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Quick Flick Guide

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The AMSORB® PLUS Quick-Flick Guide has been designed to provide you with key information extracted from published clinical papers on the subject of AMSORB®, AMSORB® PLUS and other CO_2 absorbents. This information has been categorised into 20 key focus areas which have been color coded so you can quickly and easily navigate through the Guide.

This Guide should be used in conjunction with other AMSORB® PLUS sales support tools that will be made available to you.

If you have any questions or queries relating to this Guide please email **marketing@armstrongmedical.net**

Contents

CARBON MONOXIDE

1.1	Kharasch ED et al
1.2	Knolle E et al
1.3	Knolle E et al
1.4	Knolle E et al
1.5	Berry PD et al
1.6	Stabernack CR et al
1.7	Frink EJ et al
1.8	Moon RE et al
1.9	Epstein RA
1.10	Woehlck HJ
1.11	Di Filippo A et al
1.12	Higuchi H et al
1.13	D'Eramo C
1.14	Kharasch ED et al
1.15	Kharasch ED et al
1.16	Reichle FM et al
1.17	Murray JM et al
1.18	Renfrew C et al
1.19	Schuler HG et al
1.20	Baxter PJ et al
1.21	Fang ZX et al
1.22	Lentz R
1.23	Frink EJ et al
1.24	Moon RE
1.25	ECRI Hazard Report
1.26	Keijzer et al
1.27	Magee et al

1.1 Kharasch ED et al

For desflurane and isoflurane, the order of inspired CO and COHb formation was dehydrated Baralyme® >> soda lime > Amsorb®. For desflurane and Baralyme®, 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®.

Peak CO concentrations from isoflurane were significantly different for Amsorb® versus all other absorbents, and peak CO concentrations for desflurane were significantly different for Amsorb® versus Baralyme®.

Using a single canister of fully desiccated sodalime with 7% desflurane and 1.5% isoflurane, Bonome et al. observed approximately 5,500 and 1,000 ppm peak CO and 58% and 18% COHb, respectively.

Consistent with its lack of compound A formation, dehydrated Amsorb® did not increase COHb concentrations.

The current investigation, using a clinically relevant animal model, demonstrates that Amsorb® 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®, there seems to be less need to replace Amsorb® at arbitrary time intervals or to discard Amsorb® that has become desiccated before exhaustion of CO_2 scavenging capacity. In summary, in comparison with sodalime and Baralyme®, Amsorb® caused minimal if any CO formation, minimal compound A formation, and the least amount of sevoflurane degradation. These findings seem relevant to patient safety.

Anesthesiology, V 96, No 1, Jan 2002

1.2 Knolle E et al

In the first experimental series, no CO formation was measured in the Amsorb (Sample H) when 0.5% isoflurane was directed through them. For all the other tested absorbents (A–G), there were reproducible CO concentration curves (Fig. 1). The corresponding cal-culated values of CO formation (CO and CO_{Mean}) differed significantly among the absorbents.

See Table 2 attached.

When the inlet isoflurane concentration was increased to 4% from 0.5%, the mean CO formation with LoFloSorb was approximately twofold larger, but with Superia, CO formation was approximately the same. Amsorb produced no CO. The differences in CO formation and CO_{Mean} among the three absorbents were significant.

Because CO formation in absorbents increases with increasing anesthetic concentration (1,3), CO concentration values of more than 1000 ppm can easily be expected in these absorbents when 4% isoflurane is used.

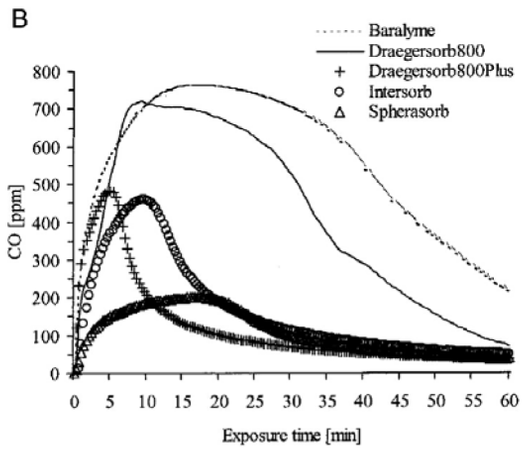
Anesth Analg 2002;95:650-5

Table 2. Characteristics of CO Formation During Passage of 0.5% Isoflurane

	Sample (brand)										
	Group 1			Group 2				Group 3			
Variable	A Baralyme	B Dragersorb 800	A-B	C Dragersorb 800 Plus	D Intersorb	E Spherasorb	C-E	F LoFloSorb	G Superia	H (Amsorb)	F-H
CO (mL)	223 ± 6	140 ± 12	181 ± 45	66±3	73 ± 3	49 ± 4	63 ± 11	8 ± 2	3 ± 2	0	4 ± 4
CO_{Mean}(ppm)	730 ± 20	458 ± 39	594 ± 146	218 ± 9	239 ± 10	162 ± 13	206 ± 35	26 ± 5	9 ± 5	0	12 ± 12
CO_{Max}(ppm)	875 ± 34	737 ± 49	806 ± 83	620 ± 17	548 ± 23	281 ± 18	483 ±152	38 ± 8	13 ± 7	-	25 ± 15
T_{COMax}(min)	24 ± 2	18 ± 1	21 ± 4	10 ± 1	12 ± 1	23 ± 1	15 ± 7	50 ± 2	25 ± 1	-	37 ± 13
$Temp_{Baseline}$(°C)	24.8±0.5	27.3 ± 1.2	26.1±1.6	26.3 ± 0.7	25.9±0.3	25.4 ± 0.2	25.9±0.6	24.8 ± 0.2	25.8 ± 0.3	26.2 ± 0.3	25.6±0.7
$Temp_{Max}$(°C)	27.7±4.2	32.0 ± 0.8	29.8±3.6	27.8 ± 0.6	27.4±0.12	26.9 ± 0.2	27.4±0.5	24.9 ± 0.2	26.2 ± 0.5	26.3 ± 0.3	25.8±0.8
$Temp_{Mean}$(°C)	25.4±1.1	28.7 ± 0.4	27.0±1.9	27.2 ± 0.5	26.6±0.05	25.9 ± 0.1	26.6±0.6	24.5 ± 0.1	25.9 ± 0.3	26.1 ± 0.2	25.5±0.8
ISO_{Loss}(%)	63 ± 1	36 ± 1	50 ± 15	26 ± 3	31 ± 1	50 ± 2	36 ± 11	89 ± 5	41 ± 2	20 ± 4	50 ± 15
$T_{ISO<0.4\%}$(min)	>60	38 ± 2		16 ± 2	20 ± 0	33 ± 1		>60	26 ± 4	15 ± 3	
$T_{ISO<0.4\%}$(min) (fresh soda lime)	<1, <1	1, 1		1, 1	<1, 1	1, 2		2, 2	1, 1	1, 1	

CO = carbon monoxide; ISO = Isoflurane

1.3 Knolle E et al



Anesthesiology, V 97, No 2, Aug 2002

1.4 Knolle E et al

Methods: For 60 minutes 0.5% isoflurane in O2 (flow: 5 l/min) was passed through completely dried samples (600g, residual humidity < 0.3g) of
A: Draegersorb800(Draeger,GER,n=6),content:Ca(OH)2,KOH,NaOH
B: Draegersorb800Plus(Draeger,GER,n=5)content:Ca(OH)2,NaOH
C: Intersorb(Intersurgical,GB,n=5),content:Ca(OH)2,NaOH
D: Spherasorb(Intersurgical,GB,n=6),content:Ca(OH)2,NaOH
E: Amsorb(Armstrong,Northern Ireland,n=4),content:Ca(OH)2
F: Amsorb exposed to 4% isoflurane.

But only the complete lack of both potassium and sodium hydroxide in soda lime composition (Amsorb) prevents CO formation.

Ref.: (1) Anesth Analg 1999;89:768-73

	CO max (ppm)	CO (ml)	T Max °C
A	755 ± 61	147 ± 20	32.1 ± 0.8
B	620 ± 17	67 ± 3	27.8 ± 0.6
C	548 ± 23	73 ± 3	27.4 ± 0.1
D	280 ± 16	49 ± 4	26.9 ± 0.3
E	Below detection limit	-	26.3 ± 0.3
F	Below detection limit	-	26.1 ± 0.1
	P < 0.05	P < 0.05	P < 0.05

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1.5 Berry PD et al

We present the most severe case of intraoperative carbon monoxide exposure yet reported, in which the diagnosis was suggested by a combination of moderately decreased oxygen saturation by pulse oximetry (SpO2) and an erroneous gas analyzer reading.

A 24-yr-old woman, ASA physical status 1, was anesthetized for a clinical research study that involved combined epidural and general anesthesia. The subject's weight was 62 kg; height was 1.66 m; hematocrit level was not measured. She had undergone an identical general anesthetic 2 weeks previously as part of the same study, with no alteration of SpO2 or other complications.

Five minutes after induction of anesthesia, SpO2 decreased to 93%. Bilateral auscultation of the lungs was normal, endotracheal suction returned no secretions; end-tidal pressure of carbon dioxide (PCO2) was 34–35 mmHg. Heart rate was 96 beats/min, and blood pressure was 110/60 mmHg, both similar to preinduction levels. The three-lead electrocardiogram tracing showed normal rhythm and QRS- and ST-segment appearance. Automated ST-segment analysis was not available on the monitor used. Clinical appearance of the subject was entirely normal, with no cyanosis and no "cherry red" appearance. Ten minutes after induction of anesthesia, the Datex Capnomac Ultima end-tidal gas analyzer (Datex-Ohmeda)—set in "automatic" mode—indicated the presence of enflurane followed after a few minutes by "mixed agent." Until this point, it indicated desflurane. No enflurane vaporizer was attached to the anesthetic machine. At this point, carbon monoxide toxicity because of desiccation of the carbon dioxide absorbent was suspected, and the Baralyme (Allied Healthcare Products, St Louis, MO) was therefore immediately replaced with fresh Baralyme. The time interval from induction of anesthesia to replacement of the Baralyme was approximately 15 min. After an additional 15 min, an arterial blood sample was obtained for cooximeter analysis with the following results: oxygenated hemoglobin (HbO2): 63%; COHb: 36%; and methemoglobin (MetHb): 1%. The study protocol was aborted and the subject was ventilated with 100% oxygen using a fresh gas flow of 8 l/min. Anesthesia was maintained with a desflurane vaporizer setting of 6%. Twenty minutes after replacement of the Baralyme, the anesthetic agent analyzer no longer indicated mixed agent, and instead indicated an end-tidal desflurane concentration of 5–5.5%, which was consistent with the vaporizer setting. The SpO2 returned to 99%. Cooximetry was repeated 45 min after the original sample, and COHb concentration was 21%. After an additional hour, COHb concentration decreased to 12%. Neuromuscular blockade was then antagonized, the anesthetic was discontinued, and the subject emerged from anesthesia with no apparent abnormal sequelae. The total duration of anesthesia was approximately 140 min. The subject remained in the postanesthesia care unit with routine monitoring for 2 h and was then discharged to home. Before discharge, she was informed about her carbon monoxide exposure.

Production of carbon monoxide within breathing circuits occurs when desiccated carbon dioxide absorbent comes into contact with and degrades volatile anesthetics. Production is greatest with desflurane, isoflurane, and enflurane; the most probable source of carbon monoxide is the –CHF2 moiety, which is missing on halothane and sevoflurane.

This case illustrates the possibility of desiccated carbon dioxide absorbent reacting with desflurane to cause significant carbon monoxide exposure in the clinical setting. The presence of an unexpectedly low SpO2 and an erroneous gas analyzer reading led to the diagnosis in this case. Nevertheless, the diagnosis of intraoperative carbon monoxide exposure is difficult because specific monitoring for carbon monoxide is not routinely available and the clinical features are vague. It is therefore possible that a significant number of undiagnosed carbon monoxide exposures occur. A high index of suspicion, awareness of possible diagnostic feature, and institution of measures to prevent carbon dioxide absorbent desiccation may help to prevent future exposures.

Anesthesiology 1999; vol. 90; pp613-616 (case report)

1.6 Stabernack CR et al

Concern persists regarding the production of carbon monoxide (CO) and Compound A from the action of carbon dioxide (CO_2) absorbents on desflurane and sevoflurane, respectively.

However, the effect of KOH versus NaOH was not consistent in its impact on CO production. Furthermore, the effect of KOH versus NaOH versus Ca(OH)2 was inconsistent in its impact on Compound A production.

The presence of polyvinylpyrrolidine, calcium chloride, and calcium sulfate in Amsorb® appears to have suppressed the production of toxic products. All absorbents had an adequate CO_2 absorbing capacity greatest with lithium hydroxide. Grace 2M and 3M had still lower, however, significant values, whereas Amsorb® and LiOH produced minimal or no CO during the first 60 min. These relationships did not change for averages during 120 and 240 min of anesthetic delivery.

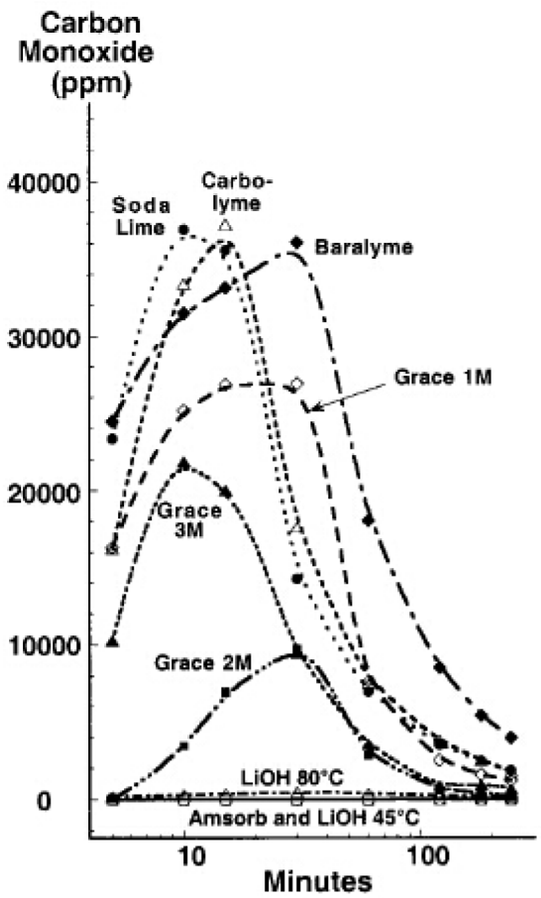


Figure 2. Under the circumstances outlined in the legend to Fig. 1, degradation of desflurane produced carbon monoxide (CO) with peak CO concentrations appearing in the outflow in 10–30 min and decreasing thereafter, to minimal concentrations with all but Baralyme® (Chemetron) by 240 min. The highest peak values were found

Anesth Analg 2000;90:1428-35

1.7 Frink EJ et al

An oxygen flow rate of 10 l/min for 24 h in a conventional anesthesia circuit can dry carbon dioxide absorbents sufficiently to produce extremely high levels of carbon monoxide with high carboxyhemoglobin concentrations in desflurane-anesthetized pigs. When the reservoir bag is in place on the anesthesia machine or when a lower oxygen flow rate (5 l/min) is used, carbon dioxide absorbent drying still occurs, but 24-48-h exposure time is insufficient to allow for carbon monoxide production with desflurane.

Nine animals were included in the studies using 48-h absorbent drying (which were performed with the reservoir bag removed) and Baralyme as the carbon dioxide absorbent. Of these nine animals, three died of cardiac arrest within 20 mins of initiation of desflurane anesthesia and six were resuscitated with administration of intravenous epinephrine and discontinuation of the desflurane anesthetic. For this reason, further evaluation of 48-h drying times were discontinued.

48-Hour Drying Studies (Reservoir Bag Removed)
Exposure of Baralyme to 10 l/min oxygen flow for 48-h resulted in a decrease in water content from 11.9 +/- 0.4% (fresh) to a water content of 3.9 +/- 0.8% at the top of the upper canister and 1.2 +/- 0.2% water content in the upper portion of the lower canister. This concentration of drying resulted in extremely high circuit carbon monoxide concentrations (mean peak concentration, 37,000 +/- 3,500 ppm) occurring within 10 to 15 min of initiation of desflurane anesthesia. All animals had carboxyhemoglobin concentrations greater than 80%, with seven of nine animals achieving concentrations of 90% or more. Three pigs died during anesthetic administration. The remaining six animals were successfully resuscitated by discontinuing anesthetic and administering 100% oxygen and epinephrine, intravenously (dose range, 0.25-2.0 mg given intravenously). None of the animals tolerated anesthesia with desflurane beyond 30 mins due to hypotension (systolic blood pressure < 60mmHg) from carbon monoxide exposure.

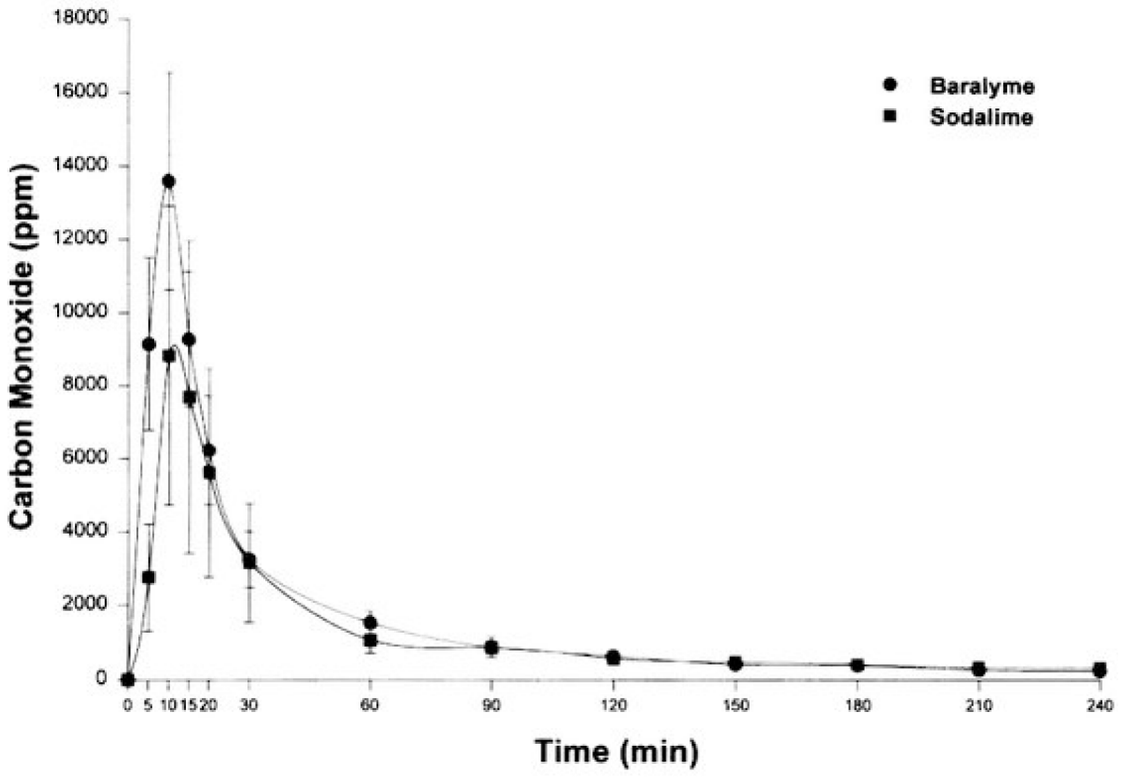


Figure 3. Carbon monoxide concentrations within the anesthesia circuit (sampled at the inspiratory limb of the circuit distal to the one-way valve) during desflurane anesthesia using dry Baralyme or soda lime (24-h drying studies). Carbon monoxide concentrations did not differ between the Baralyme and soda lime groups.

