

## Changing from Isoflurane to Desflurane toward the End of Anesthesia Does Not Accelerate Recovery in Humans

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**Background:** In an attempt to combine the advantage of the lower solubilities of new inhaled anesthetics with the lesser cost of older anesthetics, some clinicians substitute the former for the latter toward the end of anesthesia. The authors tried to determine whether substituting desflurane for isoflurane in the last 30 min of a 120-min anesthetic would accelerate recovery.

**Methods:** Five volunteers were anesthetized three times for 2 h using a fresh gas inflow of 2 l/min: 1.25 minimum alveolar concentration (MAC) desflurane, 1.25 MAC isoflurane, and 1.25 MAC isoflurane for 90 min followed by 30 min of desflurane concentrations sufficient to achieve a total of 1.25 MAC equivalent ("crossover"). Recovery from anesthesia was assessed by the time to respond to commands, by orientation, and by tests of cognitive function.

**Results:** Compared with isoflurane, the crossover technique did not accelerate early or late recovery ( $P > 0.05$ ). Recovery from isoflurane or the crossover anesthetic was significantly longer than after desflurane ( $P < 0.05$ ). Times to response to commands for isoflurane, the crossover anesthetic, and desflurane were  $23 \pm 5$  min (mean  $\pm$  SD),  $21 \pm 5$  min, and  $11 \pm 1$  min, respectively, and to orientation the times were  $27 \pm 7$  min,  $25 \pm 5$  min, and  $13 \pm 2$  min, respectively. Cognitive test performance returned to reference values 15–30 min sooner after desflurane than after isoflurane or the crossover anesthetic.

Isoflurane cognitive test performance did not differ from that with the crossover anesthetic at any time.

**Conclusions:** Substituting desflurane for isoflurane during the latter part of anesthesia does not improve recovery, in part because partial rebreathing through a semiclosed circuit limits elimination of isoflurane during the crossover period. Although higher fresh gas flow during the crossover period would speed isoflurane elimination, the amount of desflurane used and, therefore, the cost would increase. (Key words: Volatile anesthetics; pharmacokinetics; cost.)

THE relatively low solubility of newer inhaled anesthetics such as desflurane<sup>1,2</sup> allows rapid elimination after their use is discontinued.<sup>3</sup> This results in an earlier emergence than with older anesthetics with higher solubilities, such as isoflurane.<sup>4-8</sup> However, depending on fresh gas flow rates used, their higher cost may offset this potential advantage of newer anesthetics.<sup>9</sup>

In an attempt to combine the advantages of rapid emergence from desflurane anesthesia with the lesser cost of isoflurane, some clinicians use isoflurane to maintain anesthesia, and they substitute desflurane during the last 30 min of anesthesia. We hypothesized that this technique would not achieve its aims: that it would only slightly accelerate early recovery (emergence) and would not accelerate later recovery from anesthesia. We based our hypothesis on two observations. First, using pharmacokinetic data,<sup>3</sup> we modeled this practice using a computerized program (Gas Man; Med Man Simulations, Chestnut Hill, MA) and found that brain anesthetic concentrations did not decrease to those equaling the minimum alveolar concentration (MAC)-awake<sup>10</sup> faster than if isoflurane had been used throughout the anesthetic. Second, in rats in which a non-rebreathing system was used, we observed an acceleration of early emergence from anesthesia, but only a small advantage over the use of isoflurane alone for late recovery.<sup>11</sup> Although the aim of a more rapid recovery was partially met in that study<sup>11</sup> the aim of economy was not. Use of a non-rebreathing system during the substitution period

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permits maximal elimination of the first anesthetic (isoflurane) but greatly increases the cost of administration of the second anesthetic (desflurane). Economic considerations dictate that inhaled anesthetics be delivered by a closed or semiclosed system, systems that would not permit maximal elimination of isoflurane during the "crossover," and, therefore, would delay emergence.

In the present study, we tested our hypothesis in humans breathing from a semiclosed anesthesia circuit, with a fresh gas inflow of 2 l/min. We substituted desflurane for the last 30 min of a 2-h anesthetic, predicting that this would result in a clinically unimportant improvement in awakening compared with isoflurane alone, and in a slower early and late recovery than if desflurane had been used for the entire anesthetic.

