laboratory. The existence even now of a number of "liver function tests" and the increasing interest in discriminant function analysis of their results only serve to emphasize the fact that there is no unique test of hepatocellular dysfunction which can be readily applied routinely to large numbers of specimens. We accept the role of hepatocyte preparations as models for the investigation of the toxic effects of drugs; their use may serve as a valid screening procedure before in vitro tests, but will not detect the possibility of idiosyncratic reactions or determine the extent to which such factors as obesity, smoking or drug-taking may affect the condition of a patient's liver after anaesthesia.

Regarding some of the enzymes which Dr Sear puts forward as useful, the late J. H. Wilkinson, Inaugural President of the International Society of Clinical Enzymology, says (Wilkinson, 1976) that there have been few studies of the diagnostic possibilities of the serum activity of alcohol dehydrogenase, although one group of workers reported in 1968 that the test was a useful indicator of acute parenchymal liver damage; and that sorbitol dehydrogenase (of which the richest source is the liver, while some occurs in the prostate and kidney) is of limited use in diagnosis owing to its relative instability in serum, with the result that the finding of a normal activity does not exclude liver disease. These, and the other enzymes mentioned by Dr Sear, are obviously not yet been shown to be of great value in the study of liver dysfunction. Further, in discussing liver cell necrosis and abnormal membrane permeability, we find Rosalki (1976) stating that "aspartate transaminase may be elevated in several non-liver diseases (especially heart disease) whereas non-hepatic alanine transaminase elevation is unusual." Further support for our choice of enzymes could be quoted (Schmidt, 1978).

It would seem to be best to do as we have done; that is, to use those methods of testing which, whatever their shortcomings, are widely accepted as of proven value, and which can be readily applied under the conditions of a prospective study. There is a parallel in the diagnosis of diabetes: "it could be argued that undue diagnostic emphasis has been placed on blood glucose, in that many other aspects of metabolism are also deranged in diabetes, but no useful alternative diagnostic measure has yet emerged" (Keen, Jarrett and Alberti, 1979).

REFERENCES


on ketamine requirement. Following atropine premedication ketamine 5 mg lb⁻¹ was administered i.m. They found that i.v. supplementation was required to prevent limb movement before surgery in 70% of patients less than 1 year of age and showed that i.v. ketamine requirements for surgical anaesthesia were associated with age, weight and surface area, age being most significant:

\[ \text{mg} \cdot \text{h}^{-1} \cdot \text{m}^{-2} = 12.9 - 0.56 \times \text{age (yr)} \]

Other authors have described an increased MAC value for halothane in this age group (Gregory, Eger and Munson, 1969; Nicodemus et al., 1969).

Alternative possibilities for the greater ketamine requirement of younger children include differences in cerebral blood flow and neuronal density, incomplete myelination with impaired transmission, differences in cardiac output and larger extracellular fluid volumes. Regardless of the possibility of abnormal neuronal pathways within the brain, the ketamine requirement of young children should be expected to exceed that of adults.

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REFERENCES


RESPIRATORY DEPRESSION AFTER EXTRADURAL MORPHINE

SIR,—The editorial by Spence (1980) advocates the use of extradural narcotics as a new and efficient method of relieving pain after operation. It also mentions the risk of inadvertent ventilatory depression from excessive doses of narcotics entering the spinal fluid. Magora and colleagues (1979) reported their experiences of extradural morphine in both large (15 mg) and smaller doses (3–5 mg) (Glynn et al., 1979), and extradural pethidine 50–100 mg (Scott and McClure, 1979). It seems pertinent to report respiratory depression after extradural morphine 4 mg in 10 ml normal saline.

Respiratory depression has been reported after the use of intrathecal morphine in both large (15 mg) (Liolios and Andersen, 1979) and smaller doses (3–5 mg) (Glynn et al., 1979), and extradural pethidine 50–100 mg (Scott and McClure, 1979). It seems pertinent to report respiratory depression after extradural morphine 4 mg in 10 ml normal saline.

A healthy 83-yr-old man had no premedication before transurethral resection of the prostate gland; extradural analgesia was achieved with carbocaine injected through an extradural catheter inserted at L2–3. Postoperative analgesia was provided by morphine 4 mg in 10 ml normal saline administered through the catheter before it was removed shortly after the cessation of surgery. Six hours later, the patient was comatose with inadequate ventilation and pinpoint pupils.

He responded to naloxone 0.4 mg i.v., his arterial \( P_{\text{CO}_2} \) changing from 13.0 to 6.9 kPa and \( P_{\text{O}_2} \) from 3.2 to 8.8 kPa.

Three further doses of naloxone were given to maintain adequate ventilation during the following 4 h.

Ventilatory depression after extradural pethidine has been reported as occurring approximately 30 min after extradural administration (Scott and McClure, 1979). In contrast, the time of onset in the patient described was 6 h later, about the same time observed after intrathecal morphine: 6 h and 11 h (Glynn et al., 1979) and 7 h (Liolios and Andersen, 1979).

Prolonged observation of the patient may be required to detect late respiratory complications.

The safe limits of dosage and volume of extradural morphine are still to be defined. It would be interesting to know to what extent the age of the patient may influence these limits.

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OXYGEN TRANSPORT DURING DOPAMINE INFUSION

SIR,—Dr Scott and his colleagues (1979) contribute a potentially valuable paper on the effect of dopamine on whole body oxygen transport. However, their conclusions do not seem to be borne out by their data.

Oxygen and carbon dioxide production. Their increases in \( V_{\text{O}_2} \) and \( V_{\text{CO}_2} \) were only significant after 60 min at the greater dose of dopamine (30 \( \mu \text{g kg}^{-1} \text{min}^{-1} \)) when compared with initial control. The smaller dose of dopamine produced no significant changes.

Oxygen availability and ratio. At no time was oxygen availability significantly changed compared with initial control, and the oxygen availability ratio did not change under any of the test conditions.

Their conclusion that dopamine increased oxygen delivery is not correct. Comparison with the post-dopamine state appears inappropriate as the haemodynamic and metabolic state is very different. Oxygen utilization only changed in one test condition and so any inferences about the relationship between oxygen transport and utilization are not possible.

I question the value of giving percentage changes when the absolute value of two control means are different. If we consider the example of carbon dioxide production, a change from 4.9 to 7.30 represents a change of 49%. If the same absolute change (i.e. 2.4) had occurred from the initial control of 6.0, then this would be a 40% change.

Is the second change any less significant biologically than the first?

Last, the technique of comparing each of the means of