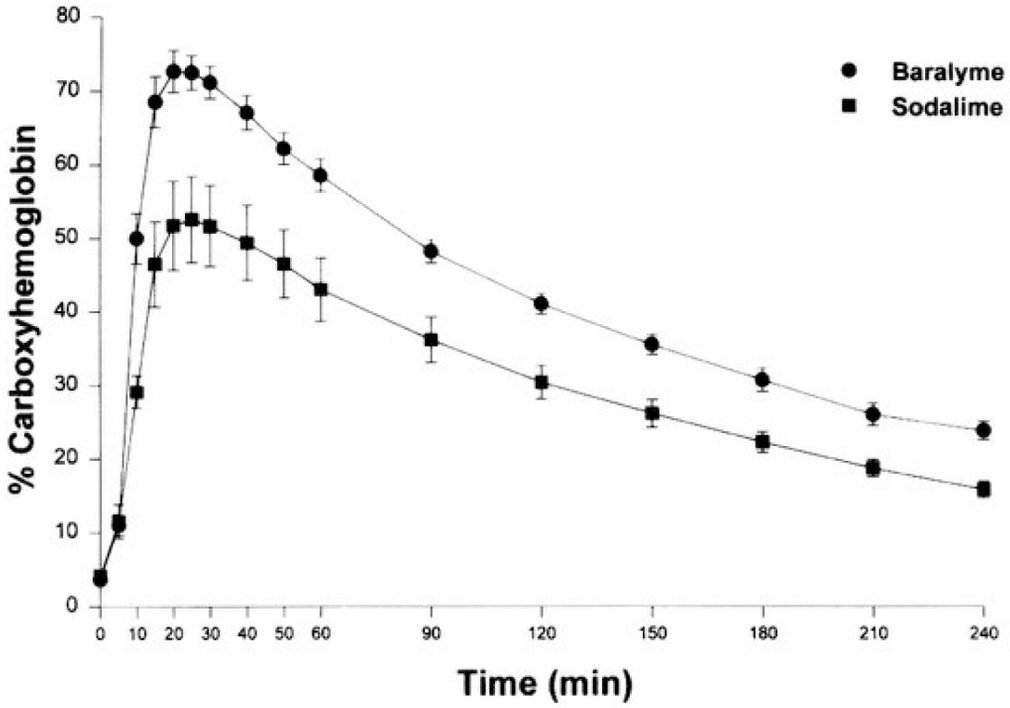


Figure 4. Carboxyhemoglobin concentrations in pigs during desflurane anesthesia using Baralyme or soda lime exposed to 24 h of 10 l/min oxygen flow. Carboxyhemoglobin concentrations are greater for the Baralyme group than for the soda lime group for all times after five min ($P < 0.01$).

We analyzed samples from the canister sectioned into thirds. Therefore, the water contents (eg 1.9% for the bottom of the lower canister) represent a mean value for the lower region. The water content of the absorbent at the very bottom was likely lower than this value. Given these limitations, we still believe that our results indicate that high carboxyhemoglobin levels can develop if desflurane is administered with partially dried carbon dioxide absorbent to humans.

Anesthesiology 1997; vol 87; No 2

1.8 Moon RE et al

For an eight hour exposure the Occupational Safety and Health Administration (OSHA) has set the maximum limit at 50 ppm. Using data on the effect of low level CO exposure on anginal threshold in individuals with coronary artery disease, the Environmental Protection Agency (EPA) has set the levels at 35 and 9 ppm for one and eight hour exposures, respectively.

Symptoms and signs of CO poisoning include headache, nausea, vomiting, dizziness, motor weakness, impaired consciousness, cardiac arrhythmias and ischemia. In some instances, particularly if there are neurological abnormalities at the time of the exposure, there can be prolonged or permanent sequelae consisting of cognitive deficits, mood changes, dementia and extra-pyramidal motor abnormalities. CO poisoning can also be fatal by preventing normal oxygen delivery to the tissues. A typical non-smoker may normally have 1-2% COHB, derived from endogenously produced CO. Smokers may have around 4 7% COHB. Although there is a poor correlation between COHB level and clinical severity of CO poisoning, generally a COHB level greater than 15-20% is associated with symptoms and greater than 50% with impaired consciousness.

The case reported by Dr. Lentz is similar to a number of others which have occurred in at least three other institutions in this country. Our own experience at Duke Medical Center dates back to January of 1990, at which time a 76-year-old nonsmoking female was undergoing general anesthesia for thyroid resection. It is the policy of our Blood Gas Lab to do co-oximetry on all samples sent for blood gas analysis. An arterial catheter had been inserted preoperatively and 25 minutes after anesthesia induction, a routine ABG sample was sent to the laboratory. Carboxyhemoglobin (COHB) level was 9.1%. SaO2 by pulse oximetry was 99 100% throughout the anesthetic. Another blood gas was sent an hour after the first one and the COHB level was 28%. Upon receipt of this result, another sample was sent and the COHB level was 29%.

The second case became evident about six weeks later when a patient undergoing total hip replacement under general anesthesia had a COHB level of 24.7%. Similar investigations were carried out; no source was found. However, the anesthesia circuit had been left in place and, using an electrochemical CO monitor, it was noted that gas exiting the Sodasorb canister had a CO concentration > 500 ppm. Heating of one of the two soda lime canisters liberated high levels of CO.

A total of eight instances occurred at Duke Medical Center. After publication of an ASA abstract, we were immediately contacted by Dr. Ed Brunner at Northwestern and Dr. Chuck Ingram at Emory, reporting, respectively, three and eighteen similar cases with COHB levels ranging from 8.5 to 32%. Many of the cases had baseline measurements and therefore a documented rise in COHB during anesthesia.

One patient had received a spinal anesthetic and had presumably been exposed to CO while receiving supplemental 02 via the anesthetic circuit. There was, however, one interesting factor: most instances had been the first case anesthetized on a Monday morning; all cases occurred in a room which had not been used for at least two days.

The guidelines listed above were only intended to be temporary, pending definitive elucidation of the cause. Investigations had begun at Duke Medical Center. While actual cases of CO poisoning were uncommonly discovered, in part because blood gases were measured on only about 10% of patients, 'footprints' of the phenomenon, in the form of measurable gaseous CO within unused anesthesia circuits, were relatively common. On Sunday afternoons dangerously high CO levels (> 1000 ppm) within the soda lime compartments of anesthesia machines were detected in over 2% of measurements (320 observations).

Anesthesia Patient Safety Foundation Newsletter 1994; vol. 09; pp13-14

1.9 Epstein RA

Carbon monoxide is toxic in very low concentrations. The severity of toxicity depends both on the duration of exposure and on the concentration inhaled. Other influencing factors include the level of exercise and coexisting medical conditions. From a practical standpoint, exposure to greater than 50 ppm for eight hours should be avoided. Even brief exposure to greater that 200 ppm is considered hazardous. Carbon monoxide reacts with hemoglobin to form deoxyhemoglobin. Textbooks of environmental medicine provide standard tables which predict carboxyhemoglobin level as a function of carbon monoxide concentration in inspired air and of duration of exposure. (1) For example, exposure to 1,000 ppm for one hour would be expected to produce 30% carboxyhemoglobin.

Although it was not stated until an explanatory note appeared in the Fall issue,
the patient was receiving desflurane. The author astutely recognized that the case occurred Monday morning and postulated that something happened to the anesthesia system during prolonged disuse which ultimately led to the release of carbon monoxide. Without understanding the specific mechanism, he made the common sense (but probably incorrect) recommendation that, after a weekend of disuse, the anesthesia system should be purged with a high flow of fresh gas prior to use. This seemed reasonable, particularly because it did not appear that there would be any disadvantage from such a strategy.

In this laboratory situation, the concentration of carbon monoxide produced was alarmingly high. With the worst case combination of desflurane and completely dry barium hydroxide lime, the carbon monoxide concentration was almost 20,000 ppm. Desflurane produced a carbon monoxide concentration of about 15 times isoflurane and barium hydroxide lime about two times soda lime. However, even the best case combination of isoflurane and completely dry soda lime produced a concentration of 500 ppm, about 10 times more than is reasonable for chronic exposure. Fortunately, even moderate degrees of hydration of the absorbents greatly decreased the concentration of carbon monoxide produced. No carbon monoxide was produced in the presence of normally hydrated absorbents with any anesthetic agent.

Anesthesia Patient Safety Foundation Newsletter, Vol 9, No 4, Winter 1994-95

1.10 Woehlck HJ

At a time when it appears that nearly all clinically relevant information is known and the issue of CO poisoning has become tiresome and passé, we are presented with a case report that might be construed as a near miss, a preventable fatality barely averted by recognition and treatment of the exposure.

Even the minimum fresh gas flow, given sufficient time, can desiccate absorbents enough to produce severe anesthetic breakdown. This suggests that the configuration and features of the anesthesia machine, such as the minimum fresh gas flow rate, can enhance or degrade patient safety.

Regarding intraoperative CO poisoning, and with tongue in cheek, I have categorized anesthesia providers into two groups: the Overconcerned and the Apathetic. The Overconcerned may have become so after a patient was actually exposed to CO via anesthetic breakdown. The Overconcerned may note similarities in the care of their machines to those that predispose to CO exposures, or the Overconcerned may just be the worrying sort; forever fearful that some harm may come. Just because one is paranoid does not mean others are not out to get him or her.
And then there are the Apathetic. The Apathetic may be overconfident, uninformed, or in denial of the possibility of a problem.

The Overconcerned can reply that in the report by Berry et al.,[1] the patient who attained 36% carboxyhemoglobin had an ASA physical status 1 and was the subject of a clinical study.
Do unrecognized episodes of intraoperative CO exposure result in or exacerbate cardiac morbidity? If so, what is the cost of these episodes?

The ASA Web site provides the estimate that 25 million anesthetic procedures are performed each year in the US. Although hard statistics are difficult to obtain, if as little as 33% of these anesthetics involve isoflurane, enflurane, or desflurane, and if four cases are performed in the average operating room each day so that 25% of cases will be first cases, then up to 2 million patients may be at risk each yr for intraoperative CO exposure. If the published incidence of CO exposures can be generalized to other institutions and remains between 1/2,000 and 1/200 first cases,[3] then approximately 1,000–10,000 patients may actually be exposed to CO each yr in the US as a result of anesthetic breakdown. Worldwide, these numbers may be far greater. The incidence of massive CO exposures analogous to that reported by Berry et al.[1] is also unknown, and even greater exposures are possible, as predicted by mathematic modeling[4,5] and demonstrated in animals by Frink et al.[6] In the absence of effective means of detection, it is possible that the majority of these cases go undiagnosed. Berry et al.[1] noted no specific signs of CO poisoning during anesthesia in the current report, so it remains possible that any potential problems caused by CO poisoning during anesthesia may be attributed to other causes. The true morbidity from intraoperative CO poisoning is uncertain. The economic costs of intraoperative CO poisoning and its prevention remain unknown.
Is it politically correct to join the ranks of the Apathetic? Or is it safer to affiliate with the Overconcerned? Today, we may still have insufficient knowledge to place this problem in perspective. Perhaps common sense and further study should prevail.

Anesthesiology 1999;90:353-359

1.11 Di Filippo A et al

Another advantage of the Amsorb is the non-production of carbon monoxide, which makes this new absorber particularly effective and advantageous in closed circuit anesthesia techniques with an ability of reducing the waste products enhancing closed circuit anesthesia.

Applied Cardiopulmonary Pathophysiology 9: 103-106, 2000

1.12 Higuchi H et al

Amsorb is chemically unreactive with volatile anesthetics. However, soda lime degrades sevoflurane to Compound A and desflurane, enflurane, and isoflurane to CO (1,3,4,10).

Anesth Analg 2001;93:221-5

1.13 D'Eramo C

In our study Amsorb® causes minimal CO production by Sevoflurane or Isoflurane; these results agree with Neumann's findings (4) and demonstrate that CO production results from use of CO2 absorbents containing large quantities of strong alkali, even if mechanism remains unclear (2). Furthermore, in our study, Amsorb® and Soda Lime demonstrate a substantially equal longevity in CO2 removing during low-flow anaesthesia.

Preliminary clinical experience

1.14 Kharasch ED et al

Amsorb® caused minimal if any CO formation, no increase in blood COHb concentration, and no oxyHb desaturation.

Anesthesiology 2001; 95:A1125

1.15 Kharasch ED et al

Unless a CO monitor is installed on an anesthesia machine or CO–hemoglobin concentrations are routinely measured, there is no way to reliably detect CO exposure or CO poisoning. We cannot rely on clinical signs of CO toxicity, and pulse oximeters are grossly insensitive.

In contrast, and of extraordinary importance, is that calcium hydroxide lime did not degrade sevoflurane to compound A, or desflurane, enflurane, or isoflurane to CO, even when desiccated.

Anesthesiology, V 91, No 5, Nov 1999

1.16 Reichle FM et al

	Sodasorb	Soda Lime	Spherasorb	Draegersorb 800+	Amsorb	p-value
max. CpA (ppm)	17.3 ±1.5	17.3 ± 2.2	12.3 ±1.2	37.0 ±1.5	<1	<0.001
t 0.5% (min)	138 ± 11	145 ± 21	144 ± 1	178 ± 4	73 ± 2	<0.001
t 1.0% (min)	182 ± 4	187 ± 18	178 ± 2	211 ± 3	102 ± 2	<0.001
CO_2 0.5% (L)	82 ± 7	86 ± 13	85 ± 1	107 ± 2	41 ± 1	<0.001
CO_2 1.0% (L)	110 ± 3	113 ± 12	107 ± 1	128 ± 3	59 ± 1	<0.001
max. Temp. (°C)	46.3 ± 2.3	45.5 ± 0.9	40.2 ± 2.1	48.8 ± 0.3	40.6 ± 0.4	0.013

2000 ASA Meeting Abstracts

1.17 Murray JM et al

Volatile Agent	Soda Lime (100 g)	Amsorb (100 g)
Oven-dried		
Desflurane (n = 3)	600 (10.0)*	1.7 (1.1)
Enflurane (n = 3)	580 (9.8)*	1.5 (1.2)
Isoflurane (n = 3)	620 (10.1)*	1.4 (1.1)
Gas flow-dried		
Desflurane (n = 3)	223 (9.7)*	1.2 (1.0)
Enflurane (n = 3)	201 (4.1)*	2.3 (1.6)
Isoflurane (n = 3)	190 (5.8)*	1.5 (1.1)

Data are mean ± SD.

Amsorb as tested under the conditions of this study does not produce clinically significant amounts of carbon monoxide in the first minute of reaction. Levels of carbon monoxide far in excess of 600 ppm have been observed in previous studies[4,5,16,18]. The important issue in the present study is the complete absence of carbon monoxide generation observed at the specific measurement interval when Amsorb was exposed to desflurane, isoflurane, and enflurane.

Anesthesiology, V 91, No 5, Nov 1999

1.18 Renfrew C et al

Carbon monoxide content of gas sample when a dried sample of soda lime or the new mixture was exposed to desflurane, enflurane or isoflurane

	Soda Lime	New Mixture
Desflurane	600 ppm	1 ppm
Enflurane	580 ppm	1 ppm
Isoflurane	620 ppm	2 ppm

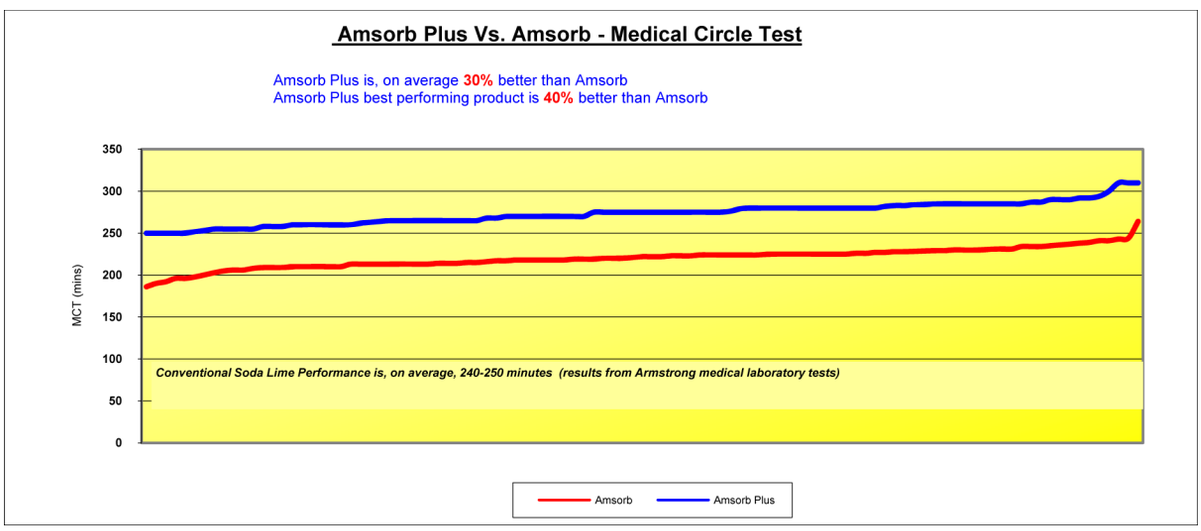
In conclusion we have shown that carbon dioxide can be absorbed effectively without the aid of strong base if water is present at a consistent percentage. We have also shown that calcium hydroxide is not capable of initiating the Canizarro reaction responsible for Compound A production when Sevoflurane is exposed to soda lime and is not capable of initiating the reaction responsible for carbon monoxide production when Desflurane, enflurane and isoflurane are exposed to desiccated soda lime.

ACTA Anaesthesiologica Scandanavica 1998; vol 42;pp58-55

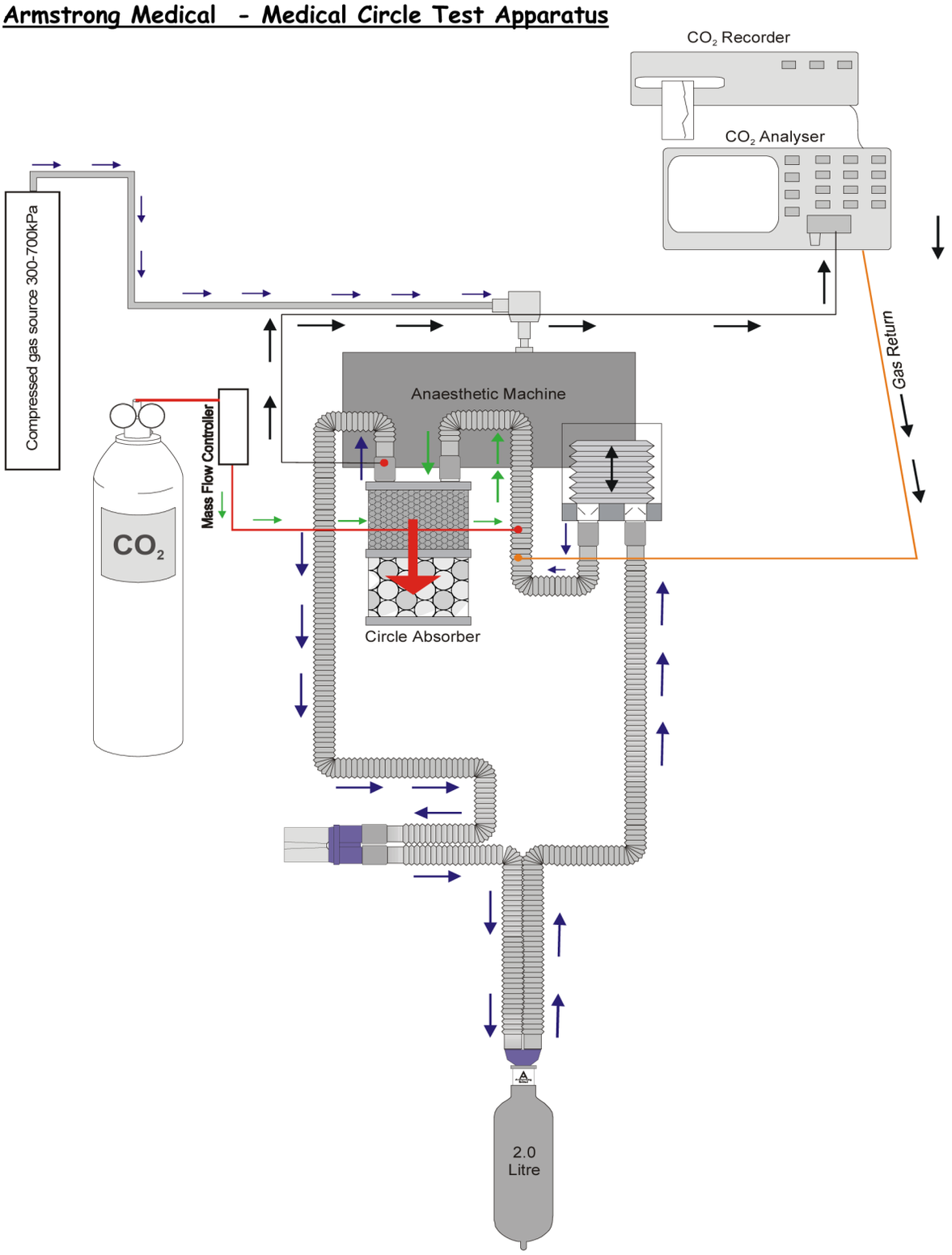
1.19 Schuler HG et al

The ability of Amsorb® to prevent anesthetic degradation is sufficiently advantageous to justify its routine clinical use despite its shorter duration for CO2 absorption (see medical circle test).