## Methods

After we received approval for our study by the University of California, San Francisco Committee on Human Research and with informed consent, we anesthetized five healthy (classified as American Society of Anesthesiologists physical status I) male volunteers for 2 h on three separate occasions: first with desflurane alone, then in a random order with isoflurane alone or with isoflurane for the first 90 min followed by desflurane for the final 30 min of the anesthetic. At least 7 days elapsed between anesthesia sessions. Entry criteria included normal findings of a medical history and physical examination; normal plasma activity of alanine aminotransferase and aspartate aminotransferase; normal plasma concentrations of bilirubin and creatinine; normal results of urine analysis; negative results of screening tests for hepatitis B and C and the human immunodeficiency virus infection; and negative results of urine tests for illicit drugs.

Electrocardiogram, automated blood pressure cuff, and pulse oximeter monitors were applied, and a peripheral intravenous cannula was inserted. Lactate Ringer's solution was infused at  $2-3 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  (replacement of physiologic fluid loss). After preoxygenation, anesthesia was induced with propofol (2 mg/kg given intravenously) and tracheal intubation was facilitated by administering mivacurium (0.2 mg/kg given intravenously). Ventilation was controlled by a standard anesthetic ventilator (Ohmeda 7000; Madison, WI) with a semiclosed circuit with a fresh gas inflow of 2 l/min of 50% oxygen and 50% air. Respiratory frequency was 10

breaths/min with the tidal volume adjusted to maintain the end-tidal carbon dioxide level at 30 mmHg, measured by infrared spectrometry (A/S3; Datex, Helsinki, Finland). Esophageal temperature was maintained at 37°C by surface application of warm air (Bair Hugger; Augustine Medical, Eden Prairie, MN).

Volunteers received 1.25 MAC desflurane (9.1% end-tidal concentration) for 120 min in one session and in the other two sessions either 1.25 MAC isoflurane alone (1.6% end-tidal concentration) or 1.25 MAC isoflurane for 90 min followed by 30 min of sufficient desflurane to achieve an end-tidal sum of both inhaled anesthetics (the residual isoflurane and the added desflurane) equal to 1.25 MAC equivalent.

Inspired and end-tidal anesthetic concentrations were measured using an infrared gas analyzer (Datex A/S3) calibrated with secondary tank standards that had been calibrated with primary volumetric standards by gas chromatography. We also sampled end-tidal and inspired gas for gas chromatographic analysis (Gow-Mac 580; Bethlehem, PA) of the concentrations of isoflurane and desflurane. During anesthesia, samples were taken at 1, 5, 10, 30, 60, 90, and 120 min. During the crossover procedure, additional samples were collected at 95, 100, 105, 110, and 115 min (5, 10, 15, 20, and 25 min of the crossover period).

After 115 min of anesthesia, the fresh gas inflow was changed to 100% oxygen at 2 l/min, and mechanical support of ventilation was decreased to a minimum level. Anesthetic administration was continued during this period. As soon as spontaneous ventilation was established, we gave 30 mg propofol intravenously, aspirated secretions from the throat, and removed the tracheal tube. When spontaneous ventilation resumed, anesthetic administration was discontinued and a non-rebreathing system was applied *via* a mask. End-tidal anesthetic gases were sampled and analyzed 1, 3, 5, 10, 15, 20, 30, 45, and 60 min after discontinuing anesthetic administration (end of anesthesia).

During elimination of the anesthetic, the volunteers were asked at 1-min intervals to open their eyes and to squeeze the investigator's hand, and the time from discontinuation of the anesthetic to performance of the appropriate response to both commands was noted. Thereafter, the volunteers were asked to identify place and date at 1-min intervals until the correct answer was given for each question. As soon as wakefulness permitted, we obtained results from a series of tests to evaluate recovery of psychomotor function, including the Trieger test (volunteers are asked to connect a series



Table 1. Vital Signs

	0 min			60 min			120 min		
	DES	ISO	XOVER	DES	ISO	XOVER	DES	ISO	XOVER
Heart rate (beats/min)	74 ± 30	93 ± 17	98 ± 18	73 ± 7	71 ± 6	72 ± 11	83 ± 15	76 ± 6	80 ± 9
MAP (mmHg)	80 ± 25	93 ± 23	98 ± 14	67 ± 7	66 ± 10	66 ± 10	72 ± 3	71 ± 10	80 ± 12
PETCO <sub>2</sub> (mmHg)	33 ± 3	33 ± 4	31 ± 2	30 ± 1	30 ± 1	30 ± 1	30 ± 1	31 ± 1	31 ± 1
Temperature (°C)	36.2 ± 0.2	36.1 ± 0.4	35.9 ± 0.4	36.7 ± 0.2	36.5 ± 0.2	36.4 ± 0.2	37.0 ± 0.2	37.0 ± 0.1	37.1 ± 0.1

DES = desflurane; ISO = isoflurane; XOVER = "crossover" technique (see text); MAP = mean arterial pressure; PETCO<sub>2</sub> = partial pressure of CO<sub>2</sub> in end-tidal gas.

