"Gassing" a Water Bath

To the Editor:—We would like to point out that in none of several recent publications concerning anesthetic actions on the heart *in vitro* is the effective anesthetic partial pressure actually measured. Some authors measure the concentration in the bath and report the results as mg/100 ml, which is meaningless unless a partition ratio is specified. Others apparently measure the anesthetic content of gas samples but do not indicate the sampling site; this is an important omission because uptake of anesthetic molecules in the apparatus used to deliver the agent can modify the gas composition distal to the source. A particular instance of this kind has recently come to our attention.

The standard muscle chamber is "gassed" by passing gases into the bottom of the bath through a sintered glass filter disk which poses considerable resistance to flow. Not only does this resistance produce a "back pressure" that affects vaporizer performance, but it apparently impedes the flow of individual gas molecules in proportion to the density of each gas. Thus, a mixture of oxygen, carbon dioxide, and halothane may accumulate halothane proximal to the disk; a reduced concentration will be found downstream, that is, in the bath itself. Using one muscle bath we found, using a Fluotec vaporizer, that the halothane concentration proximal to the sintered glass disk was 1.7 per cent, that distal to the disk was 1.2 per cent.

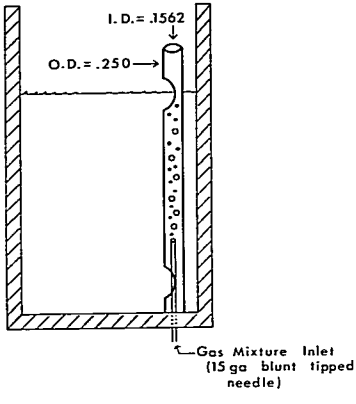

FIG. 1. Plexiglass chamber.

We now use a chamber which eliminates the need for a high resistance gassing device (fig. 1). This device can be simply and inexpensively constructed of plexiglass, and operates at atmospheric pressure, thus obviating the difficulties cited above.

A major purpose of this note is to report that we do not agree with the findings of Brown and Crout (ANESTHESIOLOGY 34:236–245, 1971) with respect to the actions of halothane. They report a 40 per cent depression of isometric contractile force at 0.8 per cent halothane (site of measurement not specified). We find an equal depression at half this concentration, or less, whether measured at the entry of gas into the chamber or at its exit above the bath. Thus, we question all of their findings on methodological grounds.

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To the Editor:—We agree with Vongvises, Webster, and Price that vaporizers of the Fluotec type are inaccurate used within a high-pressure system such as a muscle bath with a sintered glass disc. A conventional rotameter flowmeter is also inaccurate in such a system. However, we do believe that maximal dispersion of the inflowing anesthetics and oxygen into a tissue bath is mandatory, as optimal oxygenation of these muscles in an electrolyte solution is critical. Since the surface area of a given volume of gas bubbling through a liquid is greater the smaller the size of the bubbles, fine dispersion is essential. Figure 1 illustrates the apparatus we used to volatilize inhalation anesthetics. Liquid anesthetic in the Hamilton gastight syringe was

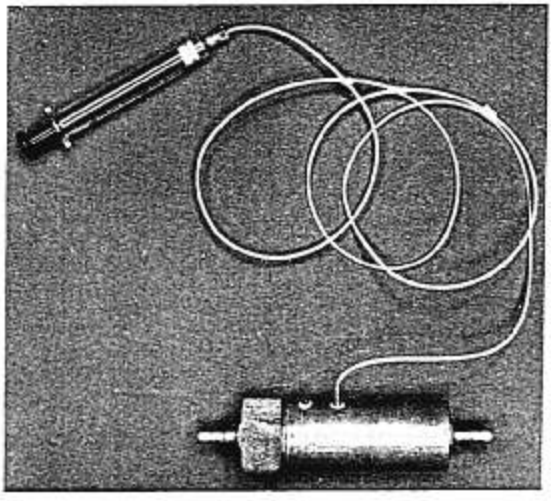

FIG. 1. In-line vaporizer and injection system used in high-pressure muscle bath apparatus.

infused by a variable-speed Harvard infusion pump through the Teflon catheter onto a stainless steel fine-mesh grid within the torpedo-shaped vaporizer. This vaporizer has internal baffles to promote a turbulent flow causing complete volatilization of liquid anesthetics. This vaporizer was kept in a water bath at 37 C. Gas flows were measured with a calibrated Matheson mass-flow flowmeter, an instrument accurate when subjected to back pressures as high as 1,000 psi. Samples for gas chromatographic analyses were taken from a three-way valve approximately six inches downstream from the vaporizer.