Anesthesiology 2001 ; 95:A510



Armstrong Medical - Medical Circle Test Apparatus



1.20 Baxter PJ et al

RECOGNITION of carbon monoxide (CO) production in anesthesia circuits resulting from volatile anesthetic degradation has necessitated changes in clinical practice and product labeling. [1-7] Intraoperative CO formation from desflurane, enflurane, and isoflurane has been reported, with CO concentrations exceeding Environmental Protection Agency safety limits. [8] There are no clinical reports of CO formation from halothane or sevoflurane. Prospective analyses have suggested that the incidence of patient CO exposure (> 30 ppm) is 0.46% for the first case of the day (2.9% in remote locations other than operating rooms), and the overall incidence is 0.26%. [4-7] Desflurane, enflurane, and isoflurane degradation to CO occurs when these anesthetics interact with relatively dry barium hydroxide lime and soda lime and is thought to be catalyzed by the strong bases in these carbon dioxide absorbents. [1,3,4,6,9] Practitioners have been cautioned by the Food and Drug Administration to replace carbon dioxide absorbent, which they suspect may be desiccated.

Anesthesiology 1998; vol. 89; pp929-941

1.21 Fang ZX et al

Two articles in the APSF Newsletter (Summer, 1994) indicate that carbon monoxide toxicity represents a potential hazard of the administration of modem halogenated volatile anesthetics.

Although no report has indicated that patient harm has resulted from the production of carbon monoxide during general anesthesia, avoidance of such a risk would seem prudent and in the best interest of patient safety.

With soda lime, at a 4.8% water content, no carbon monoxide was produced.

Dry soda lime at 45celsius

Des 4% peak CO = 8700 ppm
Enf 1.2% peak CO + 3900 ppm
Isoflurane 1% 580 ppm

Dry Baralyme at 45°C produced still higher peak levels:

Des 4% peak CO = 19700 ppm
Enf 1.2% peak CO = 5400 ppm
Isoflurane 1% 1200 ppm

The findings reported here lead to specific recommendations for the avoidance of carbon monoxide production from the interaction of potent volatile anesthetics with carbon dioxide absorbent:

1. Ensure the use of standard absorbents containing the full complement of water. Use of relatively low fresh gas inflow rates for the majority of procedures should provide a sustained level of water content in the absorbent to avoid carbon monoxide production.

2. A corollary to (1) is to discontinue the use of high inflow rates when they are no longer needed (eg after equilibration of the patient to the desired maintenance level of volatile anesthetic).

Anesthesia Patient Safety Newsletter Vol 9, No. 3, 25-36 Fall 1994

1.22 Lentz R

CO poisoning during anesthesia poses puzzles: new agent used in Florida case.

A 46-year-old white female was scheduled as an outpatient for septoplasty, endoscopic bilateral anterior ethmoidal sinus surgery, and excision of a left tonsillar cyst. During her pre-op interview, the patient denied any cardiac or respiratory history. The patient also denied any prior anesthetics and she was not taking any chronic medications. The patient did, however, admit to being a smoker, with a 20 pack/year smoking history.

Routine pre-op labs were within normal limits, and specific values were: Hgb 14.1, Na 141, K 3.8, Cl 108, C02 23, and Ca 9.6.

Following induction, the vital signs were: BP 110/60, HR 95, SaO2=100% (FiO2=40%), Temp 36.5 C.

Approximately 40 minutes into the case, the patient's 02-Hgb saturation decreased to 96% over a period of 2-3 minutes. The pulse oximeter probe was inspected to verify proper placement on the finger. Breath sounds remained equal bilaterally, without wheezes, and there was no change in PIP. The endotracheal tube was also checked for its position, and it was noted to still be secured at 20 cm at the lips. At this point, the patient was placed on 100% 02 and hand ventilated with up to 40 cmH20 pressure. This also failed to bring the patient's O2 saturation above 96%. The surgeon was made aware of these findings and was asked to complete the procedure as quickly as possible.

Arterial blood gases were sent to check the 02 saturation a COHb level was also requested. The blood gas report read the following values: pH 7.46; PC02=28 mm Hg; P02 467 mm Hg; HCO3 20.3 MEq/l; COHB 31.5%. At this point, the patient's 02-Hgb saturation remained at 97%. The surgeon was made aware of the new findings, and the procedure was completed over the next 10 minutes. The entire time interval from when the 02Hgb saturation started to decrease to the completion of the surgery was 30 minutes.

In any patient who develops the type of hemoglobin desaturation described here and who fails to respond to the usual therapeutic measures used to correct this problem, do not hesitate to send either a venous or, preferably, an arterial blood sample for the possibility of COHB "poisoning' (see article on page 13).

Anesthesia Safety Foundation Newsletter 1994: vol. 09; pp13-14

1.23 Frink EJ et al

Pigs received a 1.0 (human) minimum alveolar concentration desflurane anesthetic 7.5%) for 240 min using a 1 l/ min oxygen flow rate with dried absorbent. Carbon monoxide concentrations in the circuit and carboxyhemoglobin concentrations in the pigs were measured. RESULTS: Pigs anesthetized with desflurane using Baralyme exposed to 48 h of 10 l/min oxygen flow (reservoir bag removed) had extremely high carboxyhemoglobin concentrations (more than 80%). Circuit carbon monoxide concentrations during desflurane anesthesia using absorbents exposed to 10 l/min oxygen flow (reservoir bag removed, 24 h) reached peak values of 8,800 to 13,600 ppm, depending on the absorbent used. Carboxyhemoglobin concentrations reached peak values of 73% (Baralyme) and 53% (soda lime). The water content of Baralyme decreased from 12.1 +/- 0.3% (mean +/- SEM) to as low as 1.9 +/- 0.4% at the bottom of the lower canister (oxygen flow direction during drying was from bottom to top). Absorbent temperatures in the bottom canister increased to temperatures as high as 50 degrees C. With the reservoir bag in place during drying (10 l/min oxygen flow), water removal from Baralyme was insufficient to produce carbon monoxide (lowest water content = 5.5%). Use of 5 l/min oxygen flow (reservoir bag removed) for 24 h did not reduce water content sufficiently to produce carbon dioxide with desflurane.

Anesthesiology 1997; vol 87; No 2

1.24 Moon RE

CO has a molecular weight of approximately 28, and with commonly used mass spectrometers cannot be distinguished from nitrogen. The only reliable method of detection is direct measurement of blood COHB.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

1.25 ECRI PROBLEM REPORTING SYSTEM

Hazard Report

We concluded that dangerous levels of the gas were generated within the anesthesia system.

Many incidents have occurred during Monday morning cases, and all appear to be associated with the first delivery of an anesthetic after a lengthy period.

It should also be stressed that CO exposures are unlikely to be detected intraoperatively.

Health Devices – November 1998 – Vol. 27, No. 11

1.26 Keijzer at al

Results: Peak concentrations of CO were very high in Medisorb® (Datex-Ohmeda, Hoevelaken, The Netherlands) and Spherasorb® (Intersurgical, Uden, The Netherlands)
(13317 and 9045 p.p.m., respectively). It was lower with Loflosorb® (Intersurgical, Uden, The Netherlands) and Superia® (Datex-Ohmeda, Hoevelaken, The Netherlands) (524 and 31 p.p.m., respectively). Amsorb® (Armstrong, Coleraine, N. Ireland) and lithium hydroxide produced no CO at all.

Conclusion: Medisorb® and Spherasorb® are capable of producing large concentrations of CO when desiccated. Loflosorb® and Superia® produce far less CO under the same conditions. Amsorb® and lithium hydroxide should be considered safe when desiccated.

Acta Anaesthesiologica Scandinavica 2005; vol. 49; pp. 815-818

1.27 Magee at al

CO production
Test results show that LoFloSorb produces CO in vitro when in contact with vapourous anaesthetics, in the order sevoflurane → isoflurane → desflurane for fresh absorbent and in the order isoflurane → sevoflurane → desflurane for fresh-desiccated absorbent (see tables 1-3). Peak CO levels found with fresh LoFloSorb, across all three anaesthetic agents, reached 7ppm±4 with isoflurane at 4% - less with the other agents. Peak CO levels found with fresh-desiccated LoFloSorb across all three anaesthetic agents, were 48ppm±18 with isoflurane. Fresh or fresh-desiccated AMSORB PLUS did not produce CO beyond background interference (1ppm) in a small number of tests. It should be noted that, when desiccated, neither absorbent has the required capability to absorb clinical loadings of CO2. This data supports the earlier findings of Knolle.

Table 1.

Sevoflurane 8%	Peak CO	Median CO
AMSORB PLUS, fresh	0	0
LoFloSorb, fresh	5	2
Medisorb, fresh	10	6
AMSORB PLUS, fresh desiccated	1	<1
LoFloSorb, fresh desiccated	40	24
Medisorb, fresh desiccated	410	287

Table 2.

Isoflurane 4%	Peak CO	Median CO
AMSORB PLUS, fresh	0	0
LoFloSorb, fresh	7	3
Medisorb, fresh	25	8
AMSORB PLUS, fresh desiccated	0	0
LoFloSorb, fresh desiccated	48	28
Medisorb, fresh desiccated	810	537

Table 3.

Desflurane 16%	Peak CO	Median CO
AMSORB PLUS, fresh	0	0
LoFloSorb, fresh	6	1
Medisorb, fresh	45	23
AMSORB PLUS, fresh desiccated	0	0
LoFloSorb, fresh desiccated	35	17
Medisorb, fresh desiccated	1,010	693

COMPOUND A

2.1	Higuchi H et al
2.2	Di Filippo A et al
2.3	Kobayashi S et al
2.4	Mchaorab A et al
2.5	Schuler HG et al
2.6	Versichelen LFM et al
2.7	Di Filippo A et al
2.8	Higuchi H et al
2.9	Kharasch ED et al
2.10	Kharasch ED et al
2.11	Stabernack CR et al
2.12	Murray JM et al
2.13	Renfrew CW et al
2.14	Versichelen LFM et al
2.15	Yamakage M et al
2.16	Frink EJ et al
2.17	Abbott Labs Brief Summary - Sevoflurane
2.18	Yamakage et al

COMPOUND A

2.1 Higuchi H et al

Amsorb is chemically unreactive with volatile anesthetics. However, soda lime degrades sevoflurane to Compound A and desflurane, enflurane, and isoflurane to CO (1,3,4,10).

Anesth Analg 2001;93:221-5

2.2 Di Filippo A et al

Our results confirm that Amsorb, *in vitro* test at high temperature but also in the clinical one, obtains good results to reduce the production of Compound A because of the absence of strong bases in its formulation. This is confirmed by the literature about the new products that have been put on the market in the recent past (4, 14, 15).

Acta Anaesthesiol Scand 2002: 46: 1017-1020

2.3 Kobayashi S et al

Amsorb® is far superior to soda lime with regards to compound A concentration in a circle system during low-flow sevoflurane anesthesia.

Anesthesia 2002 Vol 97 No 3 A82 ASA Abstract 2002 Orlando

2.4 Mchaorab A et al

In summary, the formation of compound A during sevoflurane anesthesia with the use of barium hydroxide lime or soda lime absorbent did not occur during sevoflurane anesthesia with Amsorb absorbent.

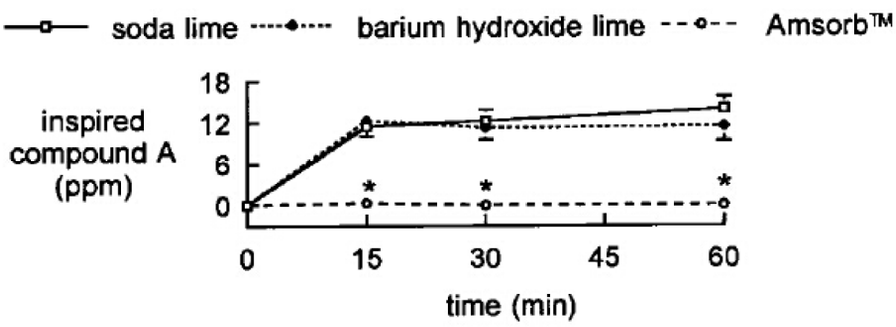


Fig. 1. Compound A concentrations produced from three carbon dioxide absorbents during sevoflurane anesthesia in volunteers (mean ± SEM). Gas samples were taken from the inspired limb of the anesthesia circuit. *Different from barium hydroxide lime or soda lime ($P < 0.05$).

Anesthesiology, V 94, No 6, Jun 2001

2.5 Schuler HG et al

The ability of Amsorb® to prevent anesthetic degradation is sufficiently advantageous to justify its routine clinical use despite its shorter duration for CO_2 absorption.

Anesthesiology 2001 ; 95:A510

2.6 Versichelen LFM et al

Our most striking results are that two carbon dioxide absorbents, Amsorb and lithium hydroxide, are devoid of compound A production. In the Amsorb-containing or lithium hydroxide–containing systems, compound A_{insp} was present in concentrations almost equal (maximum median value for Amsorb was 1.3 ppm and for lithium hydroxide was 1.6 ppm) to those contained intrinsically in commercial sevoflurane (1.06 ± 0.28 ppm)[10].

Our in vitro assessment clearly shows that Amsorb is devoid of significant compound A generation and is the answer for the clinical practice, as has already been reported[12,13]

Anesthesiology, V 95, No 3, Sep 2001

2.7 Di Filippo A et al

Our study shows that the use of Sevoflurane with a FGF of 500 ml/min produces, in some ventilators, a noticeable dose of compound A.

Applied Cardiopulmonary Pathophysiology 9: 103-106, 2000

2.8 Higuchi et al

Moreover, sevoflurane was not degraded at all using Amsorb®, which contains neither KOH nor NaOH. Consequently, these results suggest that the degradation of sevoflurane to Compound A is directly related to the presence of monovalent hydroxide bases.

Anesth Analg 2000; 91:434-9

2.9 Kharasch ED et al

Neither fresh nor dehydrated Amsorb® caused Compound A formation.

Consistent with its lack of Compound A formation, dehydrated Amsorb® did not increase COHb concentrations.

Anesthesiology, V 96, No 1, Jan 2002

2.10 Kharasch ED et al

In contrast, and of extraordinary importance, is that calcium hydroxide lime did not degrade sevoflurane to compound A, or desflurane, enflurane, or isoflurane to CO, even when desiccated.

Anesthesiology, V 91, No 5, Nov 1999

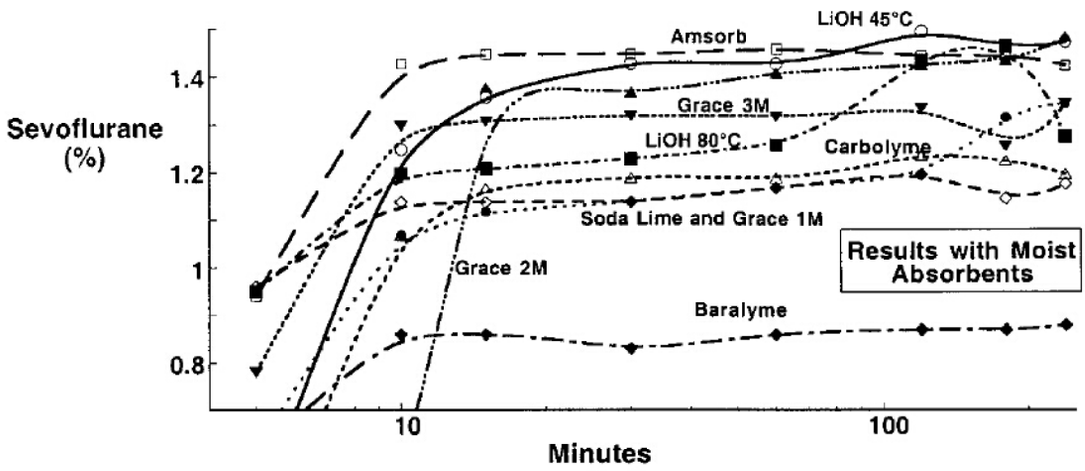
2.11 Stabernack CR et al

Concern persists regarding the production of carbon monoxide (CO) and Compound A from the action of carbon dioxide (CO_2) absorbents on desflurane and sevoflurane, respectively.

However, the effect of KOH versus NaOH was not consistent in its impact on CO production. Furthermore, the effect of KOH versus NaOH versus Ca(OH)2 was inconsistent in its impact on Compound A production.

The presence of polyvinylpyrrolidine, calcium chloride, and calcium sulfate in Amsorb® appears to have suppressed the production of toxic products. All absorbents had an adequate CO_2 absorbing capacity greatest with lithium hydroxide.

For moist absorbents, sevoflurane degradation was greatest with Baralyme® (Chemetron) (i.e., the effluent concentration was smallest) and was least with Amsorb® (Armstrong Medical) and LiOH. The other absorbents produced results intermediate to those produced by Baralyme® (Chemetron) versus Amsorb® (Armstrong Medical) and LiOH.



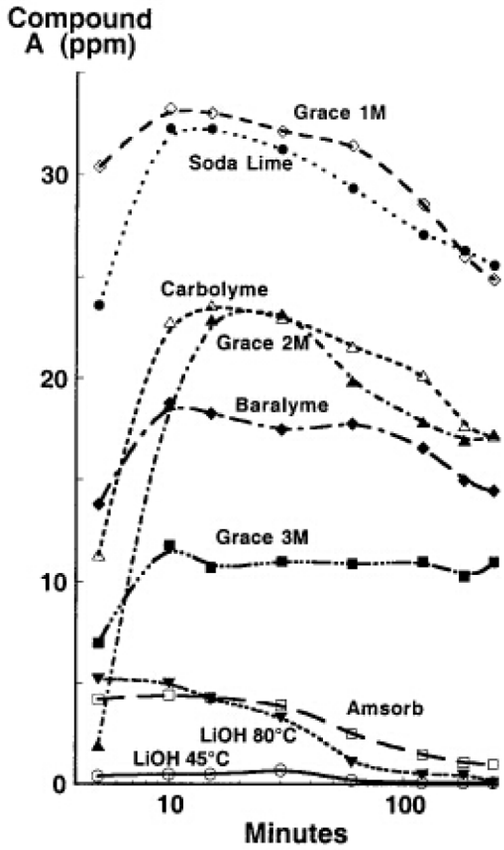


Figure 5. Under the circumstances outlined in the legend to Fig. 4, degradation of sevoflurane produced various concentrations of Compound A. Unlike the result for degradation of desflurane to CO (Fig. 2), the outflow concentrations of Compound A tended to be sustained. The highest peak Compound A values were reached in the outflow from Grace 1M and soda lime. In contrast Amsorb® (Armstrong Medica) and lithium hydroxide (LiOH) produced only small or negligible peak concentrations of Compound A. The other absorbents, including Baralyme® (Chemetron) (which produced the greatest degradation of sevoflurane—see Fig. 4) produced results intermediate to those produced by Grace 1M and soda lime versus Amsorb® (Armstrong Medica) and LiOH.

