

Title: IN VIVO  $^{19}\text{F}$  NMR STUDY OF HALOTHANE AND ISOFLURANE ELIMINATION FROM A RABBIT BRAIN

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**Introduction.** Volatile anesthetics have been assumed to be rapidly eliminated from the body with minimal amounts retained in tissues.(1) A recent study,(2) using a direct noninvasive technique, has shown that after a brief exposure to halothane, a significant amount of this agent resided in a brain of a rabbit for several days. Using the same technique, in vivo  $^{19}\text{F}$  NMR spectroscopy, we compared the elimination of halothane and isoflurane, the two most widely used inhalation anesthetics.

**Methods.** New Zealand White rabbits were premedicated with ketamine (50 mg/kg) and xylazine (5 mg/kg), intubated, and positioned in the bore of the magnet. After a background spectrum was taken, halothane (1%) and isoflurane (1.5%) were delivered using a 'nonrebreathing' system. Fluorine-19 spectra were acquired at 75.5 MHz by using a surface coil,(3) on an Oxford Research System TMR-32 spectrometer equipped with a 20-cm-bore magnet (1.89T). The surface coil (3.5 cm in diameter) was positioned on the frontal bones, midway between the eyes. Each spectrum is an accumulation of 500 transients collected with 0.5 second acquisition time. Chemical shifts are reported relative to an external 2.5%  $\text{C}_2\text{Br}_2\text{F}_4$  in  $\text{CHCl}_3$  standard, contained in a sealed 4 mm sphere. After administration of a volatile agent was terminated, anesthesia was maintained with ketamine/xylazine injections.

**Results.** 1% halothane was administered for a period of 1 hour and its elimination from a rabbit brain was followed for several days. In addition to the free halothane, another  $^{19}\text{F}$  signal was observed. This resonance has been identified as halothane covalently bound to the phospholipid fraction of the brain tissue. Both resonances were clearly visible in the  $^{19}\text{F}$  NMR spectrum accumulated at 5 hrs after administration of halothane was discontinued. The signal corresponding to 'free' halothane continued to diminish in intensity whereas the covalently bound species continued to increase.

1.5% isoflurane was administered for a period of 1 hr 30 min. and its elimination followed for several hours. 45% of the original amount of this agent remained at 4 hrs after its administration had been discontinued. As shown in Figure 1, additional resonances, shifted downfield to the original ones, were observed in the case of isoflurane as well. This observation may indicate either a covalently bound species or a shift in the environment of isoflurane within the brain tissue with time. Isoflurane elimination was followed for 8 hrs at which time the  $^{19}\text{F}$  signals were still observed.

**Discussion.** We show by a direct in vivo observation that the initial elimination of both halothane and isoflurane follows a similar pattern. 40-45% of the originally administered amount is eliminated within the first 4 to 5 hours. In addition to 'free' anesthetics, other resonances are observed which in the case of halothane have been identified as covalently bound species to membrane phospholipids.

#### References.

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