

# Comparison of Amsorb<sup>®</sup>, Sodalime, and Baralyme<sup>®</sup> Degradation of Volatile Anesthetics and Formation of Carbon Monoxide and Compound A in Swine In Vivo

Evan D. Kharasch, M.D., Ph.D.,\* Karen M. Powers, B.S.,† Alan A. Artru, M.D.‡

**Background:** Consequences of volatile anesthetic degradation by carbon dioxide absorbents that contain strong base include formation of compound A from sevoflurane, formation of carbon monoxide (CO) and CO toxicity from desflurane, enflurane and isoflurane, delayed inhalation induction, and increased anesthetic costs. Amsorb<sup>®</sup> (Armstrong Ltd., Coleraine, Northern Ireland) is a new absorbent that does not contain strong base and does not form CO or compound A *in vitro*. This investigation compared Amsorb<sup>®</sup>, Baralyme<sup>®</sup> (Chemtron Medical Division, Allied Healthcare Products, St. Louis, MO), and sodalime effects on CO (from desflurane and isoflurane) and compound A formation, carboxyhemoglobin (COHb) concentrations, and anesthetic degradation in a clinically relevant porcine *in vivo* model.

**Methods:** Pigs were anesthetized with desflurane, isoflurane, or sevoflurane, using fresh or partially dehydrated Amsorb<sup>®</sup>, Baralyme<sup>®</sup>, and new and old formulations of sodalime. Anesthetic concentrations in the fresh (preabsorber), inspired (post-absorber), and end-tidal gas were measured, as were inspired CO and compound A concentrations and blood oxyhemoglobin and COHb concentrations.

**Results:** For desflurane and isoflurane, the order of inspired CO and COHb formation was dehydrated Baralyme<sup>®</sup> >> sodalime > Amsorb<sup>®</sup>. For desflurane and Baralyme<sup>®</sup>, peak CO was 9,700 ± 5,100 parts per million (ppm), and the increase in COHb was 37 ± 14%. CO and COHb increases were undetectable with Amsorb<sup>®</sup>. Oxyhemoglobin desaturation occurred with desflurane and Baralyme<sup>®</sup> but not Amsorb<sup>®</sup> or sodalime. The gap between inspired and end-tidal desflurane and isoflurane did not differ between the various dehydrated absorbents. Neither fresh nor dehydrated Amsorb<sup>®</sup> caused compound A formation from sevoflurane. In contrast, Baralyme<sup>®</sup> and sodalime caused 20–40 ppm compound A. The gap between inspired and end-tidal sevoflurane did not differ between fresh absorbents, but was Amsorb<sup>®</sup> < sodalime < Baralyme<sup>®</sup> with dehydrated absorbents.

**Conclusion:** Amsorb<sup>®</sup> caused minimal if any CO formation, minimal compound A formation regardless of absorbent hydra-

tion, and the least amount of sevoflurane degradation. An absorbent like Amsorb<sup>®</sup>, which does not contain strong base or cause anesthetic degradation and formation of toxic products, may have benefit with respect to patient safety, inhalation induction, and anesthetic consumption (cost).

ALL currently used volatile anesthetics undergo degradation by carbon dioxide absorbents that contain sodium and/or potassium hydroxides.<sup>1-4</sup> There are three consequences of such degradation. First, sevoflurane degradation results in the formation of the haloalkene compound A. Compound A is nephrotoxic in rats,<sup>5,6</sup> although compound A formation during sevoflurane anesthesia in surgical patients has been extensively evaluated using standard and experimental markers of renal function and has been found not to have clinically significant effects.<sup>7-13</sup> Second, desflurane, enflurane, and isoflurane are degraded to carbon monoxide (CO) by desiccated and partially desiccated absorbents.<sup>14</sup> CO production from volatile anesthetic degradation is a safety issue that has necessitated changes in clinical practice and product labeling.<sup>15-21</sup> The incidence of CO exposure was 0.46% for the first case of the day (2.9% in nonoperating room locations), and the overall incidence was 0.26%.<sup>18,20</sup> CO poisoning is more frequent on Mondays, the first case of the day, and with anesthesia machines unused for long periods of time, owing to a greater risk of fresh gas flow being left on for a protracted period of time and resultant absorbent desiccation.<sup>17,20</sup> Serious CO poisoning resulting from intraoperative desflurane degradation has been reported, with neurologic injury and carboxyhemoglobin (COHb) concentrations approaching lethal levels.<sup>22</sup> Third is the destruction of volatile anesthetic *per se*, thereby diminishing inspired concentrations. Loss of inspired anesthetic may increase cost and/or adversely affect anesthetic induction. Specifically, cases of delayed sevoflurane inhalation induction due to degradation have been reported.<sup>23,24</sup> In summary, although compound A formation seems not to be a clinical concern, CO formation and reduction of inspired anesthetic concentrations are clinically relevant and significant patient safety issues.

Sodium and potassium hydroxides in absorbents such as sodalime and barium hydroxide lime (Baralyme<sup>®</sup>; Chemtron Medical Division, Allied Healthcare Products, St. Louis, MO), acting to abstract a labile proton from anesthetic molecules possessing certain structural features rendering them susceptible to degradation, were identified as the root cause of anesthetic break-

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\* Professor of Anesthesiology and Medicinal Chemistry (Adjunct), Vice-Chair for Research, Department of Anesthesiology, † Research Scientist, ‡ Professor of Anesthesiology, Department of Anesthesiology, University of Washington.

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Address correspondence to Dr. Kharasch: Department of Anesthesiology, Box 356540, University of Washington, 1959 Northeast Pacific Street, Room RR442, Seattle, Washington 98195. Address electronic mail to: kharasch@u.washington.edu. Reprints will not be available from the authors. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