Anesthesia Analgesia 2000 Vol 90 pp1428-1435

2.12 Murray JM et al

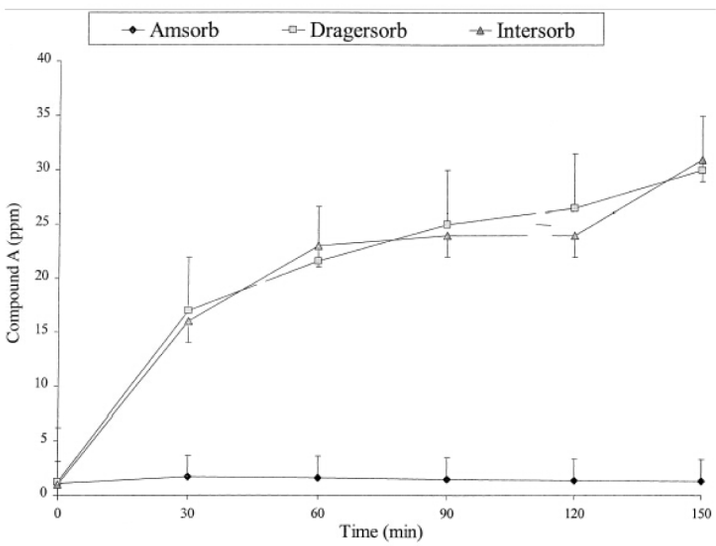


Fig. 2. Concentrations of compound A (ppm) when Amsorb (n = 3), Intersorb (n = 3), and Dragersorb (n = 3) were exposed to sevoflurane (2%) in oxygen (1 l/min). Data are mean ± SD.

Anesthesiology, V 91, No 5, Nov 1999

2.13 Renfrew CW et al

In conclusion we have shown that carbon dioxide can be absorbed effectively without the aid of strong base if water is present at a consistent percentage. We have also shown that calcium hydroxide is not capable of initiating the Canizarro reaction responsible for Compound A production when Sevoflurane is exposed to soda lime and is not capable of initiating the reaction responsible for carbon monoxide production when Desflurane, enflurane and isoflurane are exposed to desiccated soda lime.

ACTA Anaesthesiologica Scandanavica 1998; vol 42;pp58-55

2.14 Versichelen LFM et al

It was shown that with Amsorb and lithium hydroxide no compound A was generated during 2.1 % end-tidal sevoflurane, whereas with Sofnolime and KOH-free Sodasorb a significant amount of compound A was formed (~30-35 ppm), somewhat more than with Sodasorb (~20-25 ppm). Furthermore the canister temperatures during the 4 h duration administration were almost identical with the 5 CO_2 absorbents.

Conference Notes, ALFA Congress 2002, Pisa, Italy

2.15 Yamakage M et al

In conclusion, our clinical study shows that novel CO_2 absorbents without strong bases, especially Amsorb™, are effective absorbents because little, or no, Compound A was detected during low-flow anesthesia with sevoflurane.

Anesth Analg 2000;91:220-4

2.16 Frink EJ et al

Concentrations of compound A increased during the first 4 h of anesthesia with soda lime and baralyme and declined between 4 and 5 h when baralyme was used. Mean maximum inhalation concentration of compound A using baralyme was 20.28 +/- 8.6 ppm (mean +/- SEM) compared to 8.16 +/- 2.67 ppm obtained with soda lime, a difference that did not reach statistical significance. A single patient achieved a maximal concentration of 60.78 ppm during low-flow.

Exhalation concentrations of compound A were less than inhalation concentrations, suggesting patient uptake.

Anesthesiology 1992; vol. 77; pp1064-1069

2.17 Abbott Labs Brief Summary - Sevoflurane

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

ULTANE®

sevoflurane

volatile liquid for inhalation

INDICATIONS AND USAGE

Sevoflurane is indicated for induction and maintenance of general anesthesia in adult and pediatric patients for inpatient and outpatient surgery.

Sevoflurane should be administered only by persons trained in the administration of general anesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available. Since level of anesthesia may be altered rapidly, only vaporizers producing predictable concentrations of sevoflurane should be used.

CONTRAINDICATIONS

Sevoflurane can cause malignant hyperthermia. It should not be used in patients with known sensitivity to sevoflurane or to other halogenated agents nor in patients with known or suspected susceptibility to malignant hyperthermia.

WARNINGS

Although data from controlled clinical studies at low flow rates are limited, findings taken from patient and animal studies suggest that there is a potential for renal injury which is presumed due to Compound A. Animal and human studies demonstrate that sevoflurane administered for more than 2 MAC•hours and at fresh gas flow rates of <2 L/min may be associated with proteinuria and glycosuria.

While a level of Compound A exposure at which clinical nephrotoxicity might be expected to occur has not been established, it is prudent to consider all of the factors leading to Compound A exposure in humans, especially duration of exposure, fresh gas flow rate, and concentration of sevoflurane. During sevoflurane anesthesia the clinician should adjust inspired concentration and fresh gas flow rate to minimize exposure to Compound A. To minimize exposure to Compound A, sevoflurane exposure should not exceed 2 MAC•hours at flow rates of 1 to <2 L/min. Fresh gas flow rates <1 L/min are not recommended.

Because clinical experience in administering sevoflurane to patients with renal insufficiency (creatinine >1.5 mg/dL) is limited, its safety in these patients has not been established.

Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The safety of low flow sevoflurane on renal function was evaluated in patients with normal preoperative renal function. One study compared sevoflurane (N=98) to an active control (N=90) administered for ≥2 hours at a fresh gas flow rate of ≤1 Liter/minute. Per study defined criteria (Hou et al.) one patient in the sevoflurane group developed elevations of creatinine, in addition to glycosuria and proteinuria. This patient received sevoflurane at fresh gas flow rates of ≤800 mL/minute. Using these same criteria, there were no patients in the active control group who developed treatment emergent elevations in serum creatinine.

Ref 58-6547-R7-Rev Aug 2001 Abbott Labs 2001

2.18 Yamakage 2009 et al

Performance of four carbon dioxide absorbents in experimental and clinical settings

Summary

To evaluate the performance of four kinds of carbon dioxide (CO_2) absorbents (Medisorb® GE Healthcare, Amsorb® Plus Armstrong Medical, YabashiLime® Yabashi Industries, and Sodasorb® LF Grace Performance Chemicals), we measured their dust production, acceptability of colour indicator, and CO_2 absorption capacity in in vitro experimental settings and the concentration of compound A in an inspired anaesthetic circuit during in vivo clinical practice. In vitro, the order of the dust amount was Sodasorb LF > Medisorb > Amsorb Plus = YabashiLime both before and after shaking. The order of the color acceptability was similar: Sodasorb LF > Amsorb Plus = Medisorb > YabashiLime both initially and 16 h after CO_2 exhaustion. During exposure to 200 ml.min)$^{-1}$ CO_2 in vitro, the period until 1 kg of fresh soda lime allowed inspired CO_2 to increase to 0.7 kPa (as a mark of utilisation of the absorbent) was longer with Medisorb (1978 min) than with the other absorbents (1270–1375 min). In vivo, compound A (1.0% inspired sevoflurane) was detected only when using Medisorb. While Medisorb has the best ability to absorb CO_2, it alone produces compound A.

Conventional carbon dioxide (CO_2) absorbents containing strong bases (sodium hydroxide, NaOH and potassium hydroxide, KOH) can absorb CO_2 in a semi-closed anaesthetic circuits [1, 2] but also degrade sevoflurane to fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether (CF2 = C(CF_3)-O-CH_2F, compound A) [3, 4]. Compound A has a dose-dependent nephrotoxic effect in rats [5–7], although clinically adverse effects are rare [8–11]. Absorbents which include no or small amounts of NaOH /KOH produce smaller quantities of compound A [12–14], but their CO_2 absorption capacity seems poorer [12]. More recently, absorbents have been developed that use different size and shape of the absorptive granules (YabashiLime®; Yabashi Industries, Gifu, Japan), or different components to improve absorbent capacity (Amsorb® Plus; Armstrong Medical Ltd., Coleraine, Northern Ireland), or that reduce dust and also improve colour indication (a colour change occurring irreversibly when the absorbent becomes exhausted; Sodasorb® LF; Grace Performance Chemicals, Cambridge, MA, USA). Therefore, we investigated the degree of dust production, the acceptability of color indicator, and the capacity of CO2 absorption in in vitro experiments and the concentration of compound A in the inspired anaesthetic circuit in in vivo clinical practice, using these four absorbents.

Methods

We investigated one CO2 absorbent (which only contains a small amount of NaOH /KOH Medisorb®; GE Healthcare Technologies, Waukesha, WI, USA) and three third-generation CO2 absorbents (Amsorb® Plus, YabashiLime®, and Sodasorb® LF). The chemical compositions as well as the costs of these CO_2 absorbents are listed in Table 1.

Anaesthesia 2009; vol. 64; pp287-292

FORMALDEHYDE

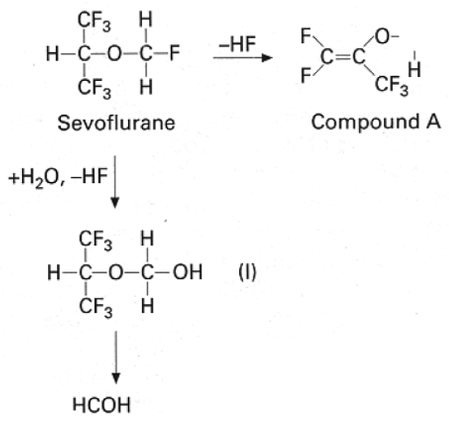
3.1	Bedi et al
3.2	Bedi et al
3.3	Funk W et al
3.4	Perry PD et al

FORMALDEHYDE

3.1 Bedi A et al

Formaldehyde is a strong reducing agent, especially in the presence of alkali. It is a potent respiratory tract irritant, a carcinogen and has been shown to cause nausea and vomiting.

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to formaldehyde in the occupational environment be controlled to a concentration no greater 1 ppm for any 30-minute sampling period (3)



The possibility of sevoflurane being degraded to formaldehyde has clinical implications. Sevoflurane has been implicated in the aetiology of post operative nausea and vomiting. Temperature and the presence of strong base in a desiccated absorbent may both be factors, which increase its production.

Sevoflurane is degraded to formaldehyde when passed through dry CO2 absorbents that contain strong alkali. Formaldehyde was not detected when sevoflurane was exposed to either fresh or dry Amsorb™.

Acknowledgement: This work was in part funded by an educational grant

3.2 Bedi et al

Sevoflurane is degraded to formaldehyde when passed through dry CO2 absorbents that contain strong alkali. Degradation to formaldehyde was associated with the greatest canister temperatures. Formaldehyde was not detected when sevoflurane was exposed to either fresh or dry Amsorb®.

References.

1. Fang ZX, Eger EI II. Anesthesia and Analgesia 1995:81:564-8
2. Funk W, Gruber M, Wild K, Hobbhahn J. British Journal of Anaesthesia 1999;82:193-8
3. National Institute for Occupational Safety and Health: Criteria for a Recommended Standard. Occupational Exposure to Formaldehyde. DHEW (NIOSH) Publication No.
77-126 (1976)

Table. Formaldehyde concentrations (ppm) and canister temperature (°C) for fresh (F) and dry(D) absorbents.
*Values exceeding NIOSH recommended limits (1 ppm).

	8% Sevo/O2	Temp °C
Amsorb (F)	0.05	39.6
Amsorb (D)	0.08	34.9
Sodasorb (F)	0.15	49.5
Sodasorb (D)	8.53*	55.0
Medisorb (F)	0.19	45.3
Medisorb (D)	1.16*	51.2

ASA Abstract 2001; 95:A1190 New Orleans

3.3 Funk W et al

With dry soda lime, the patient may inhale potentially toxic degradation products in significant amounts. Sevoflurane degradation is aggravated by a high KOH content of the lime. The observed airway irritation may be caused by formic acid, which is generated in isomolar concentrations with methanol (Cannizzaro reaction). The amount of compound A found with dry KOH-containing lime is unlikely to be noxious.

After 2 min, we detected methanol and compound A (CH_2F-O-C(=CF_2) (CF_3)). Total amounts over 20 min were: methanol 1125 mg (D dry), 334 mg (S dry) and <5 mg (fresh soda lime): compound A 148 mg (D dry), 13 mg (S dry) and 3-8 mg (fresh): and fluoride 8.5 mg (D dry), 3.3 mg (S dry) and 1 mg (fresh). Formaldehyde was detected only with dry lime (D>2.5 mg, S>0.6 mg). In summary, the use of moist soda lime is of crucial importance during inhalation induction. With dry soda lime, the patient may inhale potentially toxic degradation products in significant amounts. Sevoflurane degradation is aggravated by a high KOH content of the lime. The observed airway irritation may be caused by formic acid, which is generated in isomolar concentrations with methanol (Cannizzaro reaction).

The aim of our study was to analyse and quantify the substances that a patient might inhale under clinical conditions. Of potential interest were not only gaseous components, but formaldehyde, formic acid and fluorinated products such as fluoric acid (HF), which are known airway irritants produced during sevoflurane degradation.

Our results suggest that the observed airway irritation may be caused primarily by formic acid, which is generated in isomolar concentrations with methanol from formaldehyde (Cannizzaro reaction Fig 5).

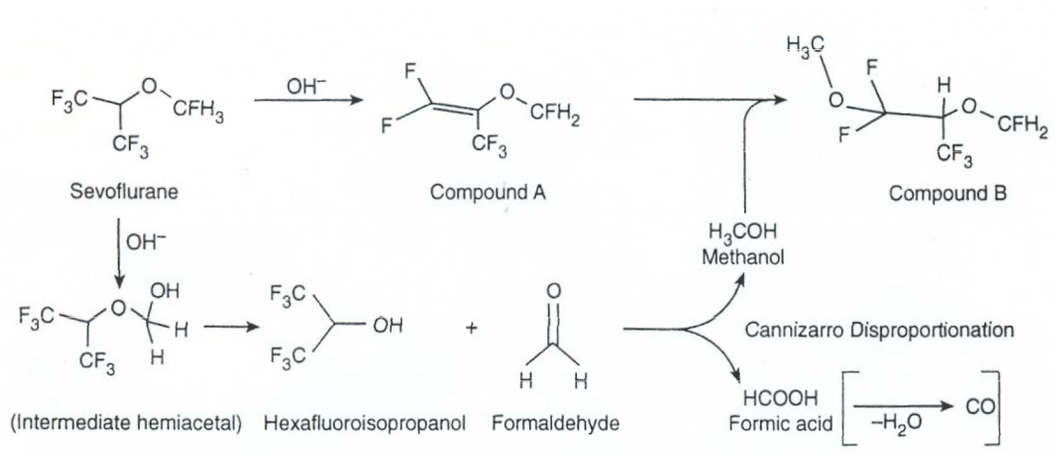


Fig 5 Degradation of sevoflurane, reproduced according to Morio and colleagues[16].

British Journal of Anaesthesia 1999; vol 82; pp193-198

3.4 Berry PD et al

Diagnosis of carbon monoxide intoxication during anesthesia is difficult because the main clinical features of toxicity are masked by anesthesia. Furthermore, there is no routinely available means to reliably identify the presence of carbon monoxide within the breathing circuit, nor to detect when carbon dioxide absorbent has been desiccated. In our case, early diagnosis of carbon monoxide production was facilitated by the presence of a clearly erroneous gas analyzer reading (it is not possible to accidentally fill a Tec 6 desflurane vaporizer with enflurane). This false reading probably resulted from trifluoromethane, which is produced along with carbon monoxide by volatile-agent degradation.

Anesthesiology 1999;90:613-616

SAFETY

4.1	Berry PD et al
4.2	J Baum & H Van Aken
4.3	Kharasch ED et al
4.4	Kharasch ED
4.5	Reichle FM et al
4.6	Frink EJ et al
4.7	Moon RE
4.8	Epstein RA
4.9	Lentz RE
4.10	Funk W et al
4.11	Murray JM et al
4.12	Schuler HG et al
4.13	Stabernack et al
4.14	Baxter PJ et al
4.15	Fang ZX et al
4.16	Woehlck HJ
4.17	ECRI Hazard Report
4.18	A bbott Labs Brief Summary - Sevoflurane
4.19	Olympio MD et al

SAFETY

4.1 Berry PD et al

Inquiry at the time of the anesthetic and subsequently revealed that (despite the appearance of recent use) the anesthetic machine had not been used for several days and had probably been left switched on and connected to the oxygen pipeline for this entire period. It was not possible to establish the fresh gas flow during this period of disuse, nor the exact configuration of the circuit. The room used for the study was located within the operating room suite, and therefore not in a "remote location"; it was, however, not used for surgical cases and was used only infrequently for other anesthetic purposes.

Diagnosis of carbon monoxide intoxication during anesthesia is difficult because the main clinical features of toxicity are masked by anesthesia. Furthermore, there is no routinely available means to reliably identify the presence of carbon monoxide within the breathing circuit, nor to detect when carbon dioxide absorbent has been desiccated. In our case, early diagnosis of carbon monoxide production was facilitated by the presence of a clearly erroneous gas analyzer reading (it is not possible to accidentally fill a Tec 6 desflurane vaporizer with enflurane). This false reading probably resulted from trifluoromethane, which is produced along with carbon monoxide by volatile-agent degradation.

Interestingly, in a recent case report,1 an unexpectedly rapid change of soda lime color to blue after induction of anesthesia was associated with desiccation and carbon monoxide production. This may imply that desiccated absorbent has less capacity to absorb carbon dioxide and, therefore, may reveal its presence by becoming exhausted and changing color more rapidly than expected. Because of the difficulty of detecting of carbon monoxide production and toxicity, prevention is especially important. Various guidelines have been published for prevention of carbon monoxide production; most recently these have concentrated on preventing the use of desiccated carbon dioxide absorbent.|| 2 Baralyme and soda lime both are supplied wet, that is, they contain approximately 13–15% water by weight. The percentage of water that would prevent carbon monoxide production for all anesthetics is probably near 4.8% for soda lime and 9.7% for Baralyme.4 A fresh gas flow of 5 l/min or more passed through absorbent for 24 h (without a patient) is sufficient to cause critical drying of the absorbent if the reservoir bag is left off the breathing circuit (thus facilitating retrograde movement of gas through the absorber). With the bag in place, drying still occurs, but to a lesser extent. These findings are consistent with the observation in several reports,1–3 including ours, that carbon monoxide production occurred when anesthetic machines had been unused for 48 h or more. In contrast, it is unlikely that either high- or low-flow anesthesia itself can cause desiccation and carbon monoxide exposure,17 because water is released as carbon dioxide is absorbed.

Anesthesiology 1999;90:613-616

4.2 J Baum and H Van Aken

Of course, routine use of higher gas flow rates will decrease the costs per hour for absorbents, although the knock-on added costs of volatile agents will exceed these savings considerably. Thus, the additional cost resulting from the use of calcium hydroxide lime is really quite low when related to the potential improvement in patient safety, which may be gained by the use of an absorbent being completely inert with respect to all volatile agents.

European Journal of Anaesthesiology, 17, 597-600

4.3 Kharasch ED et al

An absorbent like Amsorb®, which does not contain strong base or cause desflurane or isoflurane degradation and formation of toxic CO, may have significant benefit with respect to patient safety.

Anesthesiology 2001 ; 95:A1125

4.4 Kharasch ED

The original package label for sevoflurane contained a warning stating that, because of limited clinical experience, flow rates less than 2 l/min were not recommended. In October 1998, this was revised to suggest that flow rates of 1 l/min were acceptable but should not exceed 2 minimum alveolar concentration-hour, and flow rates less than 1 l/min were not recommended. The package label for anesthetics such as desflurane and isoflurane was changed* to include a precaution that when a practitioner suspects that the CO_2 absorbent may be desiccated, it should be replaced. The fallacy in the latter warning, of course, is that we have no clue when CO_2 absorbents become partially dried or fully desiccated.

Anestheshiology 1999 Vol 92, No 5

4.5 Reichle FM et al

The clinician must choose between economically optimised absorption capacity (Dragersorb 800+®) and maximum patient safety (Amsorb®). Spherasorb®, Soda Lime® & Sodasorb® combine intermediate to low Compound A production with a good absorption capacity.

	Sodasorb	Soda Lime	Spherasorb	Draegersorb 800+	Amsorb	p-value
max. CpA (ppm)	17.3 ±1.5	17.3 ± 2.2	12.3 ±1.2	37.0 ±1.5	<1	<0.001
t 0.5% (min)	138 ± 11	145 ± 21	144 ± 1	178 ± 4	73 ± 2	<0.001
t 1.0% (min)	182 ± 4	187 ± 18	178 ± 2	211 ± 3	102 ± 2	<0.001
CO_2 0.5% (L)	82 ± 7	86 ± 13	85 ± 1	107 ± 2	41 ± 1	<0.001
CO_2 1.0% (L)	110 ± 3	113 ± 12	107 ± 1	128 ± 3	59 ± 1	<0.001
max. Temp. (°C)	46.3 ± 2.3	45.5 ± 0.9	40.2 ± 2.1	48.8 ± 0.3	40.6 ± 0.4	0.013

2000 ASA Meeting Abstracts. Copyright ©2000 American Society of Anesthesiologists

4.6 Frink EJ et al

An additional concern is the inability of the anesthetist to recognise that absorbents in the circle system may be of low water content. Unless the anesthetist detects that absorbent may have been dried due to the presence of a high gas flow, the absorbent may not be replaced.

