these two compounds were not originally present in the halothane as contaminants.

The possibility that the putative metabolites might be artifactual in origin is heightened by the fact that they appeared so rapidly, almost instantaneously, in the exhaled air. Metabolites of an inhaled anesthetic would be most rapidly detected in exhaled air if mixed-function oxidase systems in the lungs were responsible for biotransformation of the anesthetic. The rate at which other xenobiotics are known to be taken up by pulmonary microsomes and the rate at which they are known to be subsequently metabolized[2] are such that one would not expect the metabolites of halothane to appear almost immediately in end-tidal air. There should be a lag period. If the metabolites were formed by hepatic mixed-function oxidase systems the delay in their appearance in exhaled air would be even greater.

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In reply:—The present investigation was performed using a non-rebreathing anesthetic circuit. We chose this circuit because halothane vapor when repeatedly passed through soda lime can be converted partly into two substances: CF_2:CBrCl, which was reported originally by Raventos *et al.*[1] and CF_3CH_2Cl, whose concentration course in a closed anesthetic circuit with a dummy lung was reported by Morio *et al.** In the control gas chromatogram (fig. 1) of the gas sample from our nonrebreathing anesthetic circuit with a dummy lung, no obvious volatile material could be detected between the air and halothane peaks. This indicates that no artifact was generated by the breakdown of halothane in the chamber or during the gas chromatographic procedure. Furthermore, the halothane used in this study was demonstrated by gas chromatography to be pure. These two compounds were not originally present in the halothane used.

As to the microsomes in each organ, it is well known that there are large differences in drug-metabolizing abilities. In studying this problem, species difference should be taken into consideration. We have found in a subsequent study (unpublished observations) that CF_2:CHCl and CF_3CH_2Cl appear immediately after administration of halothane to a liver homogenate. A small amount of these metabolites appears when halothane is added to a kidney homogenate, but only a trace amount is found when halothane is added to lung or brain homogenate, and none in the case of whole-blood homogenate. These findings have led us to conclude that there is little delay in their appearance in the exhaled gas.

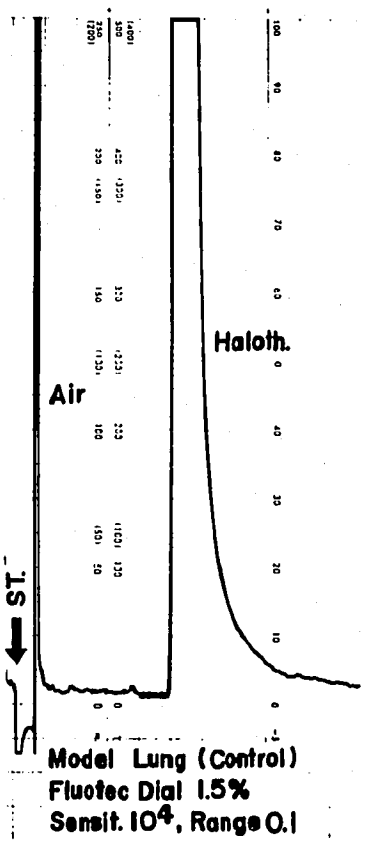

FIG. 1. Control gas chromatogram of the gas sample from the nonrebreathing anesthetic circuit. No obvious volatile material could be detected between the air and halothane peaks.

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