down and degradant formation.<sup>25</sup> Several manufacturers have developed new carbon dioxide absorbents with modified amounts, or omission of, the strong bases that initiate anesthetic degradation. Because proton abstraction and hence anesthetic degradation was greater with potassium *versus* sodium hydroxide,<sup>25</sup> reduction of potassium hydroxide content has been the primary focus. Thus, Drägerorb 800 Plus<sup>®</sup>, Medisorb<sup>®</sup>, and Spherasorb<sup>®</sup> contain little or no potassium hydroxide (but do contain sodium hydroxide), calcium hydroxide lime (Amsorb<sup>®</sup>; Armstrong Ltd., Coleraine, Northern Ireland, supplied by Abbott Laboratories, Abbott Park, IL) contains neither potassium nor sodium hydroxide,<sup>26</sup> and lithium hydroxide, long used in nonmedical devices, has also been evaluated for use in anesthesia machines.<sup>27</sup> Anesthetic degradation to compound A and/or CO by these newer absorbents has been evaluated in laboratory<sup>26,28,29</sup> and clinical<sup>27,30,31</sup> investigations. During sevoflurane anesthesia, inspired compound A concentrations with Drägerorb 800 Plus<sup>®</sup> (Dräger Medical, Telford, PA), Medisorb<sup>®</sup> (Datex Ohmeda, Helsinki, Finland), and Spherasorb<sup>®</sup> (Intersurgical, Wokingham, Berkshire, United Kingdom) were approximately half those with sodalime, whereas Amsorb<sup>®</sup> and lithium hydroxide caused little or no compound A formation.<sup>27,30,31</sup> Although compound A formation is of some interest and clinical studies have focused on sevoflurane, CO formation clearly constitutes a greater potential risk. Nevertheless, only limited data are available on anesthetic degradation to CO by newer absorbents, mostly from *in vitro* studies. This is due, in part, to ethical concerns that prevent the clinical evaluation of CO formation. *In vitro* studies usually do not incorporate carbon dioxide (CO<sub>2</sub>) effects and cannot assess the pathologic consequence of CO production (*i.e.*, formation of COHb).

The purpose of this investigation, therefore, was to compare the effects of Amsorb<sup>®</sup> with those of Baralyme<sup>®</sup> and sodalime on CO formation from desflurane and isoflurane, and COHb concentrations, in a more clinically relevant *in vivo* porcine model. Compound A formation from sevoflurane was also evaluated. Finally, absorbent effects on anesthetic degradation and inspired concentrations were also determined.

## Materials and Methods

This investigation was approved by the Animal Care and Use Committee of the University of Washington (Seattle, WA). Fourteen mixed-breed farm pigs of both sexes (16–25 kg; mean, 21 kg) were used. Animals were premedicated with an intramuscular injection of ketamine (20 mg/kg) plus xylazine (2 mg/kg). Anesthesia was induced with halothane (1.5% inspired) and nitrous oxide (3 l/min) in oxygen (3 l/min) *via* face mask. The trachea was intubated with a 6.0-mm endotracheal tube

and then connected to the standard circle system of a Narkomed (North American Dräger, Telford, PA) anesthesia machine. Release of exhaled water vapor from the lungs into the breathing system was minimized by inserting a Vital Signs filtered hygroscopic condenser humidifier (Totowa, NJ) between the endotracheal tube and the circle system. The lungs were ventilated mechanically using an Ohmeda 7000 Ventilator (BOC Health Care, Madison, WI) to maintain end-tidal CO<sub>2</sub> at 35–40 mmHg (Capnomac Ultima; Datex, Division of Instrumentarium Corp., Helsinki, Finland). Before anesthetic induction, the two anesthesia machine CO<sub>2</sub> absorber canisters were emptied of absorbent and replaced with glass beads (approximately 1.3 cm diameter). Anesthesia for surgical preparation was maintained with halothane, 0.8% expired, in oxygen, 6 l/min. A femoral incision was made and a catheter was placed in a femoral artery for determination of systolic and diastolic blood pressures and heart rate and for blood sampling for determination of blood gas tensions and pH (ABL 5; Radiometer, Copenhagen, Denmark) and hemoglobin, percent carboxyhemoglobin, and percent oxyhemoglobin (O<sub>2</sub>Hb) (482 CO-Oximometer; Instrumentation Laboratory, Lexington, MA). The incision site was injected with bupivacaine (0.5%) and closed. Mean arterial blood pressure was determined by electronic integration of systolic and diastolic blood pressures. Catheters were placed in peripheral veins, one for infusion of propofol and one for infusion at 40–50 ml/h of a 0.9% saline solution containing 0.06 mg/ml pancuronium. Animal temperature was maintained at 37°C using a rectal temperature probe and servo-controlled heat lamps.

At the conclusion of surgical preparation, halothane was discontinued and infusion of propofol (20–30 ml/h) was begun. The infusion rate was adjusted to maintain mean arterial blood pressure at 70–80 mmHg. Ventilation with oxygen and infusion of propofol was continued until the expired halothane concentration was less than 0.04%. Pigs were then assigned to five or six experimental treatments. These consisted of anesthesia with one of three anesthetics (sevoflurane, isoflurane, or desflurane) and one of three absorbents: calcium hydroxide lime (Amsorb<sup>®</sup>), barium hydroxide lime (Baralyme<sup>®</sup>), and sodalime (Sodasorb<sup>®</sup>, provided by WR Grace, Atlanta, GA). Two formulations of Sodasorb<sup>®</sup> were evaluated, a reformulation (which we refer to as “new” sodalime) and its predecessor (“classic” sodalime). The pertinent chemical composition of the absorbents was (% KOH/NaOH/H<sub>2</sub>O): calcium hydroxide lime (0/0/14), barium hydroxide lime (4.6/0/14), new sodalime (0/2.6/16), and classic sodalime (2.6/1.3/15). Absorbents were generally examined in both the fresh (hydrated) and dehydrated state, the latter accomplished by drying in an anesthesia machine (in the lower canister only, with the upper canister filled with glass beads, without a reservoir bag or circle tubing connected to the machine, and with the pop-off valve fully open) using oxygen

(10 l/min) for 24 h as described previously.<sup>§19</sup> This treatment is known to only partially dehydrate (to approximately 2–3% water content), rather than fully desiccate, the absorbent.<sup>19</sup> Partial dehydration was used because fully desiccated absorbents produced lethal CO concentrations from desflurane,<sup>19</sup> and it was desired to avoid lethality.

Each experimental condition lasted 45 min. Assignment to experimental conditions used a balanced randomization sequence designed to allocate at least four animals to each condition, for no animal to have repeated exposure to the same experimental condition, and for conditions reported in previous studies as producing the highest amounts of CO or compound A to occur toward the end of the sequence of experimental conditions (so as to minimize interference with the findings of subsequent experimental conditions within the same animal). During the conduct of the investigation, it was learned that Grace Sodorb had been reformulated (“new” sodalime with diminished KOH), and experiments had unknowingly been performed with this absorbent. A small amount of the older formulation (“classic” sodalime) was then obtained, and some of the experiments were repeated. The experimental design resulted in the following exposures (N): desflurane: dehydrated Amsorb<sup>®</sup> (7), dehydrated “new” sodalime (5), dehydrated “classic” sodalime (4), dehydrated Baralyme<sup>®</sup> (5); isoflurane: dehydrated Amsorb<sup>®</sup> (7), dehydrated “new” sodalime (7), dehydrated “classic” sodalime (4), dehydrated Baralyme<sup>®</sup> (7); sevoflurane: fresh Amsorb<sup>®</sup> (4), fresh “new” sodalime (4), fresh Baralyme<sup>®</sup> (4), dehydrated Amsorb<sup>®</sup> (4), dehydrated “classic” sodalime (4), dehydrated Baralyme<sup>®</sup> (4). Anesthetics were tested at 1 MAC end-tidal concentration (2.1% sevoflurane, 1.6% isoflurane, and 8.2% desflurane).<sup>32,33</sup>

