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## *The Role of Desflurane in the Practice of Anesthesia*

THE INTRODUCTION OF HALOTHANE in 1956 had an enormous impact upon clinical anesthesia practice.<sup>1</sup> For the first time we had available an inhalation anesthetic whose attributes included lack of pungency, permitting easy inhalation induction; nonflammability; potency sufficient to permit the use of high concentrations of oxygen; sufficient insolubility in blood to permit rapid induction and emergence; bronchodilation; uterine relaxation; and minimal postoperative nausea and vomiting. Subsequent research combined with experience gained from administration of halothane to millions of patients more clearly defined some important limitations to halothane's use, but did not diminish the importance of its discovery and acceptance by clinical anesthesiologists as a major advance in our specialty.

A somewhat less dramatic but still important advance in the development of inhalation anesthetics occurred in 1971 with the description of the clinical pharmacology of isoflurane.<sup>2-4</sup> Although I suspect that concern about halothane's potential for hepatotoxicity in part motivated a rapid acceptance of isoflurane by the anesthesia community, this new agent also had advantageous pharmacologic properties that, along with a perceived decreased propensity for hepatotoxicity, resulted in its becoming the most frequently used volatile anesthetic in the United States.

We now have the opportunity to assess the importance of what may be the next step in the evolution of inhalation anesthetics. For the past several years, the physical characteristics and pharmacologic properties of desflurane (previously identified as I-653), a volatile anesthetic structurally similar to isoflurane, have been a topic of study.

Its desirable characteristics appear to include a blood-gas partition coefficient of 0.42,<sup>5</sup> which is similar to that of nitrous oxide and far less than that of other available volatile agents, and a near indestructibility to degradation either metabolically<sup>6,7</sup> or by interaction with soda lime.<sup>8</sup> These physical characteristics became the basis of further studies investigating the suitability, and perhaps desirability, of desflurane anesthesia in humans. This issue of the Journal presents the results of a number of clinical and laboratory investigations of desflurane. These studies both confirm and extend previous observations that many pharmacologic properties of desflurane, including its effects on muscle relaxation, ventilation, cerebral, systemic, and coronary circulations, and its ability to precipitate malignant hyperpyrexia, are in fact strikingly similar to those of isoflurane.<sup>9-16</sup> This similarity between isoflurane and desflurane naturally leads us to ask: is desflurane sufficiently better than currently available inhaled anesthetics, especially isoflurane, to warrant widespread incorporation into clinical practice. In considering the answer to this question, we must remember that a nearly fifteen-year clinical experience with isoflurane has confirmed its remarkable safety record and clarified (to an extent possible after only millions of administrations) the indications and contraindications governing its use.

I foresee three stances regarding whether desflurane should be widely and rapidly adopted for clinical use. First, there are those who will advocate that the novel and potentially important differences in the physical characteristics between desflurane and isoflurane warrant adoption of desflurane for use in clinical anesthesia. For example, the difference in blood solubility suggests that induction of and emergence from anesthesia should occur more quickly in patients anesthetized with desflurane than with isoflurane. The report from Yasuda *et al.*<sup>17</sup> appears, on the surface, to confirm this prediction, as demonstrated by the more rapid increase in the alveolar concentration

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toward the inspired concentration in patients receiving desflurane compared to that with isoflurane or halothane and, after discontinuation of the volatile agent, the more rapid decrease in the alveolar concentration for desflurane than for either isoflurane or halothane. However, although the rate of increase of alveolar anesthetic concentration is often equated with rate of induction, we can also increase the speed of induction with isoflurane (or halothane) by increasing the inspired concentration above that ultimately needed to maintain anesthesia (*i.e.*, overpressure), thus diminishing this advantage of desflurane's low blood solubility. On the other hand, no technique other than increasing ventilation can hasten the rate of decrease of alveolar anesthetic concentration (or by extension, brain anesthetic concentration) during emergence. That is, there is no "underpressure" during emergence equivalent to overpressure during induction, and thus, low solubility does impart a potential special advantage to desflurane.