The observation of Vongvises *et al.* that the concentration of anesthetic in a gas mixture distal to a sintered glass disc may be different from that proximal to the disc is interesting, and surely should be taken into account in future experiments of this type. We have no data on this issue in our own system, and unfortunately it is now disassembled.

However, certain facts lead us to question the relevance of their observations to our results. First, a concentration gradient of diethyl ether across a sintered disc should be far less than that of halothane if such a gradient were present and were based on Graham's law: one would thus predict that ether would be relatively more depressant on myocardial contractility than an equal concentration (as MAC) of halothane. Our experimental result was exactly the opposite; *i.e.*, halothane was more depressant. Second, in our experiments with cyclopropane, both the inflow line containing the 95 per cent O_2–5 per cent CO_2 and the one containing the cyclopropane were monitored with Matheson flowmeters, and the predicted concentrations from these flows agreed with the analytical results of the gas mixture sampled at the level of the three-way stopcock. Hence, our data do not suggest that the differences among anesthetics described in our paper can be attributed simply to artifacts produced by a high back pressure in the gas inflow line.

Finally, the finding of Vongvises *et al.* that 0.4 per cent halothane causes 40 per cent depression of isometric contractility, whereas we found that 0.8 per cent is necessary to produce a similar degree of depression, is meaningless when considered by itself. A number of variables influence per cent depression of contractility produced *in vitro* by a given con-

centration of anesthetic, including the rate at which the preparation is driven, the temperature, the initial tension applied to the muscle, the adequacy of oxygenation, and the calcium ion concentration in the bath. One cannot interpret an isolated data point without information about these matters and the degrees of depression found at other concentratons of anesthetics.

In summary, we are interested to learn that the concentrations of certain anesthetics can be different on the two sides of a sintered glass disc, and we look forward to full documentation of the claim, and particularly its quantitative importance. We think it unlikely that this problem influenced results with cyclopropane. Our data on diethyl ether suggest to us that little quantitative error occurred in overestimation of potency ratios with the volatile anesthetics, but the possibility of error in these ratios must be acknowledged. There is no reason to believe that even if a concentration gradient existed in our system it would alter the slopes of the dose–response curves we published or the configuration of the individual isometric twitches. Therefore, we do not view the finding of Vongvises *et al.* as a serious challenge to the major conclusion of the paper: that the inhalation anesthetics studied all depress contractility via a common mechanism.

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Hyperthermia during a Second Anesthesia

To the Editor:—Increasingly numerous reports describe the development of malignant hyperthermia in patients who had undergone one or more uneventful anesthesias previously.[1-3] An additional case has been observed by us.

A healthy 30-year-old woman underwent a gynecologic operation under uneventful thiopental–nitrous oxide–oxygen–succinylcholine anesthesia lasting 75 minutes. Nine weeks later, while drunk, she lacerated one wrist severely. After three days of intensive antibiotic therapy (nafcillin, ampicillin, dicloxacillin), she was anesthetized for tendon repair. Anesthesia was induced with thiopental, followed by 50 mg succinylcholine and intubation of the trachea. Anesthesia was maintained with nitrous oxide–oxygen–halothane. A tourniquet was then applied to the arm. Thirty minutes later, blood pressure and heart rate started to increase; halothane was discontinued, but blood pressure rose to 200/90 torr and heart rate to 140 beats/min. The patient felt hot and dry, and the rectal temperature was found to be 105 F.

The operation was abandoned. External cooling brought the temperature to 102 F over a 30-minute period and to 99 F during the next hour. Hyperventilation with oxygen and intravenous fluids were employed as well. The temperature remained below 100 F, and a week later the operation was completed under brachial plexus block.

The question arises as to whether hyperthermia may have been triggered by halothane, excessive alcohol, or one of the antibiotics. Ethanol is capable of enzyme induction,[4] while antibiotics enhance the uncoupling effect of barbiturates on oxidative phosphorylation in liver and brain mitochondria.[5] Elliott[6] stated that anesthesia "must be integrated into the patient's total therapeutic regimen." I may be that a detailed retrospective history of drug and food intake as well as of exposure to pollutants in patients who have developed hyperthermia during anesthesia will provide information to elucidate the triggering factor or factors.

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