maintenance of anesthesia during the 90-minute procedure. Thirty minutes passed after discontinuation of halothane before spontaneous ventilation was adequate to allow extubation. Subsequent postoperative recovery was unremarkable.

Ketamine affords excellent cardiovascular stability and maintenance of airway reflexes and adequate spontaneous ventilation, thus permitting rapid changes in body position and positioning of the head unencumbered by anesthetic apparatus. Particularly in pediatric patients, radiologic procedures such as pneumoencephalography, carotid arteriography, and cerebral ventriculography can be performed with favorable conditions for both radiologist and anesthesiologist. Similar benefits might be gained in neurosurgical procedures such as ventriculo-peritoneal or ventriculo-jugular shunts. Many of these patients, however, may have evidence of increased intracranial pressure. Severe, acutely increased ICP in infants may cause apnea. Ketamine has been shown to cause increased CSF pressure, and presumably ICP, in humans by Gardner et al., Dawson et al., in work with animals, and Takeshita et al., studying human subjects, have shown increased cerebral blood flow with ketamine, perhaps accounting for this increased ICP.

It is postulated that in the two cases presented, pre-existing symptomatic increased ICP coupled with the added effect of ketamine on ICP caused respiratory depression and apnea. This would seem to be corroborated by the observation that both patients, when there was no evidence of symptomatic increased ICP, tolerated ketamine anesthesia without difficulty.

In selecting ketamine for certain procedures, clinicians should be alerted to its possible deleterious effect when used in the presence of increased ICP.

REFERENCES


Impurities in 14C-labeled Halothane

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Analyses of commercially available 14C-halothane by combined radio gas chromatography-mass spectrometry occasionally have indicated the presence of significant amounts of impurities. On the other hand, a sample of labeled halothane (1,1,2-bromo-2-chloro-1,1,1-trifluoroethane) recently purchased from a major manufacturer was supplied to us with the radiochromatogram in figure 1, indicating radio-purity of more than 99 per cent. Subsequent metabolic studies with this 14C-halothane sample in vivo revealed compounds which were unlikely metabolites, but which were likely precursors or side-reaction products of halothane synthesis. Radio gas chromatography in our laboratory of the original batch of 14C-

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* Although the explanation for such chromatographic purity is not clear, it is possible that column temperatures and geometry were below maximal operating efficiency levels.
halothane confirmed the presence of these same compounds (fig. 2). The assignment of these peaks by gas chromatography–mass spectrometry is:

Peak A, trans dichlorohexafluorobutene (1.2 per cent)
Peak B, cis dichlorohexafluorobutene (1.3 per cent)
Peak C, trichlorotrifluoroethane (1.8 per cent)
Peak D, monochlorotrifluoroethane (0.3 per cent)
Peak E, monobromotrifluoroethane (5.2 per cent)
Peak F, halothane (90.2 per cent)

The nature of these impurities in halothane must be seriously considered in interpreting its distribution and metabolism. The hexafluorobutenes (A and B) have an LD_{50} of 50 ppm, compared with an LD_{50} of more than 10,000 for halothane. Clayton has noted that the presence of a double bond in the polyfluoro-

alkenes, with resultant increase in chemical activity, is associated with higher levels of toxicity than is shown by the corresponding alkanes. Since in our studies, typically, 4 per cent of the halothane administered was recovered as metabolites during a four-hour period, metabolism of the hexafluorobutenes alone during this interval could introduce a significant error (as high as 62 per cent). In addition, metabolism of these impurities may lead to metabolites different from those of halothane itself, leading to incorrect conclusions as to the metabolic fate of this anesthetic.

In the final analysis, it is the responsibility of the experimenter to verify the purity of all preparations used, and to ascertain whether manufacturing standards of purity coincide with experimental demands.

REFERENCES