Several studies confirm this advantage, but only in part. Lockhart *et al.*<sup>18</sup> demonstrate more rapid elimination of desflurane than of isoflurane or halothane from brain. Ghouri *et al.*<sup>19</sup> and Smiley *et al.*<sup>20</sup> showed that after discontinuation of the volatile anesthetic, patients receiving desflurane reacted to standard stimuli and opened their eyes in about half the time required by those receiving isoflurane. However, Ghouri *et al.*<sup>19</sup> also found that the important end point of time to discharge from the hospital was not shorter for patients given desflurane than for those receiving isoflurane, a finding that would appear to minimize desflurane's potential advantage. Because patients in the study by Ghouri *et al.*<sup>19</sup> received thiopental and fentanyl for induction of anesthesia, it may be that the equal time to discharge from the hospital was a function of the time for dissipation of effect of the intravenous agents. In other words, had shorter-acting intravenous agents been used for induction of anesthesia, the advantage expected from low blood solubility of desflurane might have been more clearly demonstrated.

An additional difference between desflurane and isoflurane is the tachycardia seen at relatively light levels of isoflurane but not desflurane anesthesia.<sup>21</sup> However, this tachycardia is easily prevented by administration of a relatively small preinduction dose of opioid,<sup>22</sup> thus minimizing the importance of this advantage of desflurane.

A second stance regarding the future of desflurane will be that the added costs associated with its use are sufficient to warrant a cautious "wait and see" approach. This is a critical decision as cost constraints upon every aspect of health care delivery become more stringently imposed. Higher costs are likely, especially when the exclusive patent to manufacture isoflurane expires and because the extreme volatility of desflurane will necessitate new vaporizers. Furthermore, because desflurane is only one fifth

as potent as isoflurane,<sup>23</sup> a large liquid volume must be vaporized to produce an equal level of anesthesia. This increased cost of desflurane anesthesia can be reduced somewhat by utilization of low flows (or even closed circuit techniques).

Currently, it is difficult to assess the impact of the costs described above *versus* the potential benefits. Therefore, I recommend a third position, and that is (in the absence of unusual or undesirable pharmacologic effects being yet described) the withholding of judgment until the potential benefit of low blood solubility is more completely characterized. For example, it may well be that the increased costs associated with desflurane can be more than recovered by the savings resulting from decreased duration of stay in the recovery room. This is of particular importance because of the striking increase in redirection of patients to outpatient surgery sites. An additional potential advantage of rapid emergence and awakening may be reduced patient morbidity in recovery areas. That is, any factors that result in a more rapid elimination of residual anesthetic may lessen the likelihood of complications related to prolonged somnolence, such as intermittent airway obstruction and hypoxemia.<sup>24</sup> In addition, residual muscle paralysis may be more rapidly dissipated by more rapid elimination of volatile anesthetics.<sup>25</sup>

In conclusion, I believe it is too soon either to embrace desflurane enthusiastically or to suggest that its differences are insufficient enough to preclude wide spread use. The special uniqueness of desflurane is its low blood solubility coupled, unlike nitrous oxide, with a potency sufficient to make it capable of being an independent anesthetic. The major advantage of this low solubility should be more rapid emergence from anesthesia than that after isoflurane or the other halogenated anesthetics. Benefits that may accrue from more rapid emergence include: 1) a shortened time until discharge from the postanesthesia recovery unit or from the hospital after one-day inpatient surgical procedures, and 2) lesser morbidity from somnolence, ventilatory depression, or residual muscle paralysis. A multicenter clinical trial comparing desflurane to other anesthetics used for outpatient surgery and assessing morbidity, time to arousal and discharge, and anesthetic-related costs is a desirable next step in assessing whether this new agent indeed offers unique and important benefits to anesthesiologist and their patients.

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