

Halothane Biotransformation in Man: A Quantitative Study

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The metabolic breakdown of halothane was quantitatively determined in two patients. Trifluoroacetic acid and bromide were found as metabolites in the urine. Both metabolites have a protracted excretion rate. Since the biological half-life of trifluoroacetic acid is unknown, one can calculate only the least amount of halothane that had been metabolized on the basis of the excreted trifluoroacetic acid: 12 per cent in both patients. On the basis of the excreted urinary bromide, 20 per cent and 17 per cent, respectively, of the halothane taken up by the body was calculated to be metabolized, if one assumes a biological half-life of 12 days for bromide.

HALOTHANE has traditionally been considered an inert anesthetic. However, recent data show that halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) is metabolized in man and animals.¹⁻³ Products of the biotransformation appear in the urine: they are bromide, chloride, and trifluoroacetic acid. Quantitative determinations have been made in animals⁴⁻⁵; however, no such data are available for man. It was the purpose of this study to determine quantitatively the magnitude of metabolism of halothane in man.

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Methods and Material

Anesthesia was induced with thiopental (355 and 500 mg.) in 2 unpremedicated patients weighing 66.5 and 80.0 kg. Intubation of the trachea with a cuffed endotracheal tube was facilitated by suxamethonium (80 and 140 mg.); muscular paralysis was achieved with *d*-tubocurarine (30 and 39 mg.). The lungs were ventilated with a premixed gas consisting of 34.55 per cent oxygen in nitrogen with a modified Bird ventilator (Mark IV). Fifteen minutes after intubation, halothane^o was added to the inspired gas mixture at a constant concentration. The halothane concentration of the inspired gas mixture was continuously determined by delivering a sample (sample rate 110 ml./min.) from the inspired gas through a metal tube to a Hartmann-Braun † infrared halothane analyzer (Narkometer), calibrated with known mixtures of halothane in 35 per cent oxygen, before and after the experiment (fig. 1).

The exhaled gas was collected continuously for 15-minute periods alternately in two 120-liter counterbalanced modified gasometers which were connected by large-bore metal tubes to the exhalation port of the Bird valve. Contamination of the exhaled gas by the inspired gas mixture was avoided by appropriate valves in the nonbreathing circuit. Contamination of the inspired gas by the gas used to operate the ventilator did not occur. Gases were collected from the gasometer for analysis after they had been mixed in the gasometer for 5 minutes, which proved to be sufficient for

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