CORRESPONDENCE

Sir,—Thank you for the opportunity of replying to the letter from Drs Bradshaw and Maddison. We can assume only that these workers have been unable to confirm our observations because of some fundamental difference in technique. The difference is not immediately apparent from the information provided in their letter, but several possibilities exist. First, our patients, who were not premedicated, were ventilated mechanically throughout the investigation. Second, in each instance supramaximal stimuli were applied to the ulnar nerve at a frequency of 50 Hz for 1 s at 12-s intervals throughout the study to elicit the tetanic responses of the adductor pollicis muscle. Third, the patient’s lungs were ventilated with halothane 2% for at least 5 min before the administration of the first dose of neostigmine 2.5 mg i.v., which antagonized the tetanic transmission block and abolished the tetanic fade. Both the transmission block and the fade reappeared after the second dose of neostigmine was given 2–3 min later during the continued administration of halothane. Since our original observation, we have confirmed that this phenomenon is a consistent finding.

A further possibility is that our recording system may be more sensitive than that used by Drs Bradshaw and Maddison, as exemplified by the fact that we have been able also to demonstrate the weak neuromuscular blocking action of halothane in anaesthetized man (Hughes and Payne, 1977b).

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REFERENCES


PENTOBARBITONE DISTRIBUTION AND ENZYME INDUCTION

Sir,—I would like to make the following observations on the article on pentobarbitone distribution and enzyme induction by Drs Shin, Nakamura and Shigematsu (1977).

The summary states that the animals were treated with 100 μCi given as 30 mg kg⁻¹ of ²¹⁴C-pentobarbitone. In the "Materials and Methods", however, the solution used was stated to be 100 μCi per 30 mg in 5 ml and the animals were given 5 ml kg⁻¹. Since the mean body weight was 107 ± 9 g, the amount of radioactive material injected may have varied significantly from animal to animal. The average whole-blood volume of an adult rat is 58.0 ± 14.0 ml kg⁻¹. Therefore, 5 ml kg⁻¹ could be 10% or more of the circulating blood volume.

There is no mention of the age of the animals and why male rats only were studied. It is known that these animals mature after approximately 6 weeks of age, but, in this case, their weight should have been greater.

The authors assume that the radioactivity measured later, especially in the urine and small intestine, resulted from metabolites; but they did not demonstrate the rate of metabolism or the presence of metabolites in the strain studied.

In their conclusions, the authors overlooked the fact that, together with absorption, distribution, biotransformation and excretion, there are important genetic and also individual factors which may alter drug action (Halevy and Frumin, 1973; Halevy et al., 1974). Some of these factors may influence receptor sensitivity, local or systemic circulation, and also distribution of a drug. Genetic influences on drug metabolism are now well documented. Furthermore, the extrapolation of similar data from one strain to another and from one experimental condition to another may be erroneous.

The last line of the French translation seems incorrect: "dépression métabolique" does not really mean "degradation".

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REFERENCES


MEPTAZINOL AFTER OPEN-HEART SURGERY

Sir,—I read with interest the article by Paymaster (1977) on the use of meptazinol, pentazocine and pethidine in the period following surgery. We have studied the effects of meptazinol in 40 patients following open-heart surgery.

Immediately after anaesthesia, arterial blood was sampled with the patients breathing 40% oxygen spontaneously from a Ventimask. Following this, we administered meptazinol 30 mg i.v. to one group of 20 patients and 60 mg i.v. to another group of 20 patients, when analgesia was required. Arterial blood was taken at 30, 60 and 240 min after administration of the drug.

No significant change in $P_{aO_2}$ was noted in any patient, although $P_{aCO_2}$ was reduced significantly ($P<0.01$) in both groups, probably indicating better ventilation of the lungs once effective analgesia had been provided. No significant decrease in arterial pressure was noted in any patient.

Nausea and sweating were found following the administration of the drug in only three of the 40 patients. Meptazinol appears to be a useful analgesic in patients who have undergone open-heart surgery.

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REFERENCE