Immediately before beginning each experimental condition, baseline samples of breathing circuit gas and arterial blood were obtained, and mean arterial blood pressure, heart rate, and temperature were determined. Breathing circuit gas was sampled from the fresh gas flow line connecting the anesthesia machine to the circle system (preabsorber sample), from the inspiratory limb of the circle system tubing just distal to the one-way valve (postabsorber sample), and at the Y-connector (end-tidal sample) for determination of anesthetic and CO<sub>2</sub> concentration (Datex) and CO or compound A (drawn into gas-tight syringes and injected into autosampler vials). After obtaining these samples, infusion of propofol was discontinued. The top absorbent canister of the two canisters containing glass beads was removed and replaced with a canister containing the desired CO<sub>2</sub>

absorbent. The oxygen fresh gas flow was reduced to 1 l/min. Inspiration of sevoflurane, isoflurane, or desflurane was begun, with the inspired concentration initially set as high as possible and adjusted thereafter to achieve and maintain the desired end-tidal concentration. Samples of arterial blood and breathing circuit gas were obtained again at 5, 10, 15, 30, and 45 min for determination of hemoglobin, COHb, and O<sub>2</sub>Hb in blood, and compound A and CO concentrations in gas samples. At the same times, mean arterial blood pressure, heart rate, and temperature were determined. In addition, the temperature in the center of the absorbent canister was recorded. Arterial blood gas tensions and pH were determined at 30 min. At the conclusion of each experimental condition, the volatile anesthetic was discontinued, the canister containing CO<sub>2</sub> absorbent was removed and replaced with the canister containing glass beads, the propofol infusion was resumed, and the oxygen fresh gas flow was increased to 6 l/min. Ventilation with oxygen and infusion of propofol was continued until the expired concentration of sevoflurane or isoflurane was less than 0.10% or that of desflurane was less than 0.20% (generally > 25 min). A new set of baseline gas and blood samples was obtained, and the subsequent experimental condition was initiated as described. At the end of the study, the animal remained anesthetized and was killed by intravenous injection of potassium chloride solution.

Compound A was quantified using a modification of a published assay,<sup>34</sup> adapted to gas chromatography-mass spectrometry (GC-MS) with head space sampling. The GC-MS device was an HP 5890 II+ GC with HP 7694 head space sampler interfaced to an HP 5971 mass selective detector, using a DB-VRX capillary column (30 m × 0.32 mm; J&W, Folsom, CA). The GC injector and detector temperatures were 150 and 250°C, respectively, and the column head pressure was 2.5 psi. The head space sampler parameters were as follows: agitation = high; sample equilibration time = 0.5 min; vial pressurization = 0.05 min; loop fill time = 0.5 min; loop equilibration time = 0.15 min; sample injection time = 0.5 min; oven, loop, and transfer line temperatures = 50, 60, and 70°C, respectively. Compound A was eluted isothermally (30°C) and detected by selected ion monitoring (*m/z* 180, M<sup>+</sup>). This ion was chosen because it provides the greatest signal-to-noise ratio. Standard curves of peak area *versus* concentration were constructed by analyzing compound A standards of known amount and were used to quantify compound A concentrations in experimental samples. The limit of quantification was 3 parts per million (ppm). CO concentrations were determined by GCMS as described previously.<sup>35</sup> The limit of quantification was 8 ppm. Neither assay was optimized for sensitivity.

Results are presented as mean ± SD. CO and COHb concentrations and absorbent temperatures were com-

§ Preliminary experiments used absorbents that were dehydrated by heating in an oven, as described previously.<sup>25</sup> However, comparison experiments then showed greater CO formation from absorbent dehydrated by high fresh gas flow in an anesthesia machine compared with oven drying. Therefore, and to more realistically approximate clinical scenarios, all subsequent experiments used absorbents dehydrated by high fresh gas flow.

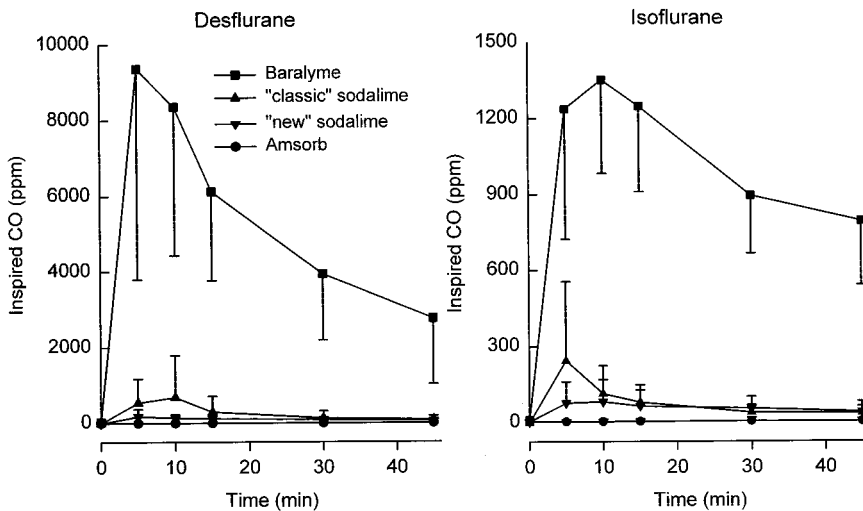


Fig. 1. Inspired carbon monoxide (CO) concentrations resulting from degradation of desflurane and isoflurane by partially dehydrated absorbents. Note the difference in scale for CO concentrations. There were 4–7 animals per group (exact numbers are provided in the Methods). Peak CO concentrations from desflurane were significantly ( $P < 0.05$ ) less for Amsorb<sup>®</sup> versus Baralyme<sup>®</sup>, and for Amsorb<sup>®</sup> versus all absorbents for isoflurane.

pared by analysis of variance. Significance was assigned at  $P < 0.05$ .

