CORRESPONDENCE

Pressure Effect on the Vernitrol Vaporizer

To the Editor.—Keet, Valentine and Riccio (page 734) have found that intermittent positive pressure ventilation results in a significant increase in halothane output of the Vernitrol vaporizer. A 1 to 2 per cent increase is obtained at the upper limit of ventilation pressures (30 cm. water) and rates (20 times per minute) ordinarily used in adults. Although there is no doubt as to the importance of this increase, it should not be assumed that it is reflected in an equal rise in inspired or alveolar halothane. The total inflow into the system was 500 ml. per minute. An average 1 to 2 per cent halothane concentration in this inflow results in a halothane input of 5 to 10 ml. per minute. This is considerably less than the average halothane uptake in man at a constant alveolar halothane concentration of 0.8 per cent.* Actual halothane uptake at 0.8 per cent alveolar concentration varies from an initial high of 80 ml. per minute to 12 ml. per minute 3 hours after the start of anesthesia. Increased Vernitrol output due to intermittent positive pressure then would ordinarily not raise the alveolar concentration by more than 0.8 per cent and would probably raise it less than 0.2 to 0.4 per cent. The external check valve reduces the halothane input to 500 times 0.003 or 1.5 ml. per minute of halothane. This is a negligible input relative to uptake and the external check valve may be considered to essentially eliminate the hazard of halothane overdoseage due to extraction of agent from the vaporizer.

The initial surge seen by the authors is of little consequence since a sudden injection of even 4 per cent halothane in 500 ml. will cause only a small increase in the inspired halothane. If the gas volume into which it were injected (anesthetic system plus patients' functional residual capacity) were 10 liters, this would result in a concentration increase of 0.2 per cent or less.

In summary, although intermittent positive pressure results in an increase in halothane output of the Vernitrol vaporizer this increase is of relatively small importance. Of greater importance is the increase input of halothane into the alveoli by the rise in ventilation. The internal check valve suggested by the authors provides absolute protection against the former hazard. The external check valve provides adequate although incomplete protection against this hazard. Neither valve eliminates the latter hazard.

E. I. Eger, II, M.D.
University of California Medical Center
San Francisco

To the Editor: Dr. Eger's comments are well taken and help to place the proper perspective on this problem. The authors did not wish to imply that it is unsafe to give halothane without a check valve. Even with no check valve, the maximal sustained rise in delivered concentration in our study was 0.6 per cent higher than expected from the flowmeter settings. This would roughly correspond to a rise in inspired concentration of 0.25 per cent during closed circuit anesthesia,† and hardly seems dangerous by any standards.

With repeated starting and stopping of IPPB, however, we are not sure how high a sustained rise in output may be possible, and it is conceivable that a dangerous rise could occur.

* Eger, E. I. and Guadagni, N. P.: Halothane uptake by man at a constant alveolar concentration, Anesthesiology, 24: 299, 1963.

† Mushin, W. W., and Galloon, S.: The concentration of anesthetics in closed circuits with special reference to halothane; clinical aspects, Brit. J. Anaesth. 32: 324, 1960.

"Kettle"-type vaporizers, when in good working order and properly used, will deliver extremely precise concentrations of halothane under free flow conditions. With closed systems and IPPB, these vaporizers are subject to a 30 per cent error in delivered concentration unless a check valve is used, and still subject to a 15 per cent error with an external check valve. The described valve is not only a more efficient remedy, but is the least expensive method suggested to date.

JOHN E. KEET, M.D.
GEORGE W. VALENTINE, M.D.
JOSEPH S. RICCIO, M.D.
Department of Anesthesia
Waterbury Hospital
Waterbury, Conn.

Halothane and Hepatic Necrosis

To the Editor.—A plague of reports of death and disease following the use of halothane is predictable.

Past and future reports should be scrutinized objectively and with intense care. Reports of liver disease following the use of halothane are utterly inconclusive, unless all of the following criteria are fulfilled:

(1) The time interval between putative cause and effect is reasonable.
(2) All other iatrogenic causes are, as nearly as possible exonerated, including, surgery itself, other anesthetic agents, and non-anesthetic agents.
(3) Indubitable evidence rules out infectious hepatitis, or, failing this:
(4) Careful epidemiologic study demonstrates incidence in time and number and place significantly higher than in a control halothane-free series.
(5) Pre-existing liver disease is, as nearly as possible, ruled out.

The report from Michigan (Brody, G. L., and Sweet, R. B.: ANESTHESIOLOGY 24: 29, 1963) fails in several ways to meet these criteria. For example, no mention is made of the length of time covered in the survey or of the comparative incidence of such liver necrosis in similar cases done without halothane in the same period of time by the same anesthesiologists in the same places. Indeed, we are not even told where the cases were except for one which is acknowledged to have been done in the authors' hospital. Little or no effort is reported to rule out causes of hepatic disease other than halothane. Two of the patients had biliary disease, and it is hardly an improbable leap from there to the liver.

The guilt of halothane is apparently given credence by implication. The authors' words, "These four cases offer no proof that halothane was the direct cause of the massive hepatic necrosis; however, the implications that such is the case are strong" are almost their only bow to the objectivity of the scientific method —scarcely more than a faint nod, really.

Indictment often has the emotional effect of conviction. The circumstantial evidence adduced to date hardly proves guilt, but it tarnishes the innocence of a useful drug.

JOHN W. FRIEND, M.D.
Central Maine General Hospital
Lewiston, Maine

To the Editor.—It becomes apparent when one reads the two reports concerning halothane toxicity in the March 7 issue of the *New England Journal of Medicine* that those articles had been submitted *concurrently* with ours, not *sequentially*. This seems to us to indicate that others using halothane have also been concerned about its possible toxicity. None of the articles submitted offers more than circumstantial evidence that halothane can, in rare instances, produce hepatic necrosis and none can be construed to be a *study* of the drug. Rather, our intent was simply to call this problem to the attention of anesthesiologists with the hope that a statistically significant scientific evaluation of halothane might be undertaken. Such a study is now being organized to include several teaching institutions.