Data are mean ± SD, n = 5. Temperature is esophageal. Times are those of anesthesia. There were no differences among anesthetics or within groups at different times of anesthesia for any variable.

of dots), P-deletion test (volunteers are asked to select all letters "p" in a text of random letters during 180 s), and the Digit Symbol Substitution test (volunteers are asked to match numbers and symbols during 90 s) 15, 30, 45, 60, 75, and 90 min after cessation of anesthesia. These tests have been used previously to study recovery from anesthesia.<sup>5,7,12,13</sup> At the same times we asked the volunteers to evaluate their "sense of clear-headedness," "sense of energy," and degree of nausea using a visual analog scale. For reference, all tests also were completed before anesthesia. The number of emetic episodes defined by one or more contiguous vomits of gastric contents was recorded.

Each volunteer remained in the study area for at least 4 h after the anesthetic was discontinued and was then discharged home.

Recovery data among the three anesthetic groups were compared by repeated-measures analysis of variance followed by a Student-Newman-Keuls *post hoc* test. We computed area under the curve of anesthetic concentration *versus* time during anesthetic elimination, and we compared these data using unpaired *t* tests, allowing for unequal variance, with Bonferroni correction. Psychomotor test performance within group during recovery was evaluated using repeated-measures analysis of variance followed by Dunnett's *post hoc* test. Statistical significance was accepted as  $P < 0.05$ .

## Results

The volunteers were aged  $25 \pm 2$  yr (mean ± SD), measured  $179 \pm 9$  cm tall, and weighed  $93 \pm 21$  kg. Vital signs during anesthesia did not differ among anesthetic groups at any time (table 1). During recovery from anesthesia, end-tidal carbon dioxide tension did not differ among groups at any time except for a slightly

higher value 3 min after cessation of desflurane compared with isoflurane. End-tidal anesthetic concentrations (MAC or MAC equivalent) measured by gas chromatography did not differ after 120 min of anesthesia: desflurane, isoflurane, and the crossover agent were  $1.26 \pm 0.02$  MAC,  $1.29 \pm 0.13$  MAC, and  $1.22 \pm 0.09$  MAC equivalent, respectively ( $P > 0.6$ ). Isoflurane concentration after 90 min, before beginning desflurane for the crossover technique was  $1.28 \pm 0.07$  MAC. During the crossover period, the sum of concentrations of isoflurane and desflurane (as determined by gas chromatography) at the six sample points ranged from a low of  $1.22 \pm 0.09$  to a high of  $1.36 \pm 0.11$  MAC equivalent (fig. 1). At the end of the crossover period (120 min of anesthesia), the isoflurane concentration was  $0.35 \pm 0.04$  MAC equivalent.

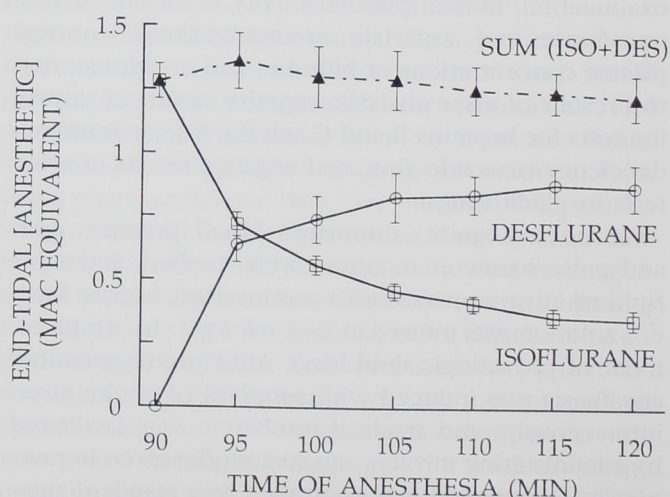


Fig. 1. End-tidal concentrations of isoflurane (□) and desflurane (○), and their sum (▲) during the last 30 min (90–120 min) of the crossover anesthetic technique, with a fresh gas inflow of 2 l/min. Results are mean ± SD.