## Results

Inspired concentrations of CO formed *via* degradation of desflurane and isoflurane by partially dehydrated absorbents are shown in figure 1. For both anesthetics, the order of CO formation was Baralyme<sup>®</sup>  $\gg$  "classic" sodalime  $>$  "new" sodalime  $>$  Amsorb<sup>®</sup>. CO increases were undetectable with Amsorb<sup>®</sup>. Peak CO concentrations from isoflurane were significantly different for Amsorb<sup>®</sup> versus all other absorbents, and peak CO concentrations for desflurane were significantly different for Amsorb<sup>®</sup> versus Baralyme<sup>®</sup>. For example, peak CO with desflurane was  $9,700 \pm 5,060$ ,  $780 \pm 1,070$ ,  $190 \pm 180$ , and  $0 \pm 0$  ppm with Baralyme<sup>®</sup>, "classic" sodalime, "new" sodalime, and Amsorb<sup>®</sup>, respectively. The area under the CO-versus-time curve for desflurane was  $3,860 \pm 1,720$ ,  $215 \pm 310$ ,  $79 \pm 47$ , and  $3 \pm 6$  ppm, respectively, for Baralyme<sup>®</sup>, "classic" sodalime, "new" sodalime, and Amsorb<sup>®</sup>, and  $779 \pm 163$ ,  $58 \pm 55$ ,  $45 \pm 42$ , and  $3 \pm 8$  ppm

with isoflurane. Areas were significantly less for Amsorb<sup>®</sup> compared with Baralyme<sup>®</sup> for both anesthetics.

Carboxyhemoglobin concentrations resulting from desflurane and isoflurane degradation to CO are shown in figure 2. Zero-time COHb concentrations with Baralyme<sup>®</sup> were slightly higher because this was usually the last experimental period per animal. Peak increases (minus preanesthesia values) in COHb concentrations and their relation to O<sub>2</sub>Hb desaturation are shown in figure 3. Peak COHb increases for desflurane were  $36.8 \pm 13.6$  and  $0.3 \pm 0.4\%$  with Baralyme<sup>®</sup> and Amsorb<sup>®</sup>, respectively, and  $10.8 \pm 2.9$  and  $0.2 \pm 0.2\%$ , respectively, for isoflurane ( $P < 0.05$ ). CO and COHb formation were accompanied by significant decreases in O<sub>2</sub>Hb saturation (fig. 3, inset). For example, with Baralyme<sup>®</sup>, O<sub>2</sub>Hb saturation decreased to  $56 \pm 18$  and  $87 \pm 3\%$  with desflurane and isoflurane, respectively. No desaturation occurred with desflurane and Amsorb<sup>®</sup> or either sodalime formulation. With both desflurane and isoflurane, and all absorbents, the percent increase in COHb concentration was mirrored by a reciprocal decrease in O<sub>2</sub>Hb saturation.

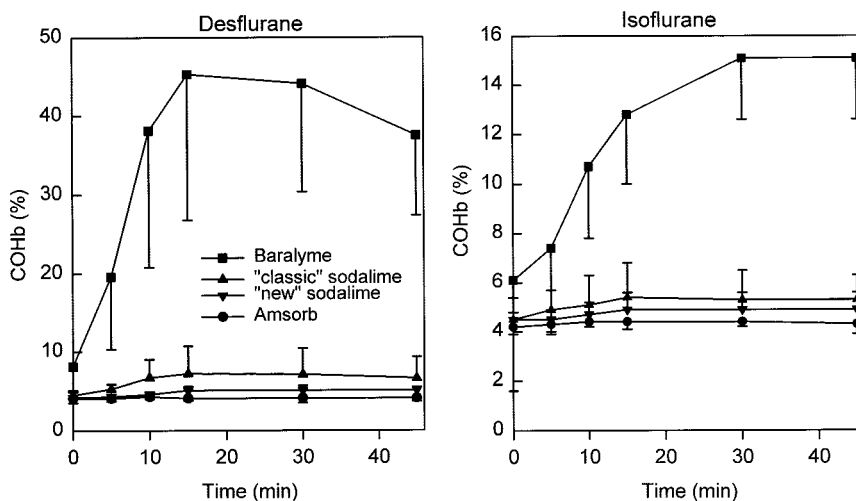
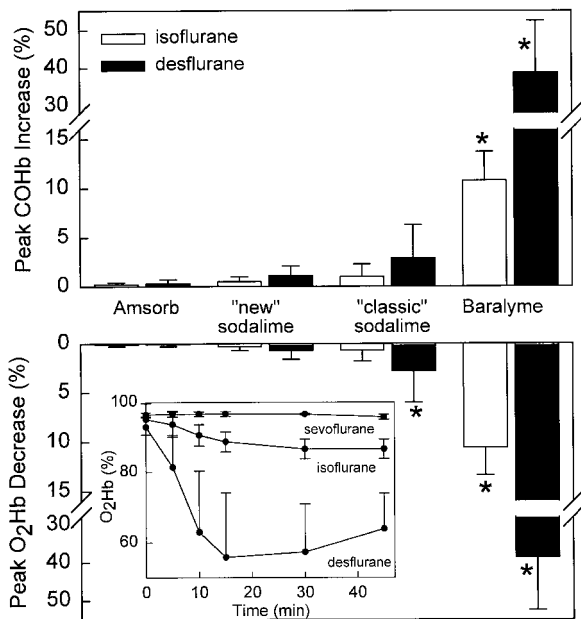


Fig. 2. Carboxyhemoglobin (COHb) concentrations resulting from desflurane and isoflurane degradation to carbon monoxide in the animals shown in figure 1. Note the difference in scale for COHb concentrations.



**Fig. 3.** Carboxyhemoglobin (COHb) formation and oxyhemoglobin (O<sub>2</sub>Hb) desaturation resulting from desflurane and isoflurane degradation by partially dehydrated absorbents. (Top and bottom) Peak increase in COHb and peak decrease in O<sub>2</sub>Hb, respectively. Asterisks denote significant differences *versus* Amsorb<sup>®</sup> ( $P < 0.05$ ). (Bottom, inset) Actual O<sub>2</sub>Hb concentrations when Baralyme<sup>®</sup> was the absorbent. With desflurane and Baralyme<sup>®</sup>, actual O<sub>2</sub>Hb saturation decreased from 97% to 56%. With desflurane and “classic” sodalime, “new” sodalime, and Amsorb<sup>®</sup>, actual O<sub>2</sub>Hb saturation decreased from 97% to 94%, decreased from 97% to 96%, and was unchanged, respectively (not shown).

Temperatures of the partially dehydrated absorbents, measured in the center of the single canister, are shown in figure 4. For both desflurane and isoflurane, temperatures were significantly lower with Amsorb<sup>®</sup> than Baralyme<sup>®</sup> at all times. For both anesthetics, temperatures of “new” sodalime tended to increase more slowly than the other absorbents and were less than Amsorb<sup>®</sup> at 5–15 min, but were equivalent at 30 min.

