Correspondence

Impurities in Halothane

To the Editor.—I should like to offer the following comments on the recent communication by Albin and his associates, (Anesthesiology 25: 672, 1964).

(1) In Dr. Albin's study the concentration of total impurity was measured in six samples of halothane. In only one instance is a control value available, and here a 50 per cent increase in impurity is noted (fresh IIIc to Residue IIIc). Unfortunately, the other samples are of limited value due to contamination (Residue IIc), or due to a chromatographic technique which permit samples of "Fresh" halothane to yield wide variations of 0.02, 0.05, and 0.06 per cent impurity on three consecutive measurements. Even the manufacturer might object to this "lack of quality control." In addition, I find no data giving measurements of the integrated peak areas, nor any information as to volumes of halothane used in the experiments from which one could evaluate evaporation effects.

(2) Despite the authors' assumption to the contrary, the mass response of all components to the flame detector is not the same (dichlorohexfluorobutene = I; halothane = 0.741). In addition, response to this detector has been shown to be nonlinear with high halothane concentration (J. Gas Chromatography 1: 14, 1963). Unless corrections are made for these factors, measurement error may be introduced.

(3) I object to the suggestion that the chromatograms in figure 2 in any way compare to the separations we obtained. I would find it impossible to make any statements with the tracings that appear in this figure. Furthermore, we have not as yet published any tracings. (Chromatographic separations and other detailed studies are published in this issue of the Journal.)

(4) Finally, this paper serves to confirm once again the presence of dichlorohexfluorobutene as a contaminant in halothane. No additional conclusions are possible from the data supplied.

ELLIS N. COHEN, M.D.
Department of Anesthesia
Stanford University School of Medicine
Palo Alto, California

To the Editor.—The comments offered by Dr. Cohen are mainly concerned with analytical details. Answers to these comments are presented under corresponding paragraph numbers. For gas chromatography with flame ionization detectors, peak areas were estimated by use of a Wheelco electronic integrator (Barber-Colman Co., Rockford, Illinois) and by multiplication of peak height by peak width at half-height. Peak areas measured on representative chromatograms were as follows: Peak A, 114, 44 mm.²; IIIc, 42 mm.²; Ic, 51 mm.²; halothane, IIc, 284 mm.². Peak A runs were with 0.04 microliters, no attenuation, and the halothane run was with 0.06 microliters at attenuation of 100. Thus, the concentration of Peak A (1,1,1,4,4,4-hexafluoro-2,3-dichloro-2-butene) was IIIc, 0.023 per cent, IIIc, 0.022 per cent, and Ic, 0.027 per cent, on the basis of peak areas. If the mass response of these two compounds is the same under our conditions, the concentrations become 0.017 per cent, 0.016 per cent, and 0.020 per cent, respectively. For sample IIIc, the increase in total impurities from 0.02 per cent to 0.03 per cent during the use was due to impurities B (1,1,1,4,4,4-hexafluoro-2-bromo-2-butene) and C (unidentified halogenated compound), not to peak A (1,1,1,4,4,4-hexafluoro-2,3-dichloro-2-butene). Data of this type are the basis of our statement "No evidence was obtained for a significant increase in the level of peak A during normal operating conditions which included refilling of the Copper Kettle vaporizer without drainage."