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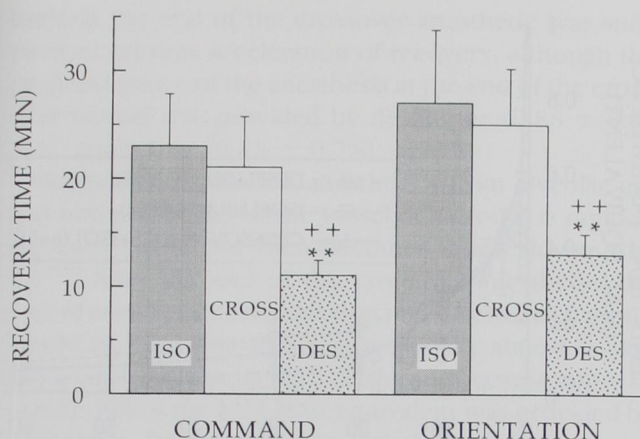


Fig. 2. Substitution of desflurane for isoflurane during the last 30 min of a 120-min anesthetic (CROSS) did not accelerate emergence from anesthesia (response to commands and orientation;  $P > 0.05$ ). Early recovery after desflurane (DES) is more rapid than after isoflurane (ISO) or after using the crossover technique. \*\* $P < 0.01$  DES vs. CROSS; ++ $P < 0.01$  DES vs. ISO. Results are means  $\pm$  SD.

#### Early Recovery (Response to Commands and Orientation)

The combined isoflurane-desflurane (crossover) anesthetic technique did not produce a more rapid emergence from anesthesia compared with the pure isoflurane technique. Emergence after desflurane was significantly faster than after isoflurane alone or after the crossover anesthetic. Time needed to respond to command was  $11 \pm 1$  min after desflurane,  $21 \pm 5$  min after crossover, and  $23 \pm 5$  min after isoflurane ( $P > 0.05$  between crossover and isoflurane;  $P < 0.01$  between desflurane and isoflurane and between desflurane and crossover; fig. 2). Orientation to place and date occurred at  $13 \pm 2$  min after desflurane,  $25 \pm 5$  min after crossover, and  $27 \pm 7$  min after isoflurane ( $P > 0.05$  between crossover and isoflurane,  $P < 0.01$  between desflurane and isoflurane and between desflurane and crossover; fig. 2).

#### Late Recovery (Cognitive Function Tests)

Fifteen minutes after desflurane anesthesia, four of five volunteers could perform all cognitive function tests, whereas after isoflurane or crossover none could do so ( $P < 0.05$  by Fisher's exact test). After 30 min, in each of the two latter groups, one volunteer could not perform the tests. Values of the P-deletion and the Digit Symbol Substitution tests returned to values that were not different from the reference values at 30 and

45 min after desflurane and at 60 and 75 min after isoflurane and the crossover technique. Performance of these tests during recovery from isoflurane anesthesia compared with after the crossover technique did not differ at any time (fig. 3). Volunteers performed significantly better after desflurane than after isoflurane or the crossover for the P-deletion test ( $P < 0.05$  at 15, 30, and 45 min), the Digit Symbol Substitution test ( $P < 0.05$  15 min through 75 min, except for crossover vs. desflurane at 60 min), and the Trieger test ( $P < 0.05$  at 15 min and 30 min after anesthesia; data not shown).

#### End-tidal Gas Concentrations

No differences were found for gas chromatographic versus infrared analysis during the 120 min of isoflurane or desflurane anesthetic. However, during the crossover period, values indicated as desflurane by infrared analysis (but that were actually a combination of desflurane and isoflurane) were 12–23% (mean) higher than those measured by gas chromatography.

During emergence and recovery from anesthesia, end-tidal anesthetic concentrations (the area under the curve of anesthetic elimination; fig. 4) were less for desflurane than for isoflurane ( $P < 0.05$ ) or for crossover ( $P < 0.05$ ), but they did not differ between isoflurane and crossover ( $P > 0.3$ ).

