brain–gas partition coefficient of 6.0[5] and a brain specific gravity of 1.07, 27 mg/100 g will be produced by an alveolar partial pressure of 0.0063 atmospheres (0.63 vol per cent) —a figure which is not far from other data for the anesthetic potency of halothane.[6] However, if the site of anesthetic action has hydrophobic solvent properties similar to those of olive oil[5,4] (olive oil–gas partition coefficient 224[5] and specific gravity 0.9), then at a partial pressure of 0.0063 atmospheres the concentration at the site of action should be 1.2 g/100 g—a value greatly different from the "BAC" of 27 mg/100 g. Such considerations suggest that the brain anesthetic concentration might deviate considerably from the concentration at the site of action. Furthermore, the deviations would be different for other anesthetics.

To avoid such difficulties, anesthetizing partial pressures have been measured in the alveolar gas phase.[3] At equilibrium such partial pressures will equal those existing at the site of action, regardless of the concentration differences. In the above example, the halothane partial pressure of 0.0063 atmospheres would apply to all sites in the brain. The experiments reported by Wolfson *et al.* are an interesting demonstration of the sharp cut-off nature of the quantal response. However, for comparisons between agents, the brain anesthetic concentration may be a misleading concept.

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To the Editor:—In considering this technique initially, we did wonder about the possible dilutional effect of brain water on our final concentration. We, too, looked at olive oil–gas partition coefficients and compared these with water–gas partition coefficients. For halothane these are 244 and 0.74, respectively, a ratio of 330:1. A brain lipid-to-water content ratio of 1:6.5 (12 per cent: 78 per cent as quoted by Dr. Halsey) would lead to a dilutional effect or error of approximately 2 per cent. Similar calculations for methoxyflurane would yield a possible error of 3 per cent. On this basis, we considered it reasonable to start our investigation.

Dr. Halsey suggests that our figure of 27 mg/100 g brain represents a concentration of 1.2 g/100 g brain at the site of action and that this site consists of only 12 per cent of brain volume. From this it may be calculated that even in the total absence of halothane in the rest of the brain (patently an oversimplification) the concentration measured should be 144 mg/100 g. This, in turn, would represent an alveolar concentration of 3.4 per cent, which is far removed from any published figures for MAC for halothane in animal or man. However, the use of olive oil partition coefficients in the study of anesthetic agents is based on tradition and availability rather than the suggestion that brain lipids have the same composition as olive oil. Indeed, it has been pointed out that anesthetic potency is more closely related to solubility in naturally occurring lipids (lecithin and cephalin) than to that in olive oil.[1]

Although recent work favors the lipid rather than the clathrate theory of anesthesia, it has certainly not been proven that lipid solubility is the only factor involved, and I think it is perhaps premature to refer to the presence of anesthetic agent in any part of the brain as "incidental" to the state of anesthesia. Indeed, in one of the publications quoted by Dr. Halsey,[2] the last sentence reads ". . . attempts to

define anesthesia as an effect in a single phase alone have been unsuccessful."

As stated by Dr. Halsey, the alveolar partial pressure of 0.63 vol per cent, equivalent to our BAC of 27 mg/100 g, is very close to the 0.71 vol per cent reported by DiFazio *et al.*[2] Preliminary work in this laboratory suggests that the BAC of methoxyflurane will be in the region of 24.5 mg/100 g of brain. Assuming a brain–gas partition coefficient for methoxyflurane of 26.4,[1] this is equivalent to an alveolar concentration of 0.13 vol per cent. There are no reported direct measurements of alveolar concentration of methoxyflurane in rats with which to compare this figure. However, when the commonly accepted human MAC for methoxyflurane of 0.16 is compared with this, a ratio of 1.23 is obtained. A similarly calculated ratio for halothane would be 1.22. Although the similarity of these relationships may be coincidental, I do not feel they can be ignored at this stage.

Finally, and perhaps most important, although it may have been inferred in our paper that we intended to compare potency of agents from estimations of brain anesthetic concentrations, this was not in fact our purpose. As we stated, our intention is to use these initial values as the bases from which to construct indices relating concentrations at anesthesia to those at respiratory and cardiac arrest. These indices will correlate not only brain but also heart concentrations. As these indices are ratios, errors due to measurement of anesthetic agent in "incidental" portions of the brain will cancel themselves out. It is these indices that we intend to use for agent comparison. We reported such indices for halothane at the ASA Annual Meeting in October 1971 and hope to publish further data in the near future.

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Cardiovascular Effects of Methylmethacrylate

To the Editor:—Drs. Cohen and Smith (ANESTHESIOLOGY 35:547–549, 1971) and Newens and Volz (ANESTHESIOLOGY 36:298–300, 1972) have drawn attention to the dangers associated with the use of large quantities of acrylic cement in reconstructive joint surgery. An animal study[1] indicated that the liquid component of the monomer reduced blood pressure and increased cardiac output and heart rate. Our more recent animal work (unpublished) has showed that, of the several components of the liquid monomer, it is the monomeric methylmethacrylate alone which is responsible for the cardiovascular changes. The hazard of acute hypotension and its sequelae, therefore, will continue until a satisfactory cement substance not based on monomeric methylmethacrylate is introduced. Until such time, we would emphasize the need to identify patients especially at risk[1] and to use acrylic cements cautiously in these individuals.

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