Why have more cases of carbon monoxide exposure with anesthetics containing a CHF2O (difluoromethoxy) moiety (ie Desflurane, enflurane and Isoflurane) not been reported? It is possible that some concentrations of carbon monoxide exposure go unrecognised because our routine monitoring modalities will not detect such exposure.

Anesthesiology 1997 vol.87; No.2

4.7 Moon RE

Symptoms and signs of CO poisoning include headache, nausea, vomiting, dizziness, motor weakness, impaired consciousness, cardiac arrhythmias and ischemia. In some instances, particularly if there are neurological abnormalities at the time of the exposure, there can be prolonged or permanent sequelae consisting of cognitive deficits, mood changes, dementia and extra-pyramidal motor abnormalities. CO poisoning can also be fatal by preventing normal oxygen delivery to the tissues.

Although high fresh gas flows appear to have played a part in reducing the likelihood of CO poisoning, the additional cost of anesthetics is substantial. At Duke Medical Center recently, the policy has been changed to remove the restriction on fresh gas flow rate, while continuing to monitor weekend CO levels. If the distribution of CO levels does not indicate greater numbers of machines with dangerous CO concentrations it may be possible to remove this most costly of the three 1990 guidelines.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

4.8 Epstein RA

Carbon monoxide is toxic in very low concentrations. The severity of toxicity depends both on the duration of exposure and on the concentration inhaled. Other influencing factors include the level of exercise and coexisting medical conditions. From a practical standpoint, exposure to greater than 50 ppm for eight hours should be avoided. Even brief exposure to greater that 200 ppm is considered hazardous. Carbon monoxide reacts with hemoglobin to form deoxyhemoglobin. Textbooks of environmental medicine provide standard tables which predict carboxyhemoglobin level as a function of carbon monoxide concentration in inspired air and of duration of exposure. (1) For example, exposure to 1,000 ppm for one hour would be expected to produce 30% carboxyhemoglobin.

It is difficult to know exactly at what carboxyhemoglobin levels mortality occurs because most victims receive therapeutic oxygen between the time of exposure and arrival at a health care facility where the carboxyhemoglobin level is determined. However, the peak level can be estimated from the known half W of carboxyhemoglobin. It is generally thought that death may result from carboxyhemoglobin levels of 50 percent in young healthy victims. Patients with underlying cardiovascular disease may be at risk from significantly lower levels.

Although it was not stated until an explanatory note appeared in the Fall issue, the patient was receiving desflurane. The author astutely recognized that the case occurred Monday morning and postulated that something happened to the anesthesia system during prolonged disuse which ultimately led to the release of carbon monoxide. Without understanding the specific mechanism, he made the common sense (but probably incorrect) recommendation that, after a weekend of disuse, the anesthesia system should be purged with a high flow of fresh gas prior to use. This seemed reasonable, particularly because it did not appear that there would be any disadvantage from such a strategy.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 4, Winter 1994-95

4.9 Lentz RE

Following induction, the vital signs were: BP 110/60, HR 95, SaO2=100% (FiO2=40%), Temp 36.5 C.

Approximately 40 minutes into the case, the patient's 02-Hgb saturation decreased to 96% over a period of 2-3 minutes. The pulse oximeter probe was inspected to verify proper placement on the finger. Breath sounds remained equal bilaterally, without wheezes, and there was no change in PIP. The endotracheal tube was also checked for its position, and it was noted to still be secured at 20 cm at the lips. At this point, the patient was placed on 100% 02 and hand ventilated with up to 40 cmH20 pressure. This also failed to bring the patient's O2 saturation above 96%. The surgeon was made aware of these findings and was asked to complete the procedure as quickly as possible.

Arterial blood gases were sent to check the 02 saturation a COHb level was also requested. The blood gas report read the following values: pH 7.46; PC02=28 mm Hg; P02 467 mm Hg; HCO3 20.3 MEq/l; COHB 31.5%. At this point, the patient's 02-Hgb saturation remained at 97%. The surgeon was made aware of the new findings, and the procedure was completed over the next 10 minutes. The entire time interval from when the 02Hgb saturation started to decrease to the completion of the surgery was 30 minutes.

The US FDA Center for Disease Control recommendations regarding this subject matter are as follows:

* All soda lime that has been dormant in the anesthesia machine for more than 24 hours should be changed, and dated.

* In addition to changing the soda lime, the anesthesia machine should also be flushed continuously with 100% 02 for at least one minute prior to the first case of the day.

In any patient who develops the type of hemoglobin desaturation described here and who fails to respond to the usual therapeutic measures used to correct this problem, do not hesitate to send either a venous or, preferably, an arterial blood sample for the possibility of COHB "poisoning' (see article on page 13).

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

4.10 Funk W et al

The aim of our study was to analyse and quantify the substances that a patient might inhale under clinical conditions. Of potential interest were not only gaseous components, but formaldehyde, formic acid and fluorinated products such as fluoric acid (HF), which are known airway irritants produced during sevoflurane degradation.

Our results suggest that the observed airway irritation may be caused primarily by formic acid, which is generated in isomolar concentrations with methanol from formaldehyde (Cannizzaro reaction Fig 5).

In summary, we observed marked degradation of sevoflurane, even in the short amount of time required for inhalation induction, when soda lime was dried, based on handling errors likely to occur in clinical practice. This reaction is aggravated by KOH contained in several carbon dioxide absorbents. Exhaled carbon dioxide slightly attenuates this reaction. Under these conditions, toxicologically meaningful amounts of methanol, formaldehyde, fluoric acid and possibly formic acid reach the T-piece. Thus drying carbon dioxide absorbents should be avoided.

British Journal of Anaesthesia 1999; vol 82; pp193-198

4.11 Murray JM et al

From a patient-safety perspective, widespread adoption of a non-destructive CO2 absorbent should be axiomatic. Assuming a reasonable and only marginally increased cost over currently used absorbents, economic arguments against a non-destructive absorbent should be moot: it represents a minute portion of total perioperative costs and might even be more cost-effective after considering medicolegal implications, potentially revised gas flow rates, and the need to replace desiccated absorbents.

Anesthesiology, V 91, No 5, Nov 1999

4.12 Schuler HG et al

The ability of Amsorb® to prevent anesthetic degradation is sufficiently advantageous to justify its routine clinical use.

Anesthesiology 2001 ; 95:A510

4.13 Stabernack et al

On the other hand, LiOH is much more corrosive than $Ca(OH)_2$ (Amsorb®), and thus, one might have to take greater care in the handling of LiOH. This difference might mandate the use of pre-packaged containers for LiOH.

Anesth Analg 2000;90:1428-35

4.14 Baxter PJ et al

RECOGNITION of carbon monoxide (CO) production in anesthesia circuits resulting from volatile anesthetic degradation has necessitated changes in clinical practice and product labeling. [1-7] Intraoperative CO formation from desflurane, enflurane, and isoflurane has been reported, with CO concentrations exceeding Environmental Protection Agency safety limits. [8] There are no clinical reports of CO formation from halothane or sevoflurane. Prospective analyses have suggested that the incidence of patient CO exposure (> 30 ppm) is 0.46% for the first case of the day (2.9% in remote locations other than operating rooms), and the overall incidence is 0.26%. [4-7] Desflurane, enflurane, and isoflurane degradation to CO occurs when these anesthetics interact with relatively dry barium hydroxide lime and soda lime and is thought to be catalyzed by the strong bases in these carbon dioxide absorbents. [1,3,4,6,9] Practitioners have been cautioned by the Food and Drug Administration to replace carbon dioxide absorbent, which they suspect may be desiccated.

Anesthesiology 1998; vol. 89; pp929-941

4.15 Fang ZX et al

Although no report has indicated that patient harm has resulted from the production of carbon monoxide during general anesthesia, avoidance of such a risk would seem prudent and in the best interest of patient safety.

Anesthesia Patient Safety Newsletter Vol 9, No. 3, 25-36 Fall 1994

4.16 Woehlck HJ

Regarding intraoperative CO poisoning, and with tongue in cheek, I have categorized anesthesia providers into two groups: the Overconcerned and the Apathetic. The Overconcerned may have become so after a patient was actually exposed to CO via anesthetic breakdown. The Overconcerned may note similarities in the care of their machines to those that predispose to CO exposures, or the Overconcerned may just be the worrying sort; forever fearful that some harm may come. Just because one is paranoid does not mean others are not out to get him or her. And then there are the Apathetic. The Apathetic may be overconfident, uninformed, or in denial of the possibility of a problem.

The Overconcerned can reply that in the report by Berry et al.,[1] the patient who attained 36% carboxyhemoglobin had an ASA physical status 1 and was the subject of a clinical study.

Anesthesiology 1999;90:353-359

DIALYZERS, HEMODIALYSIS (11-232)
See: Accession No. A3651, this issue

4.17 Health Devices Alerts™

December 11, 1998 **Number 1998-A50**

ANESTHESIA UNIT ABSORBERS, CARBON DIOXIDE (10-140)

ANESTHESIA UNIT CARBON DIOXIDE ABSORBENTS (17-509)

Devices (1) Anesthesia Unit Carbon Dioxide Absorbents; (2) Anesthesia Unit Carbon Dioxide Absorbers; (3) Semi-closed Circle Anesthesia Systems

Problems: ECRI has investigated several incidents of patient exposure to carbon monoxide (CO); a patient injury resulted in one of the incidents. CO is produced when halogenated anesthetic agents contact commonly used CO_2 absorbents that have become excessively dry due to medical gas flow during lengthy periods (eg, overnight, over a weekend) of anesthesia machine inactivity.

Action Needed: (Note; Refer to the original report, cited below, for the rationale behind the following recommendations.) ECRI recommends the following: (1) Alert anesthesia and other appropriate personnel to the problem and to the referenced document. (2) Ensure that medical gas is turned off when an anesthesia machine will not be promptly used for another procedure. At the end of each day, verify that the gas is off for all machines. (3) Before performing a pre-use check for the first case of the day, determine if there is any flow of medical gas. If there is, replace the absorbent material in both absorbent canisters before using the machine. Identify and address the cause of the gas flow. If you have any questions regarding these recommendations, contact ECRI at (610) 825-6000

Source: ECRI Carbon Monoxide exposure during inhalation anesthesia; the interaction between halogenated anesthetic agents and carbon dioxide absorbers [hazard report].

Health Devices 1998 Nov, 27 (11): 402-4

Accession No.: A3649

ANESTHESIA UNITS (10-134)

See: Accession No. A3649, this issue

DIALYZERS, HEMODIALYSIS (11-232)

See: Accession No. A3651, this issue

ECRI PROBLEM REPORTING SYSTEM

HAZARD REPORT

Carbon Monoxide Exposures during inhalation Anesthesia: The interaction between Halogenated Anesthetic Agents and Carbon Dioxide Absorbents

Anesthesia Unit Absorbers, Carbon Dioxide (10-140)
Anesthesia Unit Carbon Dioxide Absorbents (17-509)
Anesthesia Units (10-134)

Problem

ECRI has investigated several incidents of patient exposure to carbon monoxide (CO) during the administration of inhalation anesthetics through semi-closed circle anesthesia systems. In each case, after ruling out other possible sources of CO, we concluded that dangerous levels of the gas were generated within the anesthesia system under the conditions present during the incidents. These conditions included the presence of excessively dry carbon dioxide (CO_2) absorbent in an anesthesia system being used to deliver halogenated anesthetic agents for the first case of the day.

Similar incidents have been reported in the literature, with one common characteristic being the timing of the exposures. Many incidents have occurred during Monday morning cases, and all appear to be associated with the first delivery of an anesthetic after a lengthy period (eg, overnight, over a weekend) of anesthesia machine inactivity.

Background

The Dangers of Carbon Monoxide Exposure

Carbon monoxide is very toxic, even in low concentrations. Once in the blood, CO binds tightly with hemoglobin, forming carboxyhemoglobin and diminishing the ability of hemoglobin to transport and release oxygen. The level of CO exposure will be a function of both the inhaled concentration and the exposure duration. The specific effect on the patient will very depending on the patient's cardiovascular condition and the level of oxygen administered before and during administration of the anesthetic.

Circle Anesthesia Systems and Carbon Dioxide Absorbers

To understand how CO exposures can occur, readers will need a basic understanding of circle anesthesia systems and the role of CO_2 absorbers within these systems. Inhalation anesthetics are usually administered through semi-closed circle anesthesia systems, although closed circle systems are sometimes used. In either type of circle anesthesia system, some portion of the gas exhaled by the patient is re-circulated through the system and back to the patient, thus conserving medical gases, vaporous anesthetics and expired water vapor.

To prevent dangerous levels of CO_2 from accumulating in the re-circulating gas mixture, anesthesia machines that employ circle systems include an integral CO_2 absorber to remove the CO_2 exhaled by the patient. These absorbers typically consist of two stacked canisters containing granular absorbent materials that chemically neutralize CO_2 as the exhaled gas passes through. Commonly used absorbent materials include soda lime (eg Sodasorb) and barium hydroxide lime (eg Baralyme). When the ability of these materials to neutralise CO_2 becomes exhausted the absorbent is replaced. For most absorbents, the current basis for determining when replacement is needed is the change in color of a pH indicator impregnated in the absorbent material.

Discussion

Although the exact chemical mechanism by which CO can generated is not clear, published studies have indicated that a reaction between halogenated anesthetic agents and commonly used CO_2 absorbents can produce CO if the CO_2 absorbent is excessively dry. Drying out of the absorbent material can occur when (1) an anesthesia machine has been sitting idle, such as over a weekend, and (2) there is a continuous flow of medical gas (which is very dry) through the CO_2 absorber. When dry, the absorbent becomes highly reactive in the presence of certain halogenated agents, resulting in the production of CO as the agent flows through the machine's CO_2 absorber. Desflurane (Suprane) appears to be the most reactive of the halogenated anesthetic agents, although other agents – particularly enflurane and Isoflurane – have also been reported to produce CO. The reaction between the agent and the absorbent material can continue for many minutes.

Complicating matters is the fact that identifying patient exposure to CO when it does occur can be difficult because carboxyhemoglobin levels are not monitored during anesthesia. Monitoring devices such as pulse oximeters and blood gas analysers are not intended to detect carboxyhemoglobin; in fact, pulse oximeters will usually detect carboxyhemoglobin as oxyhemoglobin. Similarly, medical mass spectrometers are not configured to detect CO. And while whole blood co-oximeters can distinguish carboxyhemoglobin from oxyhemoglobin, these devices require a fresh blood sample and cannot provide real-time monitoring. As a result, CO exposure may go undiscovered unless patient morbidity leads to a comprehensive clinical and device investigation.

In the cases investigated by ECRI, anesthetists identified all the incidents of CO exposure indirectly. For example, in the incident that resulted in an injury, the patient's pulse oximetry readings had become erratic, but the heart rate and ECG waveform remained normal. After the same results were obtained using another pulse oximeter (of the same model) and a new probe, blood was drawn for a blood gas analysis, which revealed a high partial pressure of oxygen (PaO_2>600mm Hg). Suspecting a problem with the anesthesia machine, the staff switched to a different machine. The blood sample was then analysed by co-oximetry, which revealed a carboxyhemoglobin level of 60% to 70% (values that grossly exceed normal levels); thus, the cause of the patient's condition was determined to be CO exposure.

One further complication is that it can be difficult to determine when CO exposure is likely to occur because there appears to be no readily available, convenient, or reliable means of monitoring moisture within an absorber or of re-hydrating absorbent that has dried out. Thus, to prevent the conditions under which CO can be produced from developing, users will need to ensure that the absorbent does not dry out. To do this, they need to ensure that the flow ofmedical gas is discontinued whenever an anesthesia machine is not in use on a patient; it is particularly important that the gas flow be stopped at the end of the workday.

Conclusions

It should be stressed that the reactions that produce CO within an anesthesia system do not occur while the machine is idle; rather, they occur only when agent vapor flows through the absorber. Therefore, flushing the breathing circuit with fresh gas before use (such as during a pre-use check) will not prevent or relieve the problem. It should also be stressed that CO exposures are unlikely to be detected intraoperatively; thus, healthcare facilities need to ensure that the conditions under which CO can be produced during inhalation anesthesia do not occur. Specifically, users must be sure to discontinue the flow of medical gas whenever an anesthesia machine will not be promptly used on another patient. ECRI recommends that the absorbent material in both canisters of an absorber be replaced whenever there is reason to believe that a machine has been left idle with gas flowing for an undetermined time. Fresh absorbent materials are sufficiently hydrated and normally remain hydrated by exhaled water vapor in the circle system, thereby preventing reaction with halogenated agents.

There is still much to be learned both chemically and clinically about the phenomenon of CO production associated with the interaction of halogenated anesthetic agents and CO2 absorbent materials. ECRI will continue to assess relevant new findings in the medical literature and to evaluate changes in anesthesia monitoring and delivery systems. Given the present technology and knowledge of the problem, all efforts to prevent CO exposure must be directed at detecting and protecting against unintended medical gas flow when anesthesia systems are not in use.

Recommendations

1) Alert anesthesia and other appropriate personnel to the problem and to our report.
2) Ensure that medical gas is turned off when an anesthesia machine will not be promptly used for another procedure. At the end of every day, verify that the gas is off for all machines.
3) Before performing a pre-use check for the first case of a day, determine if there is any flow of medical gas. If there is, replace the absorbent material in both absorbent canisters before using the machine. Identify and address the cause of the gas flow.

Health Devices - November 1998 – Vol. 27, No. 11

4.18 Abbott Labs Brief Summary - Sevoflurane

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

ULTANE®

sevoflurane

volatile liquid for inhalation

INDICATIONS AND USAGE

Sevoflurane is indicated for induction and maintenance of general anesthesia in adult and pediatric patients for inpatient and outpatient surgery.

Sevoflurane should be administered only by persons trained in the administration of general anesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available. Since level of anesthesia may be altered rapidly, only vaporizers producing predictable concentrations of sevoflurane should be used.

CONTRAINDICATIONS

Sevoflurane can cause malignant hyperthermia. It should not be used in patients with known sensitivity to sevoflurane or to other halogenated agents nor in patients with known or suspected susceptibility to malignant hyperthermia.

WARNINGS

Although data from controlled clinical studies at low flow rates are limited, findings taken from patient and animal studies suggest that there is a potential for renal injury which is presumed due to Compound A. Animal and human studies demonstrate that sevoflurane administered for more than 2 MAC•hours and at fresh gas flow rates of <2 L/min may be associated with proteinuria and glycosuria.

While a level of Compound A exposure at which clinical nephrotoxicity might be expected to occur has not been established, it is prudent to consider all of the factors leading to Compound A exposure in humans, especially duration of exposure, fresh gas flow rate, and concentration of sevoflurane. During sevoflurane anesthesia the clinician should adjust inspired concentration and fresh gas flow rate to minimize exposure to Compound A. To minimize exposure to Compound A, sevoflurane exposure should not exceed 2 MAC•hours at flow rates of 1 to <2 L/min. Fresh gas flow rates <1 L/min are not recommended.

Because clinical experience in administering sevoflurane to patients with renal insufficiency (creatinine >1.5 mg/dL) is limited, its safety in these patients has not been established.

Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The safety of low flow sevoflurane on renal function was evaluated in patients with normal preoperative renal function. One study compared sevoflurane (N=98) to an active control (N=90) administered for ≥2 hours at a fresh gas flow rate of ≤1 Liter/minute. Per study defined criteria (Hou et al.) one patient in the sevoflurane group developed elevations of creatinine, in addition to glycosuria and proteinuria. This patient received sevoflurane at fresh gas flow rates of ≤800 mL/minute. Using these same criteria, there were no patients in the active control group who developed treatment emergent elevations in serum creatinine.

