bility of this group. Should the slightest doubt arise about the competency of liver function in such a patient, it might be prudent to chose some other anesthetic than halothane for her.

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To the Editor.—Your Editorial in the January–February 1963 issue of ANESTHESIOLOGY invited comment relating to halothane (Fluothane) and possible hepatotoxicity, and I believe that I should give what information we, the manufacturers, have, and state our views on the subject.

Experimental evidence from animals has unanimously bracketed halothane with ether and cyclopropane as being relatively free from hepatoxicity. Where halothane has been compared with chloroform under similar experimental conditions the difference has been striking.[1-10] Liver function tests have been carried out after operation by a number of investigators [11-19]; and as you stated, they have not shown halothane to be different from ether or cyclopropane, in the effect it has on these tests.

We estimate that upwards of 20 million halothane anesthetics have now been given, and the number of deaths from liver damage reported has been extremely small. We are aware of nine fatal cases. It is probable that jaundice without death has usually not been considered worth reporting, but it is interesting that Barton,[20] who reported two cases and invited other anaesthetists to report their own experiences, only provoked one reply which was a negative one.[21] We, the manufacturers, have had private reports of suspected livertoxicity from United Kingdom and Europe only three times. Two of the private reports concerned one case each, but the third dealt with 11 cases of jaundice over a seven-year period, and in two of the cases there was no obvious possible reason for the jaundice other than the anaesthetic. Pichlmayr and Stich [26] reported and subsequently published an account of 41 cases of jaundice of which 29 had received halothane. This "epidemic" was investigated and concluded to be due to the transfusion of stale blood.

In trying to assess the cause of postoperative liver damage a number of factors have to be considered, and much basic information is still required. A number of drugs, including penicillin [22] have been incriminated. The once-in-prominence "hepato-renal syndrome" (Boyce, 1941—The Role of the Liver in Surgery, Springfield, Ill.) seems to have been largely forgotten, but it is noteworthy that four out of the nine reported fatal halothane cases underwent operations involving the biliary tract. It is interesting that in 1932 Guthrie and Robertson [23] published a paper entitled: "Is ether a cause of liver death following gall-bladder surgery? Review of 434 gall-bladder and duct operations." What is it which precipitates the injury? Calvert and Brody [24] have shown that even with carbon tetrachloride it is impossible to cause liver changes experimentally unless the sympathetic nervous system is intact.[24] Do certain types of surgery and certain conditions of anaesthesia result in reflex vaso-constriction of the hepatic artery? That hepatic artery constriction provoked by the increasing use of catecholamines could be a cause of hepatic necrosis was suggested by Brunson *et al.*[25] These authors incidentally drew attention to the apparent mounting incidence of hepatic necrosis in their group of hospitals. This was prior to the introduction of halothane.

Finally you discussed the chances of infective hepatitis coinciding with the postoperative period. Using similar arguments to yours our statistical department has calculated that more than 200 cases of infective hepatitis could have occurred postoperatively following 20 million anaesthetics. These cases of infective hepatitis would have been expected to have been scattered throughout the postoperative period, as has been the case in the nine reported deaths.

In conclusion, there seems to be no real indication that halothane is toxic to the liver. All the experimental and the clinical circum-

stantial evidence points to the reverse. Nevertheless, the matter will not be settled until multi-center studies have been carried out to determine not only the incidence of hepatic necrosis after halothane administration, but its incidence after any form of anaesthesia. Such studies we understand to be under way in the United States, and are being extended in Britain.

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Since this letter was submitted for publication, several other cases of hepatic necrosis following Fluothane anaesthesia have been reported. These do not appreciably alter the arguments and opinions expressed above, though, of course, they change the figures.

Also, in the last few months we have instituted a personal enquiry to all anaesthetists in Britain. The results are not yet available, but will be published when they are.

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EPIDURAL ANESTHESIA When local anesthetic solutions are injected epidurally the number of analgesic dermatomes can be predicted with an accuracy of 15–30 per cent, less agent being required for a given spread with advancing age. In 53 patients with occlusive vascular disease, extent of segmental analgesia was one and one half to three times as great as would be expected in normal subjects of the same age, and the time interval between injection and the time to achieve the area of greatest spread was longer than in normal subjects. Thus, in an arteriosclerotic subject an ordinary dose may produce widespread analgesia at a time when no further spread of analgesia would be anticipated. (*Bromage, P. R.: Exaggerated Spread of Epidural Analgesia in Arteriosclerotic Patients, Brit. Med. J. 2: 1634 (Dec. 22) 1962.*)