Degradation of the anesthetic itself was monitored by measuring concentrations in the preabsorber fresh gas, postabsorber, and end-tidal gas. The influence of partially dehydrated absorbent on breathing system concentrations of desflurane and isoflurane is shown in figure 5. As expected, high fresh gas concentrations were initially necessary to quickly achieve and maintain the desired end-tidal concentration, and there was a spread between fresh gas (preabsorber) and postabsorber concentrations for both anesthetics. There were, however, no major differences between the various partially dehydrated absorbents in their effects on the preabsorber *versus* postabsorber or preabsorber *versus* end-tidal spread.

Inspired compound A concentrations formed *via* sevoflurane degradation by various fresh and partially dehydrated absorbents are shown in figure 6. Compound A concentrations with fresh or dry Amsorb<sup>®</sup> were not significantly different from baseline at any time and

reflected only the small amount of compound A present in the parent drug formulation. Compound A concentrations with Amsorb<sup>®</sup> were significantly less than those with fresh Baralyme<sup>®</sup> and “new” sodalime, and with “classic” sodalime at most time points. Temperatures of fresh absorbents were not substantially different from each other. However, with partially dehydrated absorbents, Amsorb<sup>®</sup> temperatures were significantly less than those of “classic” sodalime and Baralyme<sup>®</sup>, the latter reaching nearly 100°C.

Because blood samples were obtained for CO-oximeter analysis throughout all experimental periods, not just those with desflurane and isoflurane, COHb data obtained during sevoflurane administration were analyzed. There was no significant change over each 45-min experimental period with fresh absorbent or with dehydrated “classic” sodalime or Amsorb<sup>®</sup>. However, COHb did increase with dehydrated Baralyme<sup>®</sup>, from  $4.5 \pm 0.8$  to  $6.0 \pm 0.6\%$  at 45 min ( $P < 0.05$ ), and this change was significant compared with all other absorbents and conditions. There was, however, no change in O<sub>2</sub>Hb saturation (fig. 3, inset).

To monitor sevoflurane degradation, concentrations were measured in the fresh gas outflow (preabsorber), postabsorber, and end-tidal, while vaporizer settings were adjusted to achieve and maintain 2.1% end-tidal sevoflurane. The influence of fresh and partially dehydrated absorbent is shown in figure 7. For fresh absorbents, the desired end-tidal concentration was rapidly achieved, with minimal increases in vaporizer settings. However, with partially dehydrated absorbents, maximal vaporizer settings were required, and there was a substantial spread between fresh gas, postabsorber, and end-tidal sevoflurane concentrations. Using Baralyme<sup>®</sup>, even at the maximum vaporizer setting (8%), the desired end-tidal concentration could not be achieved at the early time points (5–15 min). Figure 8 shows the sevoflurane concentration gap between preabsorber fresh gas and postabsorber samples using partially dehydrated absorbents. This gap was smallest for Amsorb<sup>®</sup> and greatest for Baralyme<sup>®</sup>. Assuming a price of \$180/250 ml, the costs of sevoflurane degradation by Amsorb<sup>®</sup>, “classic” sodalime, and Baralyme<sup>®</sup> were \$2.40, 4.60, and 8.70 at the flow rate used (1 l/min). Under more conventional conditions for inhalation induction (two absorbent canisters, 6 l/min), the calculated costs would be \$28.80, 55.20, and 104.40, respectively.

## Discussion

The first purpose of this investigation was to compare the effects of Amsorb<sup>®</sup>, Baralyme<sup>®</sup>, and sodalime on CO formation from desflurane and isoflurane and COHb concentrations in a porcine *in vivo* model because ethical considerations preclude such evaluation of CO forma-

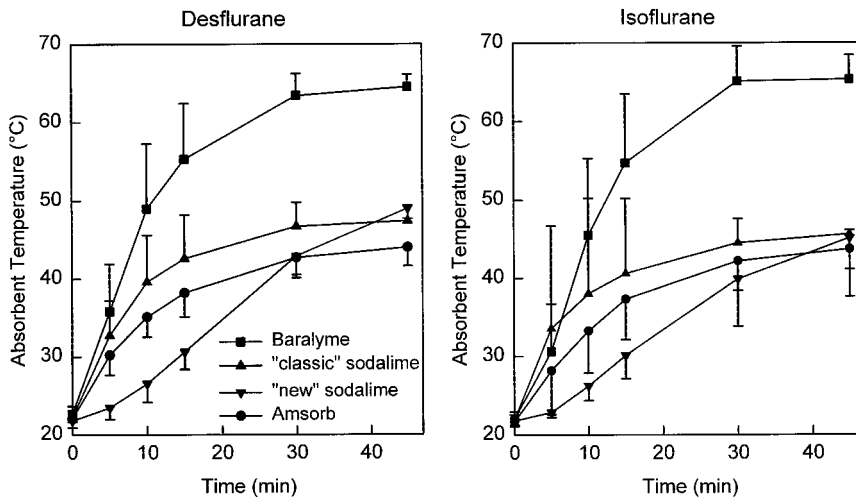


Fig. 4. Temperature in the center of the absorbent canister during anesthesia with desflurane and isoflurane using partially dehydrated absorbents. For both desflurane and isoflurane, Amsorb<sup>®</sup> temperatures were significantly lower than Baralyme<sup>®</sup> at all times and significantly greater than "new" sodalime after 5–15 min.

tion in humans, owing to known CO toxicity from isoflurane and especially desflurane degradation. Only dehydrated absorbents were evaluated because fully hydrated absorbents do not degrade these anesthetics.<sup>14,19</sup> Results for desflurane and isoflurane degradation by Baralyme<sup>®</sup> and sodalime were comparable with previous investigations in swine of comparable size.<sup>19,36</sup> Using a single canister of partially dehydrated Baralyme<sup>®</sup> with 8.2% desflurane and 1.6% isoflurane, we observed 9,400 and 1,300 ppm peak CO and 45% and 15% COHb, respectively. Using a single canister of fully desiccated sodalime with 7% desflurane and 1.5% isoflurane, Bonome *et al.*<sup>36</sup> observed approximately 5,500 and 1,000 ppm peak CO and 58% and 18% COHb, respectively. Using 7.5% desflurane and two canisters of partially dehydrated Baralyme<sup>®</sup> and sodalime ("classic"), Frink *et al.*<sup>19</sup> observed approximately 14,000 and 9,000 ppm peak CO and 73% and 52% COHb, respectively. Thus, dehydrated absorbents containing strong base (KOH, NaOH) consistently degrade desflurane and isoflurane to toxic concentrations of CO, whereas Amsorb<sup>®</sup> caused no detectable CO formation, did not increase COHb concentrations, and did not decrease O<sub>2</sub>Hb saturation. "New" sodalime (no KOH, 2.6% NaOH) caused less CO formation than "classic" sodalime (2.6% KOH, 1.3% NaOH), although the differences were not statistically significant. This confirms *in vitro* observations that Amsorb<sup>®</sup> caused minimal, if any, CO formation.<sup>26,29</sup> These are the first *in vivo* results that demonstrate greater potential safety, *vis-à-vis* CO formation and toxicity, of absorbents lacking strong base.

|| A preliminary investigation was conducted to compare desflurane degradation by various fully desiccated CO<sub>2</sub> absorbents, using the *in vitro* model used previously.<sup>25</sup> Compared with CO formation by Drägerisorb 800 > Baralyme<sup>®</sup> > sodalime > Drägerisorb 800 Plus > Carbolime (Allied Healthcare), Amsorb<sup>®</sup> caused no detectable CO formation (E. D. K., unpublished data, July 1999).