Ref 58-6547-R7-Rev Aug 2001 Abbott Labs 2001

Consensus Statement Agreed Upon

"Absorbents," From Preceding Page

One absorbent provides a graded and permanent colorimetric indicator of both expected desiccation and exhaustion (Amsorb® Plus, Armstrong Medical Ltd.), while another (Spherasorb®, Intersurgical Ltd.) contains a substance that delays the total desiccation of the absorbent. Reducing by-products to negligible levels does not require strong-base-free absorbents.

The incidence of patient exposure to carbon monoxide is unknown. ECRI, Abbott Laboratories, and other investigators have already published recommendations to minimize the risk of unintended desiccation of absorbents. Anesthesia machine manufacturers are aware that fresh gas flow through modern and unique breathing circuits may promote desiccation of absorbent in different ways. Clinicians are directed to those resources for detailed information.

Monitoring absorbent temperature is one potentially useful adjunct, but the critical location of the probe and the quantity of heat that is worrisome have not been clearly identified. Temperature is elevated during normal carbon dioxide absorption reactions, and varies widely throughout the absorbent. Furthermore, carbon monoxide can still be produced at temperatures that might otherwise be associated with normal absorption. Relative humidity of the gas flowing out of the absorbent may be directly related to, and therefore indicate, its moisture content. Simple (home) devices to measure carbon monoxide are disrupted in the presence of volatile agents, but more sophisticated monitors are available. Some desiccated absorbents will continue to absorb carbon dioxide; therefore, the presence of an acceptable capnographic waveform should not be taken as confirmation that the breathing gas is free from carbon monoxide. Alternatively, an elevated baseline of inspired carbon dioxide on the capnogram should alert the clinician to the possibility of desiccation and/or exhaustion.

Consensus Statement

At the conclusion of this conference, attendees were asked to again consider the goal of the conference, ***"to develop a consensus statement to share with anesthesia professionals on the use of carbon dioxide absorbents so as to reduce the risk of adverse interactions with volatile anesthetic drugs,"*** and make appropriate recommendations. Based on those responses, the APSF drew the following conclusions:

The APSF recommends use of carbon dioxide absorbents whose composition is such that exposure to volatile anesthetics does not result in significant degradation of the volatile anesthetic.

The APSF further recommends that there should be institutional, hospital, and/or departmental policies regarding steps to prevent desiccation of the carbon dioxide absorbent should they choose conventional carbon dioxide absorbents that may degrade volatile anesthetics when absorbent desiccation occurs.

In such circumstances of using absorbents that may degrade volatile anesthetics, conference attendees generally agreed that users could take the following steps, consistent with ECRI recommendations:

1. Turn off all gas flow when the machine is not in use.
2. Change the absorbent regularly, on Monday morning for instance.
3. Change absorbent whenever the color change indicates exhaustion.
4. Change all absorbent, not just 1 canister in a 2-canister system.
5. Change absorbent when uncertain of the state of hydration, such as if the fresh gas flow has been left on for an extensive or indeterminate time period.
6. If compact canisters are used, consider changing them more frequently.

There was also support for the APSF to create an "Expert Task Force" to define further the characteristics of carbon dioxide absorbents that do not significantly degrade volatile anesthetics.

Table 1. Invited Medical Experts, APSF, and Industry Representatives

Medical Experts	
Jerry A. Dorsch, MD Jacksonville, FL	Edmond I Eger, II, MD Professor of Anesthesiology University of California, San Francisco, CA
Evan D. Kharasch, MD, PhD Professor of Anesthesiology University of Washington School of Medicine Seattle, WA	Harvey J. Woehlck, MD Professor of Anesthesiology Medical College of Wisconsin Milwaukee, WI
Anesthesia Patient Safety Foundation	
Robert C. Morell, MD Editor, *APSF Newsletter*	Michael A. Olympio, MD Chair, APSF Committee on Technology Co-moderator of Conference
George A. Schapiro Executive Vice President	Robert K. Stoelting, MD President Co-moderator of Conference
Industry Representatives	
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Dr. Olympio is Professor of Anesthesiology, former Director and Founder of the Patient Simulation Laboratory, and former Vice Chair for Education for the Department of Anesthesiology at Wake Forest University School of Medicine in Winston-Salem, NC. He is also Chair of the APSF Committee on Technology and serves on the APSF Executive Board as well.

Recommended References

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3. Fatheree RS, Leighton BL. Acute respiratory distress syndrome after an exothermic Baralyme-sevoflurane reaction. *Anesthesiology* 2004;101:531-3.
4. Wu J, Previte JP, Adler E, et al. Spontaneous ignition, explosion, and fire with sevoflurane and barium hydroxide lime. *Anesthesiology* 2004;101:534-7.

See "Absorbents," Next Page

Editor's Note: *There is not uniform agreement among experts as to the specific types and amounts of degradation products that may form when volatile anesthetics are exposed to desiccated absorbents that contain significant amounts of KOH and NaOH. Hence, no specific conclusions can be drawn from this conference about the relative contribution of any specific degradation product or circuit material (including plastics) as a combustible fuel in a high heat, oxygen-enriched environment.*

APSF Newsletter Summer 2005, vol. 20, No. 2, pp. 25, 27-29

ADSORPTION

5.1	Knolle E et al
5.2	Funk W et al
5.3	Grodin WK et al
5.4	Kharasch ED et al
5.5	Stabernack CR et al
5.6	Versichelen LFM et al
5.7	Magee CD et al
5.8	O Ahmed, S Mannion

5.1 Knolle E et al

The largest isoflurane loss (89% ± 5%) took place in LoFloSorb, but the level of CO formation in this absorbent was among the smallest.

With Amsorb (containing no alkali hydroxide), the elapsed time of 15 ± 3 min was the shortest, whereas with LoFloSorb (also with no alkali hydroxide) and Baralyme (containing KOH), the outlet isoflurane concentration had not reached 0.4% by the end of the experimental period of 60 min.

Unexpectedly, isoflurane loss did not correlate with CO formation, and there was a relatively large isoflurane loss in LoFloSorb (89% of the inlet isoflurane).

Table 2. Characteristics of CO Formation During Passage of 0.5% Isoflurane

	Sample (brand)										
		Group 1		Group 2				Group 3			
Variable	A Baralyme	B Dragersorb 800	A-B	C Dragersorb 800 Plus	D Intersorb	E Spherasorb	C-E	F LoFloSorb	G Superia	H (Amsorb)	F-H
CO (mL)	223 ± 6	140 ± 12	181 ± 45	66±3	73 ± 3	49 ± 4	63 ± 11	8 ± 2	3 ± 2	0	4 ± 4
CO_{Mean}(ppm)	730 ± 20	458 ± 39	594 ± 146	218 ± 9	239 ± 10	162 ± 13	206 ± 35	26 ± 5	9 ± 5	0	12 ± 12
CO_{Max}(ppm)	875 ± 34	737 ± 49	806 ± 83	620 ± 17	548 ± 23	281 ± 18	483 ±152	38 ± 8	13 ± 7	-	25 ± 15
T_{COMax}(min)	24 ± 2	18 ± 1	21 ± 4	10 ± 1	12 ± 1	23 ± 1	15 ± 7	50 ± 2	25 ± 1	-	37 ± 13
$Temp_{Baseline}$(°C)	24.8±0.5	27.3 ± 1.2	26.1±1.6	26.3 ± 0.7	25.9±0.3	25.4 ± 0.2	25.9±0.6	24.8 ± 0.2	25.8 ± 0.3	26.2 ± 0.3	25.6±0.7
$Temp_{Max}$(°C)	27.7±4.2	32.0 ± 0.8	29.8±3.6	27.8 ± 0.6	27.4±0.12	26.9 ± 0.2	27.4±0.5	24.9 ± 0.2	26.2 ± 0.5	26.3 ± 0.3	25.8±0.8
$Temp_{Mean}$(°C)	25.4±1.1	28.7 ± 0.4	27.0±1.9	27.2 ± 0.5	26.6±0.05	25.9 ± 0.1	26.6±0.6	24.5 ± 0.1	25.9 ± 0.3	26.1 ± 0.2	25.5±0.8
ISO_{Loss}(%)	63 ± 1	36 ± 1	50 ± 15	26 ± 3	31 ± 1	50 ± 2	36 ± 11	89 ± 5	41 ± 2	20 ± 4	50 ± 15
$T_{ISO<0.4\%}$(min)	>60	38 ± 2		16 ± 2	20 ± 0	33 ± 1		>60	26 ± 4	15 ± 3	
$T_{ISO<0.4\%}$(min) (fresh soda lime)	<1, <1	1, 1		1, 1	<1, 1	1, 2		2, 2	1, 1	1, 1	

CO = carbon monoxide; ISO = Isoflurane

5.2 Funk W et al

With dry soda lime, sevoflurane was not detected at the T-piece for 3 min and reached 6-7% within 6-10 min.

British Journal of Anaesthesia 1999; vol 82, pp193-198

5.3 Grodin WK et al

The authors demonstrated that soda lime will adsorb enflurane or isoflurane as a function of the water content of the soda lime. Various volumes of liquid enflurane or isoflurane were placed in an equilibration flask containing fresh (15% water by weight) or dried soda lime and the vapor phase anesthetic concentrations plotted. When dry soda lime was used, the plot of concentration as a function of volume of liquid added was biphasio: initially flat and then rising linearly. This is qualitatively similar to data reported previously for halothane. The authors hypothesize that drying soda lime produces a molecular sieve-like structure, as absorption is greatest for molecules with small carbon chains lengths and kinetic diameters, or with structural characteristics such as cis/trans isomerism, which effectively reduce molecular size.

Anesthesiology 1985; Vol 62(1) pp60-64

5.4 Kharasch ED et al

However, there was a considerable spread between fresh gas and postabsorbent or end-tidal sevoflurane concentrations with dehydrated absorbents, which was smallest with Amsorb®. This is similar to laboratory findings of lesser sevoflurane degradation by desiccated Amsorb® compared with sodalime and Baralyme®.[29]

Anesthesiology, V 96, No 1, Jan 2002

5.5 Stabernack CR et al

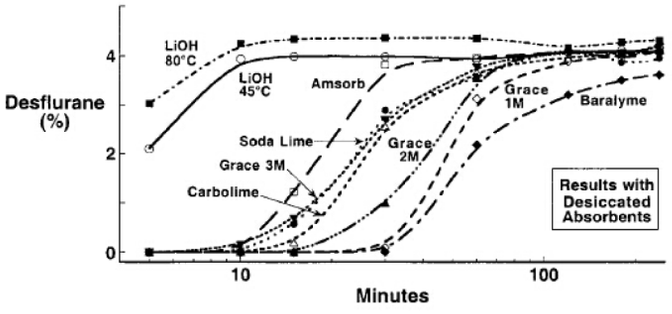

Figure 1. Desflurane, at a concentration of approximately 4.3% and a flow rate of 25 mL/min, was directed through approximately 21 g of desiccated absorbents (15 g of lithium hydroxide [LiOH]) at a temperature of 45°C (except for LiOH where an additional study at 80°C was done) and the outflow concentration of desflurane was measured. Except for LiOH, all desiccated absorbents eliminated desflurane (i.e., completely degraded the anesthetic) from the outflow for 10–30 min. Desflurane output as a fraction of input at 240 min was between 0.95 and 1.0, except for Baralyme® (Chemetron) where it was 0.85.

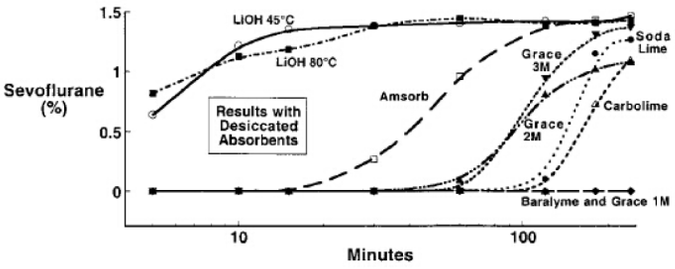

Figure 3. Sevoflurane, at a concentration of approximately 1.5% and a flow rate of 25 mL/min, was directed through approximately 21 g of desiccated absorbents (15 g for lithium hydroxide [LiOH]) at a temperature of 45°C (except for LiOH where an additional study at 80°C was done) and the outflow concentration of sevoflurane was measured. Except for LiOH, all desiccated absorbents eliminated sevoflurane from the outflow for 15–240 min (Fig. 3). An appreciable concentration of sevoflurane appeared in the first outflow sample from LiOH. The order of appearance of sevoflurane from other absorbents was Amsorb® (Armstrong Medica), Grace 3M and 2M, and finally soda lime and Carbolime® (Chemetron). Both Baralyme® (Chemetron) and Grace 1M contained the greatest amounts of KOH and prevented the appearance of sevoflurane at any time. Despite this degradation of sevoflurane, only minimal concentrations of Compound A appeared in the outflow (data not shown).

Anesth Analg 2000;90:1428-35

5.6 Versichelen LFM et al

An interesting finding is also that the amount of liquid sevoflurane injected in the system to generate a stable end-tidal concentration of sevoflurane was significantly less ($P < 0.05$) in the presence of Amsorb than with all the other absorbents.

Anesthesiology, V 95, No 3, Sep 2001

5.7 Magee et al

New Generation Non-Soda Lime Absorbents:

Factors Affecting Patient Safety During Inhalational Anaesthesia; in vitro evaluation of AMSORB® PLUS and LoFloSorb®

Short Summary

AMSORB PLUS and LoFloSorb carbon dioxide (CO_2) absorbents for anaesthesia varied in respect to carbon monoxide (CO) production, anaesthetic agent adsorption and CO_2 absorption capacity in an anaesthesia simulation model. Fresh, partially-desiccated and fresh-desiccated LoFloSorb produced small amounts of CO but markedly adsorbed or eliminated anaesthetic vapour in the order isoflurane → sevoflurane → desflurane with significant adsorption occurring during simultaneous absorption of CO_2 in the first 20 minutes of simulation. Fresh-desiccated LoFloSorb adsorbed 57% of 4% sevoflurane for 74 minutes and 48% of 4% isoflurane for 62 minutes, whereas fresh desiccated AMSORB PLUS adsorbed 19% for 24 minutes and 3% for 5 minutes respectively. Fresh LoFloSorb caused a delay in reaching 90% (3.6%) of 4% sevoflurane for 37 minutes and took 38 minutes to reach 90% (1.8%) of 2% isoflurane whereas AMSORB PLUS took 8 minutes and 6 minutes respectively. LoFloSorb appeared to possess greater adsorption capability with desflurane, when partiallydesiccated, compared to when fresh-desiccated. Fresh-desiccated and partially-desiccated LoFloSorb absorbed 45% and 90% less CO_2 respectively than fresh and partially-desiccated AMSORB PLUS. There were also differences in respect to the rate at which both absorbents became desiccated by oxygen, with LoFloSorb only marginally more resistant to desiccation compared to AMSORB PLUS. Suitability of LoFloSorb for inhalational anaesthesia should be evaluated by users in respect of their requirements for patient safety and CO_2 absorption capacity. Further research should consider what happens to anaesthetic vapour that has become adsorbed and whether potential exists for revapourisation of this vapour at some further point, perhaps triggered by an increase in absorbent temperature caused by the exothermic reaction of absorption of CO_2 and whether such unintentional anaesthetic vapourisation poses risk to patients or creates erroneous patient monitoring data.

Abstract

Desiccated soda lime degrades halogenated anaesthetics to carbon monoxide (CO), formaldehyde, methanol, dimethoxymethane and vinyl ethers of which Compound A production, resulting from interaction with sevoflurane, has been described[1]. Some desiccated absorbents may concurrently adsorb anaesthetic vapour, in phenomena first described by Grodin2. All commercially available medical CO_2 absorbents use calcium hydroxide lime ($Ca(OH)_2$) as the neutralising base for carbon dioxide (CO_2) produced during anaesthesia respiration. Absorbents differ in minor ingredients, included as absorption catalysts and hardeners, of which sodium hydroxide (NaOH) is common. These ingredients are known to compromise the proper functioning of the absorbent, under specific conditions and with specific types of absorbent. Water is an essential ingredient, common to all absorbents, and is necessary for efficient CO_2 absorption and, in the case of some absorbents, for avoiding

5.8 O Ahmed, S Mannion

Results and Discussion:

The total costs over each four week period were €4375.69 and €3150.94 for soda lime and Amsorb® respectively. Reduced cost during Amsorb® period were due to 1) less sevoflurane consumption 2) fewer Amsorb® changes because of reliable colour change, and 3) cheaper domestic waste disposal of Amsorb® as it is inert.

Conclusion

We demonstrated Amsorb® to be a cost efficient alternative to soda lime in everyday clinical practice.

Cost comparison between soda lime and Amsorb®.

	Soda lime	**Amsorb®**	**P-Value**
Number of GAs	231 patients	236 patients	
Product used and cost	34 canisters	14 canisters	0.006 (number of canisters)
	€505.24 (€14.86/canister)	€296.38 (€21.17/canister)	
Sevoflurane bottles (250mls) and cost	35 bottles	26 bottles	0.22 (number of bottles)
	€3839.85 (€109.71/bottle)	€2852.46 (€109.71/bottle)	
Waste and cost	34 kilograms	14 kilograms	0.006 (kgs)
	€30.6 (€0.9/kg*)	€2.1 (€0.15/kg^)	
Total cost (4 weeks)	**€4375.69**	**€3150.94**	

*Sodalime is disposed in healthcare waste ^Amsorb® is disposed in domestic waste

European Journal of Anaesthesiology June 2011-volume 28-issue-P12-13

DELAYED INDUCTION

6.1	Kharasch ED et al
6.2	Versichelen LFM et al
6.3	Versichelen LFM et al

DELAYED INDUCTION

6.1 Kharasch ED et al

Amsorb® would have the least potential to delay inhalation induction. Similarly, the cost of anesthetic degradation by dehydrated absorbent would be lowest with Amsorb®.

Anesthesiology, V 96, No 1, Jan 2002

6.2 Versichelen LFM et al

This study shows that Amsorb has the least potential to delay induction.

Conference Notes, ALFA Congress 2002, Pisa Italy

6.3 Versichelen LFM et al

An interesting finding is also that the amount of liquid sevoflurane injected in the system to generate a stable end-tidal concentration of sevoflurane was significantly less ($P < 0.05$) in the presence of Amsorb than with all the other absorbents.

Anesthesiology, V 95, No 3, Sep 2001

PULSE OXIMETRY

7.1	Frink EJ et al
7.2	Moon RE
7.3	Berry PD et al
7.4	Lentz RE
7.5	ECRI Hazard Report

PULSE OXIMETERY

7.1 Frink EJ et al

Carbon monoxide is not readily detected by conventional end-tidal agent monitors. Pulse oximetry does not reliably change with the presence of carboxyhemoglobin, because the absorbance spectrum of carboxyhemoglobin is similar to that of oxyhemoglobin at 660 nm. It has been observed that in dogs, even with carboxyhemoglobin concentrations of 70%, the pulse oximetry monitor will record a saturation rate of 90% or more. In adults, unless a co-oximetry blood gas analysis is performed, the presence of carboxyhemoglobin will not be detected reliably.

Anesthesiology V87, No 2 Aug 1997

7.2 Moon RE

CO poisoning during anesthesia is unlikely to be diagnosed using commonly employed monitors. COHB is not easily detected by dual wavelength devices such as pulse oximeters. Studies in dogs' and observations in patients (2) have indicated that high COHB levels result in only a trivial reduction in SaO2 measured by pulse oximetry. Detection of gaseous CO is also difficult. Dedicated CO analyzers most commonly use either electrochemical techniques or infrared absorption. However, the infrared absorption spectrum of CO is different from that of C02, and in concentrations likely to be present in cases of CO poisoning (0.05 0.1%), would not significantly alter the reading on clinical capnographs. CO has a molecular weight of approximately 28, and with commonly used mass spectrometers cannot be distinguished from nitrogen. The only reliable method of detection is direct measurement of blood COHB.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

7.3 Berry PD et al

We present the most severe case of intraoperative carbon monoxide exposure yet reported, in which the diagnosis was suggested by a combination of moderately decreased oxygen saturation by pulse oximetry (SpO2) and an erroneous gas analyzer reading.