#### Visual Analog Scales

No volunteer could complete the visual analog scale 15 min into recovery from isoflurane or crossover anesthesia. At other times there were no statistical differences for the visual analog scale data for sense of clear-headedness, sense of energy, and nausea among the groups. Episodes of emesis did not occur in the isoflurane group, occurred in one volunteer in the desflurane group (one episode), and in two volunteers in the crossover group (two and four episodes).

#### Discussion

Our findings support the hypothesis that substituting desflurane for isoflurane during the latter part of an anesthetic does not accelerate either early or late recovery (emergence from anesthesia and normalization of cognitive function, respectively). By either measure, recovery occurred significantly later than after an anesthetic with desflurane of equivalent concentration and duration. In agreement with other studies,<sup>4–8</sup> we also



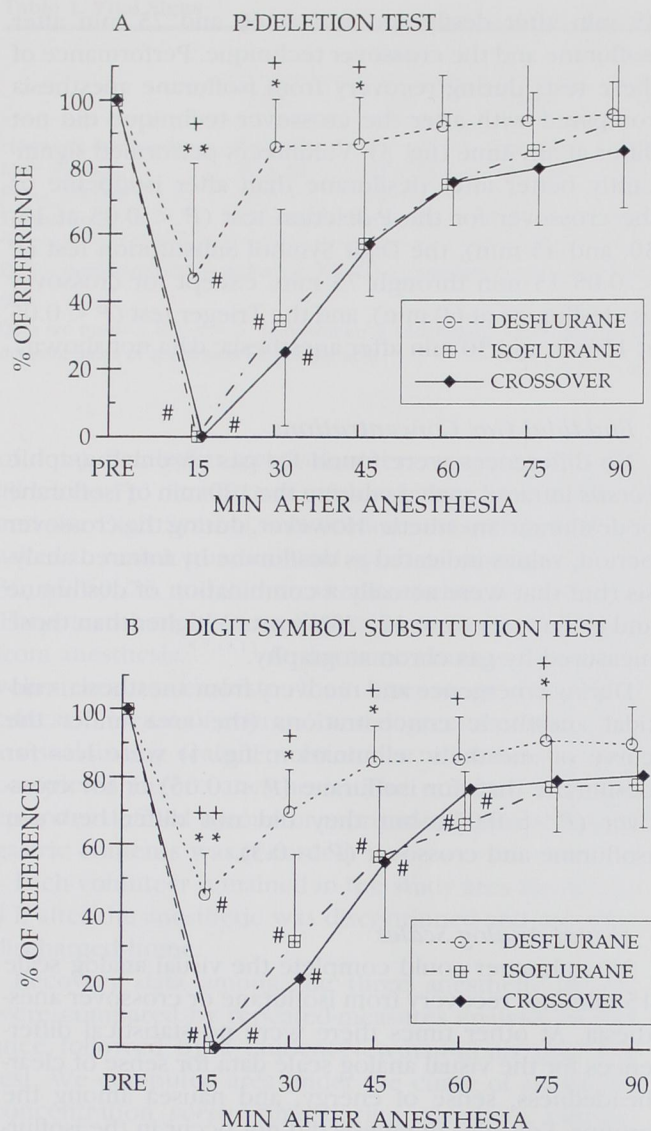


Fig. 3. Substitution of desflurane for isoflurane during the last 30 min of a 120-min anesthetic (crossover) did not accelerate late recovery as measured by P-deletion (A) or Digit Symbol Substitution (B) tests ( $P > 0.05$ ). There was no significant difference at any time for recovery of cognitive function between isoflurane and the crossover anesthetic. The values for desflurane differed significantly from isoflurane and crossover groups, through 75 min for the Digit Symbol Substitution test (DSST) and through 45 min for the P-Deletion test. Later recovery from desflurane was more rapid than after isoflurane or the crossover technique. Return to values not different from the reference value occurred for desflurane after 45 min for the DSST and after 30 min for the P-deletion test; for isoflurane and crossover after 75 min for the DSST and after 60 min for the P-deletion test.  $**P < 0.01$ ;  $*P < 0.05$  (desflurane vs. crossover);  $++P < 0.01$ ;  $+P < 0.05$  (desflurane vs. isoflurane).  $\#P < 0.05$  versus preanesthesia. Data are means  $\pm$  SD. For better visibility, data at each time point are slightly separated, but data were obtained at the same times.