# A preliminary investigation was conducted to compare sevoflurane degradation by various hydrated CO<sub>2</sub> absorbents, using our *in vitro* model.<sup>25</sup> Compared with compound A formation by Drägerisorb 800 > sodalime > Baralyme<sup>®</sup> > Drägerisorb 800 Plus > Carbolime, Amsorb<sup>®</sup> caused no detectable compound A formation (E. D. K., unpublished data, July 1999).

The second purpose of this investigation was to compare Amsorb<sup>®</sup>, Baralyme<sup>®</sup>, and sodalime effects on compound A formation. Both fresh and dehydrated absorbents were evaluated because both can degrade sevoflurane.<sup>24</sup> Compound A formation by fresh "new" sodalime was equivalent to that by Baralyme<sup>®</sup>, despite the fact that this absorbent contains no KOH and less total base (2.6%) than either "classic" sodalime (2.6% KOH, 3.9% total base) and Baralyme<sup>®</sup> (4.6% KOH, 4.6% total base). The ability of fresh newer soda limes to form compound A and negligible compound A formation by Amsorb<sup>®</sup> was similar to our preliminary *in vitro* results<sup>#</sup> and comparable with clinical investigations.<sup>27,30,31</sup> Breathing circuit compound A concentrations with dehydrated absorbents have not been previously reported. In contrast to other absorbents, partially dehydrated Amsorb<sup>®</sup> caused negligible apparent formation of compound A. Interestingly, compound A concentrations were also low with partially dehydrated Baralyme<sup>®</sup>; this may relate to compound A degradation in addition to its formation.<sup>37</sup> Thus, regardless of hydration state, Amsorb<sup>®</sup> produced negligible amounts of compound A.

Assessment of CO formation during sevoflurane degradation was not an objective of these experiments because little or no CO was formed from sevoflurane.<sup>14,25</sup> CO concentrations in gas samples were not measured. Nonetheless, indirect evidence was available from COHb data. Surprisingly, partially dehydrated Baralyme<sup>®</sup> did result in a small increase (1.5%) in COHb concentration. Thus, although sevoflurane is not degraded to CO by hydrated absorbents,<sup>14,25</sup> this may occur with dehydrated absorbents. Consistent with its lack of compound A formation, dehydrated Amsorb<sup>®</sup> did not increase COHb concentrations. A case report of increased COHb concentrations with sevoflurane was recently published.<sup>23</sup>

The third purpose of this investigation was to compare the effects of various absorbents on anesthetic degradation. Although not often evaluated, in contrast to the formation of compound A and CO, loss of inspired an-

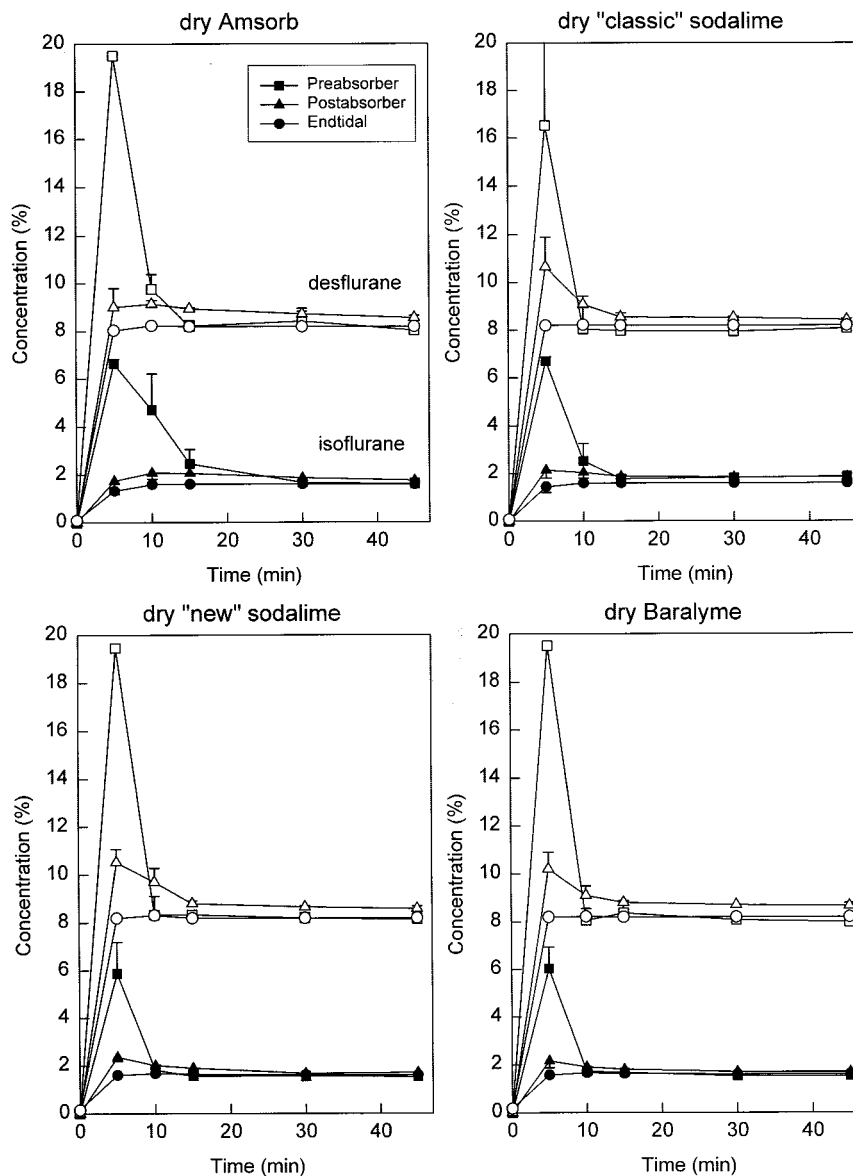


Fig. 5. Anesthesia circuit concentrations of desflurane and isoflurane during anesthesia using partially dehydrated absorbents. Gas samples were obtained from the fresh gas flow line connecting the anesthesia machine to the circle system (preabsorber sample, squares), the inspiratory limb of the circle distal to the one-way valve (postabsorber sample, triangles), and at the Y-connector (end-tidal sample, circles). Open and filled symbols denote desflurane and isoflurane, respectively.