A second important diagnostic feature of our case was the observed moderate decrease in SpO2 without other identifiable causes. It is widely believed that SpO2 remains unchanged during carbon monoxide toxicity, with COHb being detected as HbO2 by

most pulse oximeters.14,15 Our case, however, suggests that significant COHb concentrations may moderately decrease SpO2. This is consistent with animal studies in which SpO2 decreased with high COHb concentrations,16 with a COHb concentration of 70% producing a SpO2 of 90%.

Anesthesiology 1999;90:613-616

7.4 Lentz RE

Following induction, the vital signs were: BP 110/60, HR 95, SaO2=100% (FiO2=40%), Temp 36.5 C.

Approximately 40 minutes into the case, the patient's 02-Hgb saturation decreased to 96% over a period of 2-3 minutes. The pulse oximeter probe was inspected to verify proper placement on the finger. Breath sounds remained equal bilaterally, without wheezes, and there was no change in PIP. The endotracheal tube was also checked for its position, and it was noted to still be secured at 20 cm at the lips. At this point, the patient was placed on 100% 02 and hand ventilated with up to 40 cmH20 pressure. This also failed to bring the patient's O2 saturation above 96%. The surgeon was made aware of these findings and was asked to complete the procedure as quickly as possible.

Arterial blood gases were sent to check the 02 saturation a COHb level was also requested. The blood gas report read the following values: pH 7.46; PC02=28 mm Hg; P02 467 mm Hg; HCO3 20.3 MEq/l; COHB 31.5%. At this point, the patient's 02-Hgb saturation remained at 97%. The surgeon was made aware of the new findings, and the procedure was completed over the next 10 minutes. The entire time interval from when the 02Hgb saturation started to decrease to the completion of the surgery was 30 minutes.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

7.5 ECRI PROBLEM REPORTING SYSTEM

Hazard Report

In fact, pulse oximeters will usually detect carboxyhemoglobin as oxyhemoglobin. And while whole blood co-oximeters can distinguish carboxyhemoglobin from oxyhemoglobin, these devices require a fresh blood sample and cannot provide real-time monitoring.

In the incident that resulted in an injury, the patient's pulse oximetry readings had become erratic, but the heart rate and ECG waveform remained normal.

Health Devices – November 1998 – Vol. 27, No.11

FDA

8.1	Baxter PJ et al
8.2	Kharasch ED et al
8.3	Di Filippo et al
8.4	Abbott Labs Brief Summary - Sevoflurane

8.1 Baxter PJ et al

RECOGNITION of carbon monoxide (CO) production in anesthesia circuits resulting from volatile anesthetic degradation has necessitated changes in clinical practice and product labeling. [1-7] Intraoperative CO formation from desflurane, enflurane, and isoflurane has been reported, with CO concentrations exceeding Environmental Protection Agency safety limits. [8] There are no clinical reports of CO formation from halothane or sevoflurane. Prospective analyses have suggested that the incidence of patient CO exposure (> 30 ppm) is 0.46% for the first case of the day (2.9% in remote locations other than operating rooms), and the overall incidence is 0.26%. [4-7] Desflurane, enflurane, and isoflurane degradation to CO occurs when these anesthetics interact with relatively dry barium hydroxide lime and soda lime and is thought to be catalyzed by the strong bases in these carbon dioxide absorbents. [1,3,4,6,9] Practitioners have been cautioned by the Food and Drug Administration to replace carbon dioxide absorbent, which they suspect may be desiccated.

Anesthesiology 1998;89:929-941

8.2 Kharasch ED et al

Anesthetic degradation and associated concerns regarding patient safety have necessitated changes in clinical practice and product labeling and have been the focus of more than 100 laboratory and clinical reports, several editorials in this journal,[9–13] scholarly debates, public and private arguments and letters, anesthetic manufacturers' marketing and lobbying campaigns, and hearings by the Food and Drug Administration and international regulatory agencies.

Use of a nondestructive CO_2 absorbent could lead the Food and Drug Administration to revise its warnings about volatile anesthetic degradation. These changes may affect us all.

Anesthesiology, V 91, No 5, Nov 1999

8.3 Di Filippo et al

Compound A production correlates directly with Sevoflurane concentrations in the anaesthesia circuit [3], it increases by raising the temperature of the absorbents [3] and it is reduced by their humidity [4].

For these reasons The Food and Drug Administration doesn't approve the use of Sevoflurane at flows lower than 2L/min.

Applied Cardiopulmonary Pathophysiology 9: 103-106, 2000

8.4 Abbott Labs Brief Summary - Sevoflurane

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

ULTANE®

sevoflurane

volatile liquid for inhalation

INDICATIONS AND USAGE

Sevoflurane is indicated for induction and maintenance of general anesthesia in adult and pediatric patients for inpatient and outpatient surgery.

Sevoflurane should be administered only by persons trained in the administration of general anesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available. Since level of anesthesia may be altered rapidly, only vaporizers producing predictable concentrations of sevoflurane should be used.

CONTRAINDICATIONS

Sevoflurane can cause malignant hyperthermia. It should not be used in patients with known sensitivity to sevoflurane or to other halogenated agents nor in patients with known or suspected susceptibility to malignant hyperthermia.

WARNINGS

Although data from controlled clinical studies at low flow rates are limited, findings taken from patient and animal studies suggest that there is a potential for renal injury which is presumed due to Compound A. Animal and human studies demonstrate that sevoflurane administered for more than 2 MAC•hours and at fresh gas flow rates of <2 L/min may be associated with proteinuria and glycosuria.

While a level of Compound A exposure at which clinical nephrotoxicity might be expected to occur has not been established, it is prudent to consider all of the factors leading to Compound A exposure in humans, especially duration of exposure, fresh gas flow rate, and concentration of sevoflurane. During sevoflurane anesthesia the clinician should adjust inspired concentration and fresh gas flow rate to minimize exposure to Compound A. To minimize exposure to Compound A, sevoflurane exposure should not exceed 2 MAC•hours at flow rates of 1 to <2 L/min. Fresh gas flow rates <1 L/min are not recommended.

Because clinical experience in administering sevoflurane to patients with renal insufficiency (creatinine >1.5 mg/dL) is limited, its safety in these patients has not been established.

Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The safety of low flow sevoflurane on renal function was evaluated in patients with normal preoperative renal function. One study compared sevoflurane (N=98) to an active control (N=90) administered for ≥2 hours at a fresh gas flow rate of ≤1 Liter/minute. Per study defined criteria (Hou et al.) one patient in the sevoflurane group developed elevations of creatinine, in addition to glycosuria and proteinuria. This patient received sevoflurane at fresh gas flow rates of ≤800 mL/minute. Using these same criteria, there were no patients in the active control group who developed treatment emergent elevations in serum creatinine.

Ref 58-6547-R7-Rev Aug 2001 Abbott Labs 2001

IN VIVO

9.1	Moon RE
9.2	Kharasch ED et al
9.3	Frink EJ et al
9.4	Di Filippo A et al
9.5	Higuchi H et al
9.6	Ebert TJ et al
9.7	Berry PD et al
9.8	Lentz R
9.9	Mchaourab A et al

IN VIVO

9.1 Moon RE

The case reported by Dr. Lentz is similar to a number of others which have occurred in at least three other institutions in this country. Our own experience at Duke Medical Center dates back to January of 1990, at which time a 76-year-old nonsmoking female was undergoing general anesthesia for thyroid resection. It is the policy of our Blood Gas Lab to do co-oximetry on all samples sent for blood gas analysis. An arterial catheter had been inserted preoperatively and 25 minutes after anesthesia induction, a routine ABG sample was sent to the laboratory. Carboxyhemoglobin (COHB) level was 9.1%. SaO2 by pulse oximetry was 99 100% throughout the anesthetic. Another blood gas was sent an hour after the first one and the COHB level was 28%. Upon receipt of this result, another sample was sent and the COHB level was 29%.

The second case became evident about six weeks later when a patient undergoing total hip replacement under general anesthesia had a COHB level of 24.7%. Similar investigations were carried out; no source was found. However, the anesthesia circuit had been left in place and, using an electrochemical CO monitor, it was noted that gas exiting the Sodasorb canister had a CO concentration > 500 ppm. Heating of one of the two soda lime canisters liberated high levels of CO.

A total of eight instances occurred at Duke Medical Center. After publication of an ASA abstract, we were immediately contacted by Dr. Ed Brunner at Northwestern and Dr. Chuck Ingram at Emory, reporting, respectively, three and eighteen similar cases with COHB levels ranging from 8.5 to 32%. Many of the cases had baseline measurements and therefore a documented rise in COHB during anesthesia.

Endogenous CO Production

A report by Middleton published in 196511 demonstrated high CO levels within the anesthetic circuits in patients anesthetized using low flow. The authors attributed these levels to endogenous production of CO from hemoglobin breakdown. COHB measurements were not reported. Accelerated erythrocyte breakdown (e.g. hemolysis, blood transfusion) causes increased endogenous CO production and it is possible that under certain conditions exhaled CO concentrations could reach toxic levels.

Anesthesia Patient Safety Foundation Newsletter 1994; vol. 09; pp13-14

9.2 Kharasch ED et al

For desflurane and Isoflurane, the order of inspired CO and COHb formation was dehydrated Baralyme® >> soda lime > Amsorb®. For desflurane and Baralyme®
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®.

Fourteen mixed-breed farm pigs of both sexes (16-25kg; mean, 21kg) were used.

The current investigation, using a clinically relevant animal model, demonstrates that Amsorb® 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®, there seems to be less need to replace Amsorb® at arbitrary time intervals or to discard Amsorb® that has become desiccated before exhaustion of CO_2 scavenging capacity.

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

Anesthesiology, V 96, No 1, Jan 2002

9.3 Frink EJ et al

An oxygen flow rate of 10 l/min for 24 h in a conventional anesthesia circuit can dry carbon dioxide absorbents sufficiently to produce extremely high levels of carbon monoxide with high carboxyhemoglobin concentrations in desflurane-anesthetized pigs. When the reservoir bag is in place on the anesthesia machine or when a lower oxygen flow rate (5 l/min) is used, carbon dioxide absorbent drying still occurs, but 24-48-h exposure time is insufficient to allow for carbon monoxide production with desflurane.

Nine animals were included in the studies using 48-h absorbent drying (which were performed with the reservoir bag removed) and Baralyme as the carbon dioxide absorbent. Of these nine animals, three died of cardiac arrest within 20 mins of initiation of desflurane anesthesia and six were resuscitated with administration of intravenous epinephrine and discontinuation of the desflurane anesthetic. For this reason, further evaluation of 48-h drying times were discontinued.

Anesthesiology 1997; vol 87; No 2

9.4 Di Filippo A et al

Results: In vitro at 45°C Compound A concentration with soda lime and Dragersorb 800 Plus was about 10 times higher than with Amsorb. *In vivo* the Compound A concentrations in the inspiratory branch of the circuit were lower in the group with Amsorb.

Conclusion: The Compound A production is minimal with Amsorb as carbon dioxide absorber.

Acta Anaesthesiologica Scandinavica 2002: 46: 1017-1020

9.5 Higuchi H et al

An informed consent form was signed by each patient before participation in the study. The subjects were 38 patients undergoing general anesthesia for various surgeries.

Anesth Analg 2000;91:434-9

9.6 Ebert TJ et al

Methods: After IRB approval, 4 healthy volunteers (ASA PS I) provided informed consent and were anesthetized at 1 MAC for 3 hours with each of 4 volatile anesthetics (on separate days). Each hour of anesthesia consisted of a different absorber (Amsorb [Armstrong Medical Ltd, Coleraine, Northern Ireland], soda lime, barium hydroxide). Order of absorbents was random. Anesthesia was delivered in a semi-closed circuit with a fresh gas flow rate of 2 L/min. Tidal volume was 10 ml/kg and respiratory rate at 8 breaths/min. $ETCO_2$ was continuously monitored and averaged for each 1-hr session. Arterial blood gases (ABG) were obtained at baseline and after each hour of the 3-hour session. Inspired compound A concentrations were measured during sevoflurane administration.

Results: ABG's and $ETCO_2$ concentrations were not different between CO_2 absorbents for any of the anesthetics. There was no evidence of CO formation with any anesthetic (data for desflurane and sevoflurane are shown in the table, mean±SEM). Compound A formation during sevoflurane with soda lime and barium hydroxide absorbents was not evident during use of Amsorb (Figure, *Amsorb different from comparators, $p<0.01$).

Abstract at ASA 2000, Moscone Convention Center, Room E

9.7 Berry PD et al

A 24-yr-old woman, ASA physical status 1, was anesthetized for a clinical research study that involved combined epidural and general anesthesia. The subject's weight was 62 kg; height was 1.66 m; hematocrit level was not measured. She had undergone an identical general anesthetic 2 weeks previously as part of the same study, with no alteration of SpO2 or other complications.

Anesthesiology 1999; vol. 90; pp613-616 (case report)

9.8 Lentz R

CO poisoning during anesthesia poses puzzles: new agent used in Florida case.

A 46-year-old white female was scheduled as an outpatient for septoplasty, endoscopic bilateral anterior ethmoidal sinus surgery, and excision of a left tonsillar cyst. During her pre-op interview, the patient denied any cardiac or respiratory history. The patient also denied any prior anesthetics and she was not taking any chronic medications. The patient did, however, admit to being a smoker, with a 20 pack/year smoking history.

Routine pre-op labs were within normal limits, and specific values were: Hgb 14.1, Na 141, K 3.8, Cl 108, C02 23, and Ca 9.6.

Anesthesia Safety Foundation Newsletter 1994: vol. 09; pp13-14

9.9 Mchaourab A et al

Methods: Four healthy volunteers were anesthetized on different days with desflurane, sevoflurane, enflurane, and isoflurane. End-tidal carbon dioxide ($ETCO_2$) and anesthetic concentrations were measured with infrared spectroscopy; blood pressure and arterial blood gases were obtained from a radial artery catheter. Each anesthetic exposure lasted 3 h, during which the three fresh (normally hydrated) CO_2 absorbents were used for a period of 1 h each. Anesthesia was administered with a fresh gas flow rate of 2 l/min of air:oxygen (50:50). Tidal volume was 10 ml/kg; respiratory rate was 8 breaths/min. Arterial blood gases were obtained at baseline and after each hour. Inspired concentrations of compound A were measured after 15, 30, ––and 60 min of anesthetic administration for each CO_2 absorbent.

Results: Arterial blood gases and ETCO2 were not different among three CO_2 absorbents. During sevoflurane, compound A formed with barium hydroxide lime and soda lime, but not with Amsorb.

Conclusions: This new CO_2 absorbent effectively scavenged CO_2 and was not associated with compound A production.

Anesthesiology, V 94, No 6, Jun 2001

COLOUR CHANGE

10.1	Berry PD et al
10.2	Magee CD et al
10.3	O Ahmed, S Mannion

COLOUR CHANGE

10.1 Berry PD et al

Interestingly, in a recent case report,1 an unexpectedly rapid change of soda lime color to blue after induction of anesthesia was associated with desiccation and carbon monoxide production. This may imply that desiccated absorbent has less capacity to absorb carbon dioxide and, therefore, may reveal its presence by becoming exhausted and changing color more rapidly than expected.
Because of the difficulty of detecting of carbon monoxide production and toxicity, prevention is especially important. Various guidelines have been published for prevention of carbon monoxide production; most recently these have concentrated on preventing the use of desiccated carbon dioxide absorbent.|| 2 Baralyme and soda lime both are supplied wet, that is, they contain approximately 13–15% water by weight. The percentage of water that would prevent carbon monoxide production for all anesthetics is probably near 4.8% for soda lime and 9.7% for Baralyme.4 A fresh gas flow of 5 l/min or more passed through absorbent for 24 h (without a patient) is sufficient to cause critical drying of the absorbent if the reservoir bag is left off the breathing circuit (thus facilitating retrograde movement of gas through the absorber). With the bag in place, drying still occurs, but to a lesser extent. These findings are consistent with the observation in several reports,1–3 including ours, that carbon monoxide production occurred when anesthetic machines had been unused for 48 h or more. In contrast, it is unlikely that either high- or low-flow anesthesia itself can cause desiccation and carbon monoxide exposure,17 because water is released as carbon dioxide is absorbed.

Anesthesiology 1999;90:613-616

10.2 Magee et al

does not possess the ability to degrade the anaesthetic vapour through destruction of or through adsorption of the vapour, as conversely reported by Knolle. 15g±0.2 samples of fresh absorbents, LoFloSorb and AMSORB PLUS were desiccated or further hydrated to a 14% ±0.3 H2O w/w, as appropriate. These samples were conditioned in triplicate and weighed after being placed in sealed glass u-tubes with glass wool to retain the sample. After 72 hours, the contents of one u-tube of each type of absorbent sample was moisture-tested to verify the conditioned moisture content of 14% ±0.3 H2O w/w. The remaining sample pairs were then placed individually on a four decimal place balance (Adam Equipment, Milton Keynes, UK, model ACB) and weighed to determine the gross weight of the U-tube, sample material and rubber bungs and the net weight of absorbent sample. A gas line carrying 1L.min oxygen was connected to the inlet port of the u-tube at room temperature 20°C ±0.5. The time taken to reach a steady weight (for more than 15 minutes) on the balance was recorded to determine total gravimetric weight loss of water from the sample. An identical experiment was conducted on the second of the two remaining pairs and average data, across the pairs, was recorded for final analysis. The contents of the u-tube were then moisture analysed to verify remaining moisture content.

Permanency of Colour Change
Three sets of 100g samples of fresh AMSORB PLUS and LoFloSorb, which had been used in the simulation rig for CO_2 absorption studies, were further desiccated or hydrated to 6% H_2O to ensure an even colour change to violet, across the entire 100g sample. 6% H_2O was taken as the approximate hydration point where both absorbents changed from their fresh colour to violet, during CO_2 absorption studies on the simulation rig. This moisture content was verified using 10g of spare material produced in excess of the 100g sample. The 100g samples were immediately placed in a sealed vessel and inspected 48 hours later for deterioration of the colour.

Results
Data points 1-12 reported in tables 10-21

Adsorption
1. Fresh absorbent: Inspiratory anaesthetic agent concentration, relative to vapouriser setting at 5, 10, 20 and 40 minutes and at the point of equilibrium of agent to 90% of the vapouriser setting
2. Partially-desiccated absorbent: Inspiratory anaesthetic agent concentration, relative to vapouriser setting at 5, 10, 20 and 40 minutes and at the point of equilibrium of agent to 90% of the vapouriser setting
3. Fresh-desiccated absorbent: Inspiratory anaesthetic agent concentration, relative to vapouriser setting at 5, 10, 20 and 40 minutes and at the point of equilibrium of agent to 90% of the vapouriser setting
4. Fresh-desiccated absorbent: Total loss or adsorption of anaesthetic agent at the point of equilibrium of agent to 90% of the vapouriser setting

CO Production
5. Fresh absorbent: CO production at 1, 5, 10, 20 and 40 minutes from fresh absorbent
6. Partially-desiccated absorbent: CO production at 1, 5, 10, 20 and 40 minutes from partially desiccated absorbent
7. Fresh-desiccated absorbent: CO production at 1, 5, 10, 20 and 40 minutes from fresh desiccated absorbent

CO_2 Absorption Capacity, Rate of Dehydration and Permanency of Colour Change
8-10. CO_2 absorption capacity of fresh absorbent, partially-desiccated absorbent and fresh desiccated absorbent
11. Rate of dehydration
12. Permanency of colour change

Permanency of Colour Change
(12) The violet colour of all three LoFloSorb samples had receded to a consistent grey-green colour, closer to its fresh colour (green) than to its indicating colour (violet). The colour of all AMSORB PLUS samples remained violet at 48-hours and 72-hours.