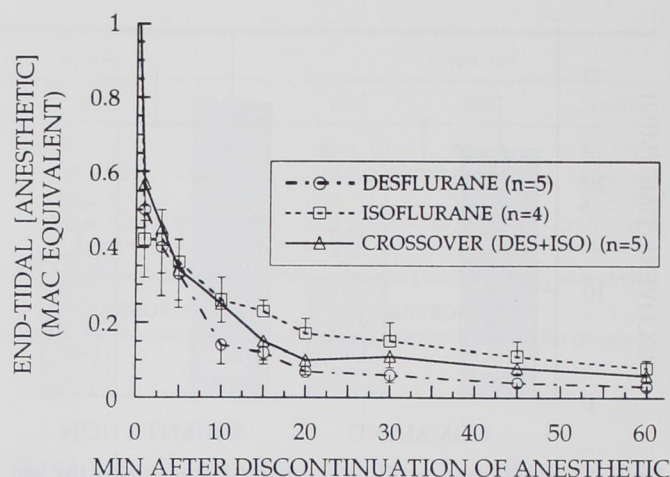


Fig. 4. After termination of anesthesia, area under the curves of end-tidal concentrations during 3–60 min of elimination differed between desflurane and isoflurane ( $P < 0.05$ ) and between desflurane and the crossover anesthetics ( $P < 0.05$ ) but not between isoflurane and the crossover anesthetics ( $P > 0.3$ ). Data are mean  $\pm$  SD.

found that recovery after desflurane is more rapid than after the more soluble isoflurane.

Several factors determine clearance of anesthetic from the brain, and thus the time to awakening from anesthesia: (1) cerebral blood flow; (2) the blood-brain partition coefficient; and (3) the partial pressure of anesthetic in arterial blood. There is no apparent difference in cerebral blood flow during isoflurane compared with desflurane anesthesia.<sup>14</sup>

The blood-brain partition coefficient for isoflurane is 33% greater than that for desflurane,<sup>2</sup> which delays the elimination of isoflurane by a proportional amount. However, this is not enough to explain the 100% longer recovery times for isoflurane and the crossover versus desflurane found in the present study.

The anesthetic partial pressure in arterial blood will be sustained at a higher level with isoflurane because of the greater solubility of isoflurane in blood.<sup>2</sup> This effect adds to the slower elimination from the brain. Together these factors help explain the differences found between desflurane alone and isoflurane alone.

In addition to the above, elimination of anesthetic from alveolar gas is important. During the crossover period, partial rebreathing from the semiclosed circuit impeded elimination of isoflurane. The isoflurane concentration decreased within 30 min from the initial 1.25 MAC (1.6%) to  $0.35 \pm 0.04$  MAC (fig. 1), which is a higher concentration than would result with an open system.<sup>15</sup> The amount of isoflurane remaining in the



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brain at the end of the crossover anesthetic was sufficient to prevent acceleration of recovery, although the preponderance of the anesthesia at the end of the crossover period was provided by desflurane ( $0.88 \pm 0.09$  MAC equivalent [ $6.4\% \pm 0.7\%$ ]; fig. 1).

Elimination of inhaled anesthetics from alveolar gas and brain, as a part of the vessel-rich group, is rapid in the early phase but then becomes much slower (fig. 5).<sup>15,16</sup> After the end of the crossover anesthetic, the sum of anesthetic concentration in the vessel-rich group would be expected to decrease initially almost as rapidly as after anesthesia with desflurane because approximately 70% of the 1.25 MAC equivalent was provided by desflurane. During this time, relatively lesser amounts of isoflurane are eliminated. However, soon thereafter, when the remaining concentration of desflurane has become small, most of the remaining anesthetic is contributed by isoflurane, and further elimination and recovery would be expected to more closely resemble anesthetic elimination and recovery from a pure isoflurane anesthetic. We modeled the three anesthetic techniques using Gas Man (version 3.1), a commercial anesthetic simulation program. The results qualitatively confirmed our predictions (fig. 5).

Differences in recovery were not caused by differences in anesthetic concentration (MAC equivalent) or duration among the three groups. Control of concentration and duration was essential to our conclusions because both parameters are important determinants of the total amount of anesthetic in the body, and thus of speed of elimination and recovery. Nor were differences caused by differences in alveolar ventilation during recovery, as assessed by end-tidal carbon dioxide tension, which did not differ among groups.