esthetic may be clinically important if it results in delayed inhalation induction<sup>23,24</sup> or economically important if it increases anesthetic consumption. Little difference was observed between dehydrated Amsorb<sup>®</sup>, "new" or "classic" sodalime, or Baralyme<sup>®</sup> in the spread between fresh gas concentrations and postabsorbent or end-tidal concentrations of isoflurane or desflurane. This model is, however, less sensitive than laboratory models, which did show a substantial difference in the degradation of desflurane by desiccated Baralyme<sup>®</sup>, sodalime, and Amsorb<sup>®</sup>.<sup>29</sup> This may relate to the overpressure used herein to rapidly achieve target end-tidal concentrations rather than the constant anesthetic concentrations used in laboratory models. For sevoflurane and fresh absorbents, the inspired end-tidal spread was much less, and there was also little difference between absorbents. However, there was a considerable spread between fresh gas and postabsorbent or end-tidal sevoflurane con-

centrations with dehydrated absorbents, which was smallest with Amsorb<sup>®</sup>. This is similar to laboratory findings of lesser sevoflurane degradation by desiccated Amsorb<sup>®</sup> compared with sodalime and Baralyme<sup>®</sup>.<sup>29</sup> It is interesting to note that there was a significant discrepancy, with dehydrated absorbents, between the inspired *versus* end-tidal gradient for sevoflurane compared with compound A. The gradient was greatest with Baralyme<sup>®</sup> despite the detection of minimal compound A, and a small gradient existed with Amsorb<sup>®</sup> even though there was no compound A formation detected. The highest amount of compound A formation occurred with "classic" sodalime, but the gradient was intermediate for this absorbent. It is unclear whether this represents sevoflurane adsorption rather than degradation, sevoflurane degradation to other than compound A, or further reactions of compound A. Nonetheless, Amsorb<sup>®</sup> did cause the least amount of sevoflurane degradation. Because

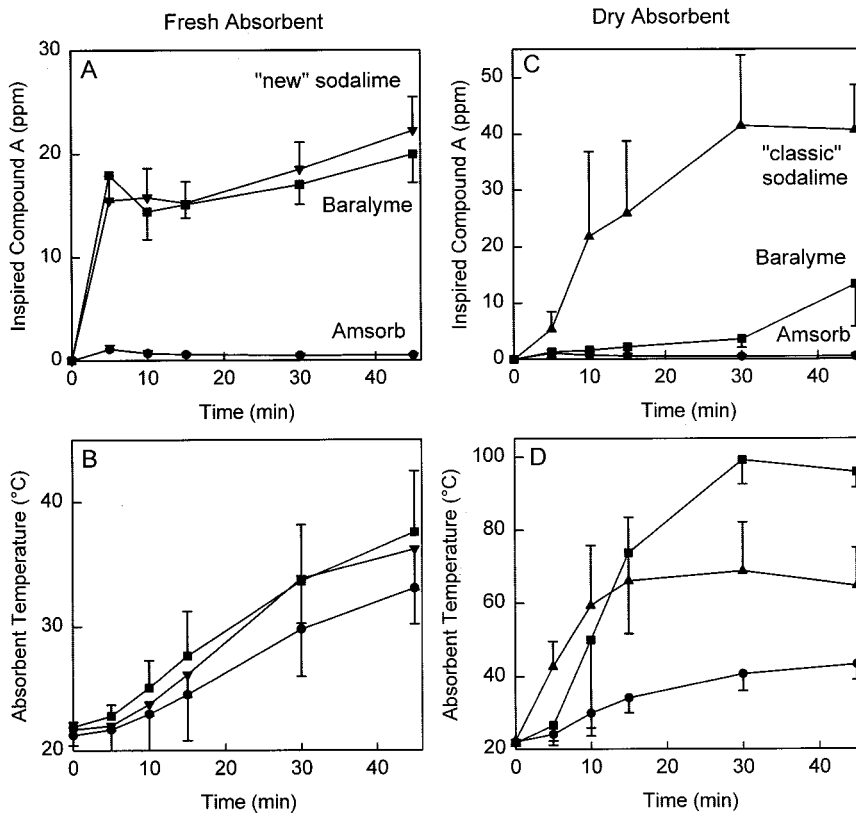


Fig. 6. Inspired compound A concentrations and absorbent temperatures resulting from degradation of sevoflurane by fresh and by partially dehydrated absorbents. Compound A concentrations with fresh or dry Amsorb<sup>®</sup> were not significantly different from baseline at any time. Compound A concentrations with Amsorb<sup>®</sup> were significantly less than those with fresh Baralyme<sup>®</sup> and "new" sodalime, and with partially dehydrated "classic" sodalime at 10–45 min. Temperatures were not different between fresh absorbents. Dehydrated Amsorb<sup>®</sup> temperatures were significantly less than those of dry Baralyme<sup>®</sup> and "classic" sodalime after 5 min.

this is the most commonly used volatile anesthetic for inhalation induction, Amsorb<sup>®</sup> would have the least potential to delay inhalation induction. Similarly, the cost of anesthetic degradation by dehydrated absorbent would be lowest with Amsorb<sup>®</sup>.

Identification of mechanisms of anesthetic degradation was not an objective of this investigation. Nonetheless, a few observations are pertinent. The absence of CO formation from desflurane and isoflurane with Amsorb<sup>®</sup> was not due exclusively to absorbent temperature because "new" sodalime was cooler but produced slightly more CO. The absence of compound A formation from sevoflurane and fresh absorbents was also not due exclusively to absorbent temperature because these were comparable for the various absorbents. Similarly, with dehydrated absorbents, there was no relation between temperature and compound A formation. The absence of strong base, rather than differences in temperature, seem more important in explaining the lack of CO and compound A formation with Amsorb<sup>®</sup>.

