked an adductor pollicis twitch in only the tourniquet-occluded (right) arm, stimulating the ulnar nerve at 1.3 Hz via skin electrodes. The evoked twitch was sensed by a transducer (Pye Ether UF 1), which had been strapped securely onto the right hand. In all our patients the magnitude of the transducer output was recorded on a Devices MX2 chart recorder, whereas Dr Holst-Larsen either recorded the twitch on a chart recorder or estimated the magnitude of the response visually.

We have studied the effect of release of the tourniquet at approximately 120 s after the injection of suxamethonium in 13 patients, and after 150 and 180 s in four and two patients respectively. The latter two groups will not be described in detail as the numbers are so small. All the patients had plasma pseudocholinesterase concentrations within the normal range of values for this hospital (0.6–1.4 unit/litre) and no abnormal dibucaine and fluoride numbers, were reported.

In the patients who had the tourniquet released at approximately 120 s after the injection of suxamethonium the overall duration of occlusion was from 160 to 240 s (mean 213 s) and the actual time between injection of suxamethonium and tourniquet release was from 110 to 123 s (mean 118 s). In common with Dr Holst-Larsen, we observed a rapid onset of block, beginning 5–14 s (mean 10 s) after tourniquet release, and reaching 75% of maximal observed twitch depression within 14–30 s (mean 26 s). Maximal twitch depression ranged from 0 to 100% (mean 73%), while duration of effect as judged by the time from cuff release to recovery of 50% of the control twitch height varied from 0 s (in the only patient in whom no block occurred) to 390 s (mean 153 s).

The only values which may be compared directly with those reported by Dr Holst-Larsen are the durations of effect after 2 min of tourniquet occlusion: in both investigations the ranges of duration were similar (0–6.5 min), but in our patients the mean duration was less (153 s compared with 198 s). Despite this difference the fact that we found appreciable neuromuscular block occurring after 2 min of tourniquet occlusion would support his contention that significant quantities of suxamethonium are present in blood at that time. Further evidence of significant amounts of suxamethonium being present for an even longer period in some patients is that twitch depression was observed in some of our patients in whom tourniquet release was delayed for 150 or 180 s.

As we were measuring only the effects of the drug in the occluded arm we have no data concerning the duration of effect in the unoccluded arm and consequently we are unable to predict the quantity of active drug remaining in the circulation at the time of tourniquet release. However, as the plasma pseudocholinesterase concentrations and the dibucaine and fluoride numbers were within normal limits, we have no reason to suppose that the duration of effect in the unoccluded arm would be outside the normal range. Similarly, we do not have any data concerning the effect of tourniquet occlusion alone upon the duration of effect of suxamethonium, but as Dr Holst-Larsen found only small effects with a similar occlusion time, we would not anticipate that this would produce a marked effect.

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REFERENCE