Administration of 30 mg propofol ( $<0.35$  mg/kg) approximately 5–10 min before terminating the anesthetic administration could have delayed emergence. However, at the time of emergence, plasma concentrations would have been  $\leq 1\%$  ( $<0.01$   $\mu\text{g/ml}$ ) of the maximal concentration.<sup>17</sup> This is unlikely to have affected the results. Even if this concentration of propofol did contribute to a delay in awakening, it would have affected desflurane most because the administration of propofol was more proximate to the time of emergence from desflurane than to that of the other anesthetics.

Two additional study conditions warrant comment. The observers rating recovery were not blinded. This could have added bias to the results, accentuating or diminishing differences among the three groups. However, there were always at least two observers (and

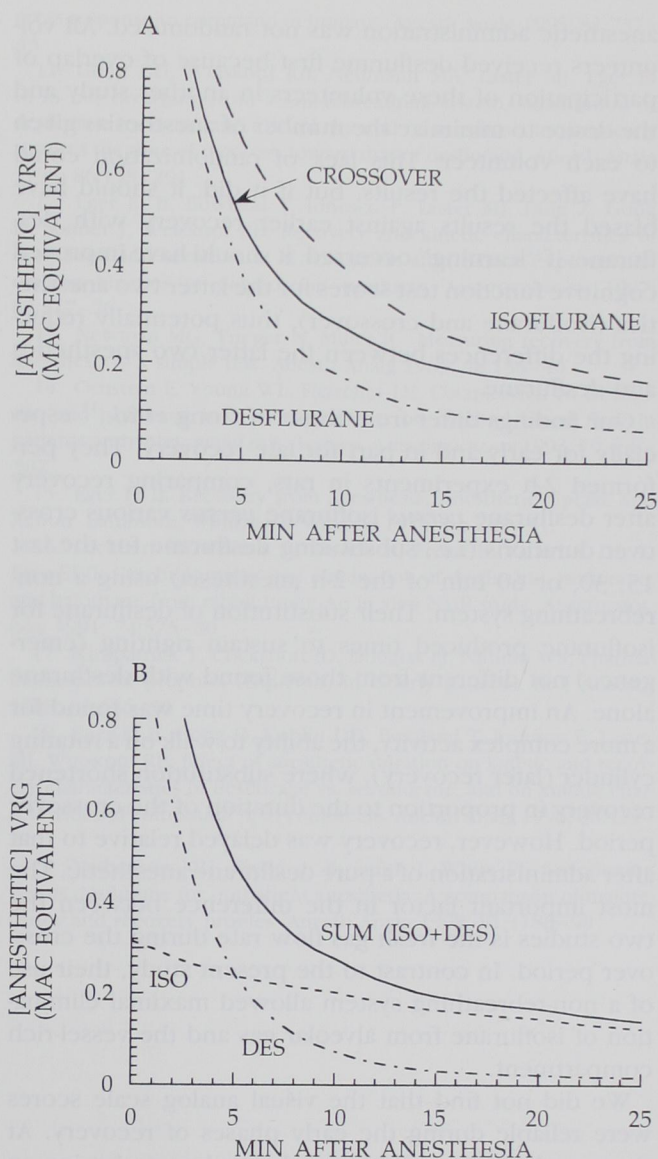


Fig. 5. Estimated anesthetic concentration (by Gas Man) in the vessel-rich group (VRG), after termination of anesthetic administration. In A the vessel-rich group anesthetic concentration of all three treatment groups is shown as a fraction of MAC. The components (desflurane and isoflurane) and the sum of the crossover anesthetic are shown in B. Values used for simulation: weight, 93 kg; alveolar ventilation during anesthesia, 6 l/min; alveolar ventilation during recovery, 3.5 l/min for 10 min, 4.5 l/min for the next 10 min, and then 5.3 l/min; cardiac output during anesthesia, 6.3 l/min; cardiac output during recovery, 8 l/min for 10 min, 7 l/min for the next 10 min, and then 6.3 l/min.

frequently three or four), and the measures are largely objective. Thus we do not believe that the lack of blinding significantly affected the results. The sequence of



anesthetic administration was not randomized. All volunteers received desflurane first because of overlap of participation of these volunteers in another study and the desire to minimize the number of anesthetics given to each volunteer. This lack of randomization could have affected the results, but if it did, it should have biased the results against earlier recovery with desflurane: if "learning" occurred, it should have improved cognitive function test scores for the latter two anesthetics (isoflurane and crossover), thus potentially reducing the differences between the latter two anesthetics and desflurane.

