enrich our hospital fare with the produce of the real tins of soup rather than the pop art form, and to treat our patients in accordance with the findings of true research rather than the computer-processed reproductions of the analog model.

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REFERENCES


SIR,—The purpose of my leader was to examine the value of pharmacokinetic analysis in determining how much effect an injection of a drug would have and for how long. Some broad generalizations are now possible for the neuromuscular blocking drugs: renal failure will prolong the action, as may obstructive jaundice. With cirrhosis it may be that larger initial doses are needed, although the duration of action is prolonged, but the studies often show only what we can expect on the average. In addition there is wide individual variation. With neuromuscular blocking drugs the answer to the anaesthetist's question is to use a nerve stimulator: individual variation will be demonstrated.

Dr Feldman has demonstrated that other individual circumstances such as manner of testing, the technique of administration and the alteration of the local environment of muscle will alter the response to neuromuscular blockers. From this evidence he deduces the pharmacokinetic approach to be invalid. It is—in his circumstances, but not for most of us who do not apply such rigid tests.

Perhaps the use of one-, two- or three-compartment modelling is justified if we use Ockham's razor. Cohen, Corbascio and Fleischli (1965) carried out an early study on the distribution and fate of tubocurarine. As a result of analysing several tissues they were able to propose a nine-compartment analog model.

Yet the decay in plasma concentration in their experiments can be described using two exponential processes (Smith, 1976).

Dr Feldman compares pharmacokinetic and pharmacodynamic modelling with Andy Warhol's pictures. These may not be exact representations, but they are illuminating. So may be these sciences.

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ADH CONCENTRATIONS AND PREMEDICATION

SIR,—We have been interested in the endocrine and metabolic stress response initiated by anaesthesia and especially by surgical trauma (Kehlet, 1979). Antidiuretic hormone (ADH) is regarded as one of the stress indicators (Feist et al., 1978). We studied the effect of premedication on ADH concentrations in 37 healthy patients undergoing major gynaecological operations under general anaesthesia. Thirteen patients received tofizopam 100 mg orally on the night before operation, and 100 mg on the morning of operation; 12 patients received nitrazepam 5 mg and 12 patients received placebo. ADH concentrations were measured by direct radioimmunoassay according to Fyhrquist, Wallenius and Holleman (1976), modified with sequential saturation. The subjective assessments of premedication were recorded in the operating room just before the induction of anaesthesia (apprehension and excitement: nil, slight, moderate, marked). In this respect there was no significant difference between the patient groups, nor was any significant change recorded in the ADH concentrations: tofizopam group = 6.2±0.7 pg ml⁻¹ before premedication and 6.4±0.7 pg ml⁻¹ before induction; nitrazepam group = 5.6±1.2 pg ml⁻¹ and 5.8±1.2 pg ml⁻¹; placebo group = 5.1±0.8 pg ml⁻¹ and 6.2±1.4 pg ml⁻¹ (mean ± SEM). However, in each patient group, some ADH concentrations increased (from 4.9±0.6 pg ml⁻¹ to 7.5±1.0 pg ml⁻¹, P<0.01, Student's t test, paired data, n = 18), and in others they decreased (from 6.2±0.8 pg ml⁻¹ to 4.9±0.8 pg ml⁻¹, P<0.001, n = 19). The patients in the former group felt more excitement (χ² = 4.350, P<0.05) than those in the latter group and when the results of excitement and apprehension (equivalent to anxiolytic effect) were combined, the difference was even more significant (χ² = 6.195, P<0.025).

Thus it appears that the endocrine stress response can be initiated before the induction of anaesthesia.

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