There are limitations with this investigation. A "worst case" scenario was not evaluated. Specifically, CO formation using two canisters filled with completely desiccated absorbent was not evaluated. Under these conditions, CO and COHb concentrations exceeded toxic thresholds and caused hemodynamic instability and/or death,<sup>19,36</sup> which we wished to avoid. Therefore, partially dehydrated absorbents and a single canister, which also more closely approximates the relation to subject

weight and absorbent mass, were used. Differences between absorbents would have been even greater had two canisters of fully desiccated absorbent been evaluated. Absorbents were not dehydrated to a specific hydration endpoint, which might have decreased experimental variability. Pigs (21 kg) were smaller than adult patients; hence, the model is not quite as clinically relevant were larger pigs to have been used, but it has been used previously<sup>19,36</sup> and is more relevant than *in vitro* systems. A small number of animals were used, and multiple absorbent and anesthetic concentrations were evaluated in each animal. This was done in accordance with Animal Use Guidelines, which aim to limit animal use to the minimal number possible. Carryover effects were minimized, however, by allowing adequate wash-out between experimental conditions and randomizing the order of exposure, except usually keeping the absorbent (*i.e.*, Baralyme<sup>®</sup>) known to cause the greatest effects last. Use of more animals might have permitted small differences between absorbents to reach statistical significance. However, the main conclusions of the investigation, that Amsorb<sup>®</sup> caused minimal if any CO formation, minimal compound A formation, and the least amount of sevoflurane degradation, would not have been different.

A previous editorial, which accompanied the first report of Amsorb<sup>®</sup> and its laboratory evaluation, cautioned that laboratory results needed to be confirmed in clinical evaluations to substantiate the lack of anesthetic degra-



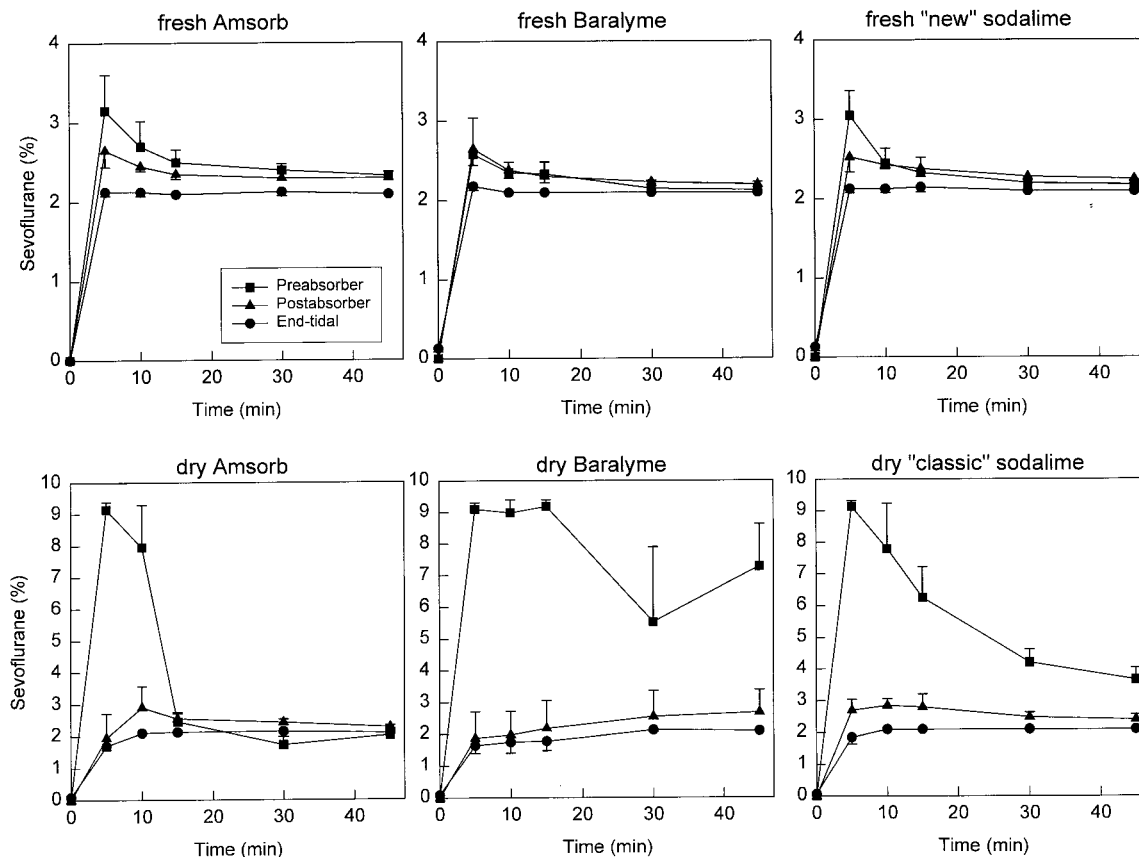


Fig. 7. Anesthesia circuit concentrations of sevoflurane during anesthesia using fresh and partially dehydrated absorbents. Gas samples were obtained as described in figure 5.

ation.<sup>3</sup> Although clinical investigations confirmed that Amsorb<sup>®</sup> caused little or no compound A formation,<sup>30,31</sup> a similar evaluation of CO formation in surgical patients is precluded by ethical concerns. The current investigation, using a clinically relevant animal model, demonstrates that Amsorb<sup>®</sup> caused minimal if any CO formation and the least amount of sevoflurane degradation. These findings suggest that the use of an absorbent that

does not cause anesthetic degradation and formation of toxic products may have benefit with respect to patient safety, inhalation induction, and anesthetic consumption (cost). Because these benefits occur with both fresh and dehydrated Amsorb<sup>®</sup>, there seems to be less need to replace Amsorb<sup>®</sup> at arbitrary time intervals or to discard Amsorb<sup>®</sup> that has become desiccated before exhaustion of CO<sub>2</sub> scavenging capacity.

In summary, in comparison with sodalime and Baralyme<sup>®</sup>, Amsorb<sup>®</sup> caused minimal if any CO formation, minimal compound A formation, and the least amount of sevoflurane degradation. These findings seem relevant to patient safety.

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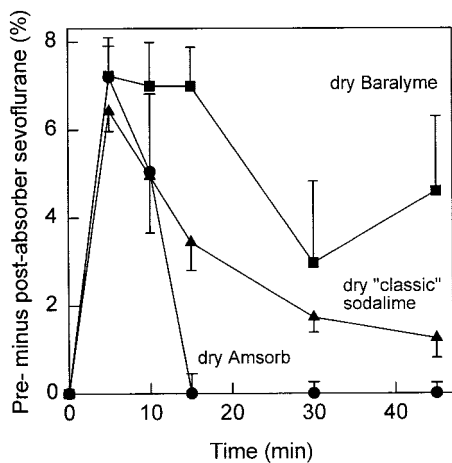


Fig. 8. Sevoflurane concentration difference between preabsorber and postabsorber samples during anesthesia using partially dehydrated absorbents.

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