Our findings differ from those of Gong *et al.*,<sup>11</sup> especially for early and in part for late recovery. They performed 2-h experiments in rats, comparing recovery after desflurane *versus* isoflurane *versus* various crossover durations (*i.e.*, substituting desflurane for the last 15, 30, or 60 min of the 2-h anesthesia) using a non-rebreathing system. Their substitution of desflurane for isoflurane produced times to sustain righting (emergence) not different from those found with desflurane alone. An improvement in recovery time was found for a more complex activity, the ability to walk on a rotating cylinder (later recovery), where substitution shortened recovery in proportion to the duration of the crossover period. However, recovery was delayed relative to that after administration of a pure desflurane anesthetic. The most important factor in the difference between the two studies is the fresh gas flow rate during the crossover period. In contrast to the present study, their use of a non-rebreathing system allowed maximal elimination of isoflurane from alveolar gas and the vessel-rich compartment.

We did not find that the visual analog scale scores were reliable during the early phases of recovery. At times, volunteers would rate themselves as having an almost "normal" sense of energy or as "clear-headed" when it was obvious that they were insufficiently awake to respond correctly. Sometimes volunteers required coaching to complete the test appropriately.

We did not study sevoflurane in this crossover design because we wanted to provide the crossover technique with the greatest likelihood of success. Desflurane has lower blood and tissue solubilities than does sevoflurane,<sup>1,2</sup> and consequently recovery from desflurane is more rapid than from sevoflurane.<sup>18,19</sup> Thus switching to sevoflurane during the crossover period would not have produced improved results compared with crossing over to desflurane. Response to command and orientation after 2 h of 1.25 MAC sevoflurane administered

in a similar, previous study in the same volunteers did not differ from that after the crossover anesthetic ( $P > 0.45$  for command and  $P > 0.60$  for orientation).

The crossover anesthetic did not improve recovery from anesthesia compared with isoflurane alone. However, it is a more expensive anesthetic to administer. Using the current US pricing of approximately \$30 per 100 ml isoflurane and \$70 per 240 ml desflurane, and applying our human pharmacokinetic data, in a manner previously described,<sup>9</sup> the cost of 120 min of 1.25 MAC isoflurane at 2 l/min is approximately \$8.87. The cost of a similar use of isoflurane for 90 min followed by 30 min of desflurane at 2 l/min is \$11.75 (\$7.04 for the 90 min of isoflurane plus \$4.71 for the 30 min of desflurane). Recovery from anesthesia would likely have been improved had we used a non-rebreathing fresh gas flow rate during the crossover period (allowing for a more rapid elimination of isoflurane). However, increasing the fresh gas flow rate increases the cost of administering an inhaled anesthetic. The cost of using a nearly non-rebreathing flow rate (6 l/min), producing a total of 1.25 MAC equivalence during the crossover period would increase the cost of the anesthetic administration to approximately \$22.98 (\$7.04 for the isoflurane + \$15.94 for the desflurane). The cost of the use of desflurane alone to produce 1.25 MAC for 120 min is approximately \$29.04 at 2 l/min and \$15.79 at 1 l/min. Thus, if a crossover technique maximally eliminates isoflurane (and probably would still not attain recovery times seen after a pure desflurane anesthetic), it can be more or less expensive than if desflurane alone were used at a moderate or low fresh gas flow rate.

During the crossover period, we maintained anesthetic concentration (MAC equivalent) at a constant level to be able to compare fairly the three techniques. However, we had to use gas chromatography to do so. Few available clinical monitors can measure concentrations of two inhaled anesthetics when both are present in a single mixture. Those that do are unlikely to do so over the range of anesthetic required to satisfactorily maintain constant anesthetic concentration.

In conclusion, we found that switching anesthetics from isoflurane to the less soluble desflurane during the last 30 min of anesthesia does not improve either early or late recovery, when using a moderate fresh gas flow (2 l/min). Recovery after desflurane is more rapid than after isoflurane or a crossover anesthetic. Substitution of desflurane for isoflurane might accelerate recovery if a higher flow rate is used, but this would increase



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cost and recovery would still not be as rapid as after desflurane alone.

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