Fig. 7. Exhausted LoFloSorb after 48 hours in a sealed vessel

Fig. 8. Exhausted AMSORB PLUS after 48 hours in a sealed vessel

Discussion

AMSORB PLUS is widely reported as a safe alternative to the use of soda limes or NaOH-containing absorbents during inhalational anaesthesia due to its inability to degrade anaesthetic vapour. AMSORB PLUS does not contain strong base alkali components, such as those in conventional soda lime absorbent formulations. The colour change mechanism of AMSORB PLUS appears to be an incidental benefit to its use, by providing an accurate indication of hydrated state and, hence, remaining absorptive capacity[8]. NaOH-containing absorbents are not capable of colouring or remaining coloured in response to desiccation and are therefore likely to be used inadvertently, as desiccated or partially-desiccated absorbent, on patients. The patient safety risks with use of this type of absorbent are widely known. LoFloSorb is a NSL absorbent, utilising silica and molecular sieve zeolites[9] within its formulation to aid absorption. Other studies confirm LoFloSorb produces CO and adsorbs anaesthetic vapour when desiccated. Knolle[10] reported a loss or adsorption of 89%±5 of the inflow of 0.5% isoflurane for over 60 minutes from the start of the test. This showed that desiccated LoFloSorb seriously inhibited the delivery of anaesthetic vapour and, in clinical use this could pose a serious risk to patient well-being and comfort. The capability of desiccated LoFloSorb to adsorb anaesthetic agent is therefore significant and is confirmed in this study but the present study additionally demonstrates significant adsorption of vapour when LoFloSorb is fresh or is partially desiccated, relative to the performance of AMSORB PLUS and Medisorb. This behaviour may be due to the use of silica and zeolites in LoFloSorb, which published clinical papers[11] show entrap vapourised drugs as well as CO_2. A common example of this is the use of molecular sieve crystals in the scavenging system of anaesthetic machines, which adsorb waste anaesthetic vapour. The extent to which fresh or partially-desiccated LoFloSorb is capable of adsorbing anaesthetic vapour, whilst simultaneously absorbing CO_2 should be carefully considered before clinical use. Inadequate delivery of anaesthetic vapour to the patient especially in the early stages of anaesthesia may expose the patient to inadequate anaesthesia and surgical pain that may be masked if muscle relaxant drugs are used concomitantly. The present study did not examine what happens to adsorbed anaesthetic vapour. It is possible that such vapour condenses to liquid on the surface of absorbent material and is re-vapourised as absorbent temperature rises due to heat produced from the absorption of CO_2. This secondary vapourisation would add vapour to the intentional delivery of vapour via the vapouriser dial setting causing anomalies between inspired/expired values and those of the vapouriser dial setting. If undetected, patients could receive elevated and/or erratic levels of anaesthetic vapour, potentially resulting in inadvertent changes to blood pressure

Results and Discussion:

The total costs over each four week period were €4375.69 and €3150.94 for soda lime and Amsorb® respectively. Reduced cost during Amsorb® period were due to 1) less sevoflurane consumption 2) fewer Amsorb® changes because of reliable colour change, and 3) cheaper domestic waste disposal of Amsorb® as it is inert.

Conclusion

We demonstrated Amsorb® to be a cost efficient alternative to soda lime in everyday clinical practice.

Cost comparison between soda lime and Amsorb®.

	Soda lime	**Amsorb®**	**P-Value**
Number of GAs	231 patients	236 patients	
Product used and cost	34 canisters	14 canisters	0.006 (number of canisters)
	€505.24 (€14.86/canister)	€296.38 (€21.17/canister)	
Sevoflurane bottles (250mls) and cost	35 bottles	26 bottles	0.22 (number of bottles)
	€3839.85 (€109.71/bottle)	€2852.46 (€109.71/bottle)	
Waste and cost	34 kilograms	14 kilograms	0.006 (kgs)
	€30.6 (€0.9/kg*)	€2.1 (€0.15/kg^)	
Total cost (4 weeks)	**€4375.69**	**€3150.94**	

*Sodalime is disposed in healthcare waste ^Amsorb® is disposed in domestic waste

European Journal of Anaesthesiology June 2011-volume 28-issue-P12-13

DRYNESS

11.1	Frink EJ et al
11.2	Kharasch ED et al
11.3	Berry PD et al
11.4	Higuchi H et al
11.5	Woehlck HJ
11.6	Kharasch ED et al
11.7	Kharasch ED et al
11.8	Frink EJ et al
11.9	Moon RE

11.1 Frink EJ et al

48-Hour Drying Studies (Reservoir Bag Removed)
Exposure of Baralyme to 10 l/min oxygen flow for 48-h resulted in a decrease in water content from 11.9 +/- 0.4% (fresh) to a water content of 3.9 +/- 0.8% at the top of the upper canister and 1.2 +/- 0.2% water content in the upper portion of the lower canister. This concentration of drying resulted in extremely high circuit carbon monoxide concentrations (mean peak concentration, 37,000 +/- 3,500 ppm) occurring within 10 to 15 min of initiation of desflurane anesthesia. All animals had carboxyhemoglobin concentrations greater than 80%, with seven of nine animals achieving concentrations of 90% or more. Three pigs died during anesthetic administration. The remaining six animals were successfully resuscitated by discontinuing anesthetic and administering 100% oxygen and epinephrine, intravenously (dose range, 0.25-2.0 mg given intravenously). None of the animals tolerated anesthesia with desflurane beyond 30

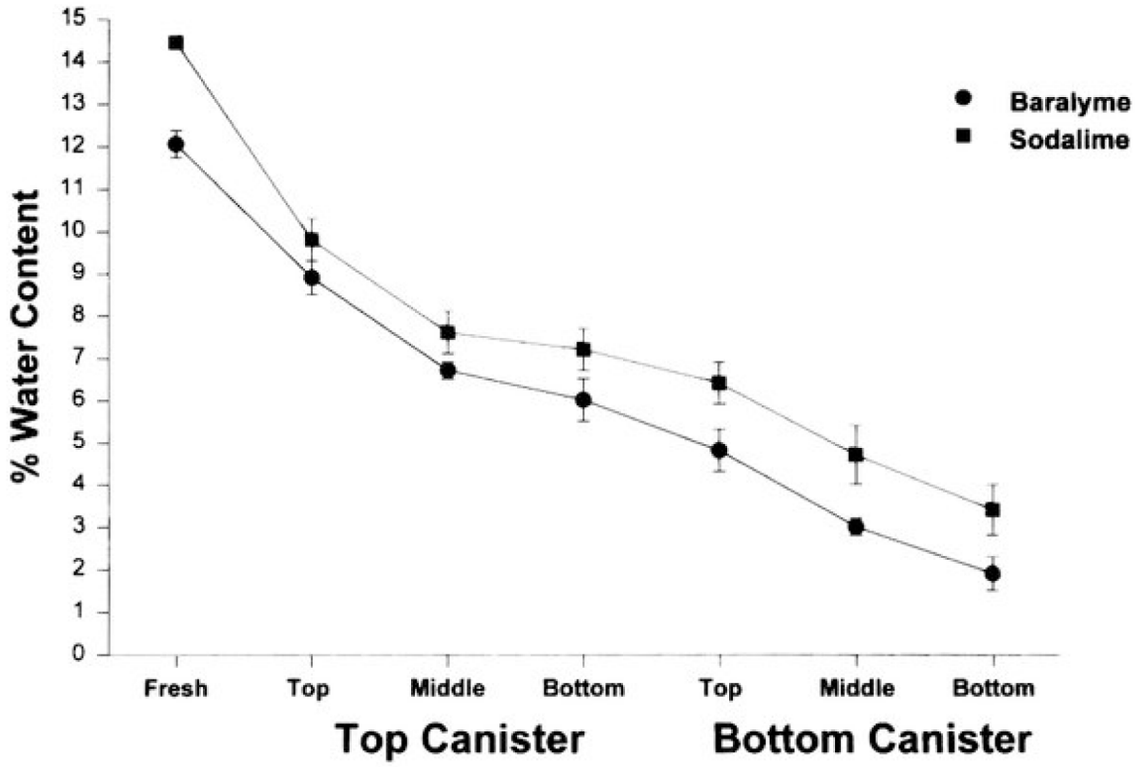

Figure 2. Water content of soda lime and Baralyme after 24-h drying with exposure to 10 l/min oxygen flow. Water contents are shown for various regions of the upper and lower carbon dioxide absorbent canisters.

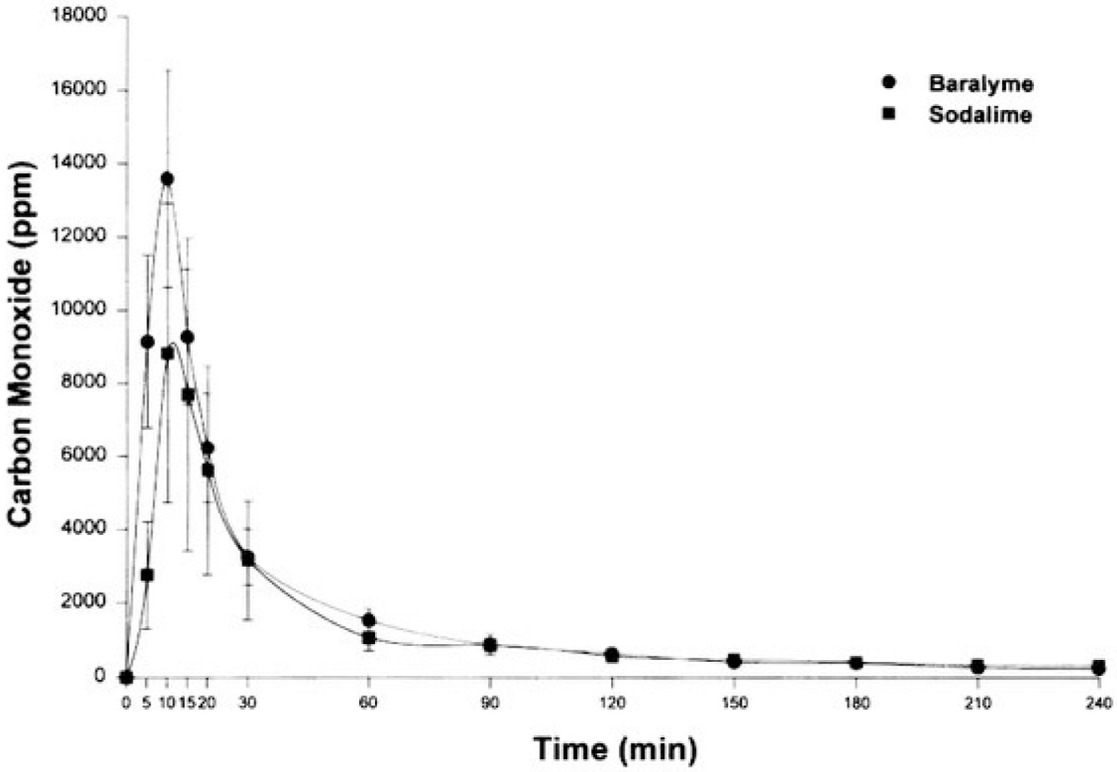

Figure 3. Carbon monoxide concentrations within the anesthesia circuit (sampled at the inspiratory limb of the circuit distal to the one-way valve) during desflurane anesthesia using dry Baralyme or soda lime (24-h drying studies). Carbon monoxide concentrations did not differ between the Baralyme and soda lime groups.

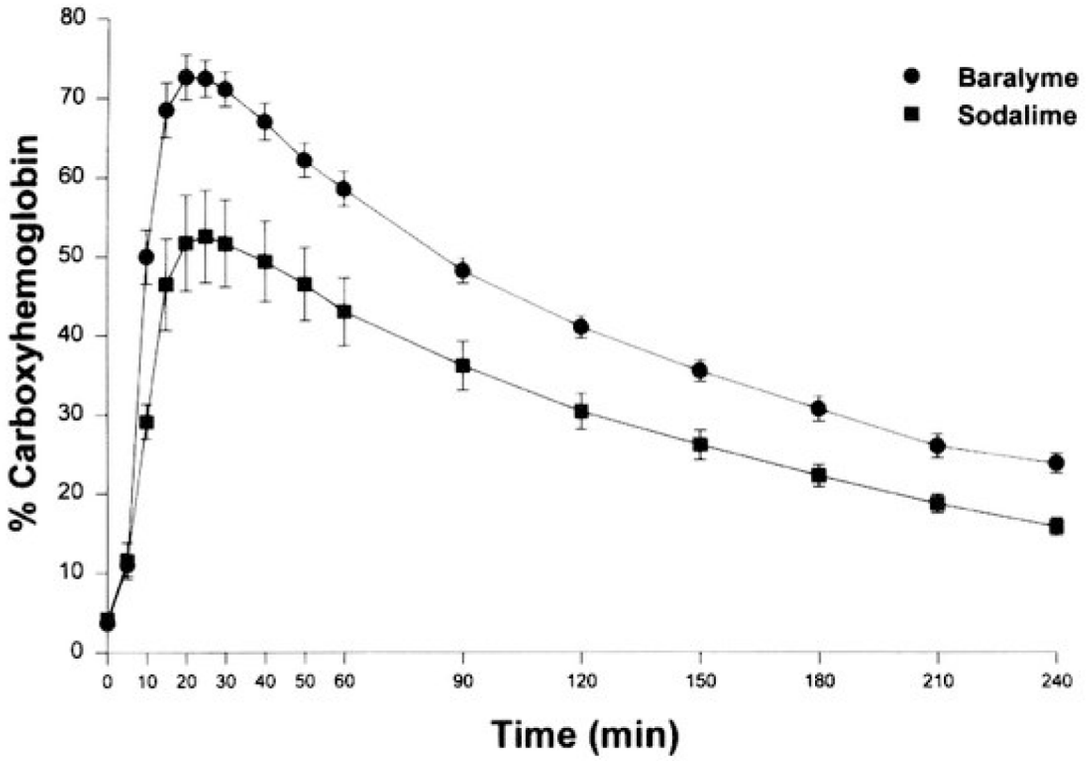

Figure 4. Carboxyhemoglobin concentrations in pigs during desflurane anesthesia using Baralyme or soda lime exposed to 24 h of 10 l/min oxygen flow. Carboxyhemoglobin concentrations are greater for the Baralyme group than for the soda lime group for all times after five min ($P < 0.01$).

We analyzed samples from the canister sectioned into thirds. Therefore, the water contents (eg 1.9% for the bottom of the lower canister) represent a mean value for the lower region. The water content of the absorbent at the very bottom was likely lower than this value. Given these limitations, we still believe that our results indicate that high carboxyhemoglobin levels can develop if desflurane is administered with partially dried carbon dioxide absorbent to humans.

An additional concern is the inability of the anesthetist to recognise that absorbents in the circle system may be of low water content. Unless the anesthetist detects that absorbent may have been dried due to the presence of a high gas flow, the absorbent may not be replaced.

Anesthesiology 1997 vol.87; No.2

11.2 Kharasch ED et al

Neither fresh nor dehydrated Amsorb® caused compound A formation.

This treatment is known to only partially dehydrate (to approximately 2–3% water content), rather than fully desiccate, the absorbent.[19] Partial dehydration was used because fully desiccated absorbents produced lethal CO concentrations from desflurane,[19] and it was desired to avoid lethality.

Using a single canister of fully desiccated sodalime with 7% desflurane and 1.5% isoflurane, Bonome et al.[36]observed approximately 5,500 and 1,000 ppm peak CO and 58% and 18% COHb, respectively.

Anesthesiology, V 96, No 1, Jan 2002

11.3 Berry PD et al

Production of carbon monoxide within breathing circuits occurs when desiccated carbon dioxide absorbent comes into contact with and degrades volatile anesthetics. Production is greatest with desflurane, isoflurane, and enflurane; the most probable source of carbon monoxide is the –CHF2 moiety, which is missing on halothane and sevoflurane.

Inquiry at the time of the anesthetic and subsequently revealed that (despite the appearance of recent use) the anesthetic machine had not been used for several days and had probably been left switched on and connected to the oxygen pipeline for this entire period. It was not possible to establish the fresh gas flow during this period of disuse, nor the exact configuration of the circuit. The room used for the study was located within the operating room suite, and therefore not in a "remote location"; it was, however, not used for surgical cases and was used only infrequently for other anesthetic purposes.

Interestingly, in a recent case report,1 an unexpectedly rapid change of soda lime color to blue after induction of anesthesia was associated with desiccation and carbon monoxide production. This may imply that desiccated absorbent has less capacity to absorb carbon dioxide and, therefore, may reveal its presence by becoming exhausted and changing color more rapidly than expected. Because of the difficulty of detecting of carbon monoxide production and toxicity, prevention is especially important. Various guidelines have been published for prevention of carbon monoxide production; most recently these have concentrated on preventing the use of desiccated carbon dioxide absorbent.|| 2 Baralyme and soda lime both are supplied wet, that is, they contain approximately 13–15% water by weight. The percentage of water that would prevent carbon monoxide production for all anesthetics is probably near 4.8% for soda lime and 9.7% for Baralyme.4 A fresh gas flow of 5 l/min or more passed through absorbent for 24 h (without a patient) is sufficient to cause critical drying of the absorbent if the reservoir bag is left off the breathing circuit (thus facilitating retrograde movement of gas through the absorber). With the bag in place, drying still occurs, but to a lesser extent. These findings are consistent with the observation in several reports,1–3 including ours, that carbon monoxide production occurred when anesthetic machines had been unused for 48 h or more. In contrast, it is unlikely that either high- or low-flow anesthesia itself can cause desiccation and carbon monoxide exposure,17 because water is released as carbon dioxide is absorbed. The Food and Drug Administration has recommended that, where desiccation is suspected, on the basis of a high fresh gas flow in an unused machine over a prolonged period, the carbon dioxide absorbent should be changed.

Anesthesiology 1999;90:613-616

11.4 Higuchi H et al

Degradation with dry absorbent is enormously more than degradation with standard absorbent (14).

Anesth Analg 2001;93:221-5

11.5 Woehlck HJ

Even the minimum fresh gas flow, given sufficient time, can desiccate absorbents enough to produce severe anesthetic breakdown. This suggests that the configuration and features of the anesthesia machine, such as the minimum fresh gas flow rate, can enhance or degrade patient safety.

Anesthesiology 1999;90:353-359

11.6 Kharasch ED et al

Neither fresh nor dehydrated Amsorb® caused compound A.

Anaesthesiology 2001; vol 95:A1124. Abstract at ASA 2001, New Orleans

11.7 Kharasch ED et al

In contrast, and of extraordinary importance, is that calcium hydroxide lime did not degrade sevoflurane to compound A, or desflurane, enflurane, or isoflurane to CO, even when desiccated.

Anesthesiology, V 91, No 5, Nov 1999

11.8 Frink EJ et al

Pigs received a 1.0 (human) minimum alveolar concentration desflurane anesthetic 7.5%) for 240 min using a 1 l/min oxygen flow rate with dried absorbent. Carbon monoxide concentrations in the circuit and carboxyhemoglobin concentrations in the pigs were measured. RESULTS: Pigs anesthetized with desflurane using Baralyme exposed to 48 h of 10 l/min oxygen flow (reservoir bag removed) had extremely high carboxyhemoglobin concentrations (more than 80%). Circuit carbon monoxide concentrations during desflurane anesthesia using absorbents exposed to 10 l/min oxygen flow (reservoir bag removed, 24 h) reached peak values of 8,800 to 13,600 ppm, depending on the absorbent used. Carboxyhemoglobin concentrations reached peak values of 73% (Baralyme) and 53% (soda lime). The water content of Baralyme decreased from 12.1 +/- 0.3% (mean +/- SEM) to as low as 1.9 +/- 0.4% at the bottom of the lower canister (oxygen flow direction during drying was from bottom to top). Absorbent temperatures in the bottom canister increased to temperatures as high as 50 degrees C. With the reservoir bag in place during drying (10 l/min oxygen flow), water removal from Baralyme was insufficient to produce carbon monoxide (lowest water content = 5.5%). Use of 5 l/min oxygen flow (reservoir bag removed) for 24 h did not reduce water content sufficiently to produce carbon dioxide with desflurane.

Anesthesiology 1997; vol 87; No 2

11.9 Moon RE

The guidelines listed above were only intended to be temporary, pending definitive elucidation of the cause. Investigations had begun at Duke Medical Center. While actual cases of CO poisoning were uncommonly discovered, in part because blood gases were measured on only about 10% of patients, 'footprints' of the phenomenon, in the form of measurable gaseous CO within unused anesthesia circuits, were relatively common. On Sunday afternoons dangerously high CO levels (> 1000 ppm) within the soda lime compartments of anesthesia machines were detected in over 2% of measurements (320 observations).

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

DRY OUT INDICATOR

12.1	Knolle E et al
12.2	Knolle E et al
12.3	Kharasch ED et al
12.4	Knolle E et al

DRY OUT INDICATOR

12.1 Knolle E et al

Conclusions: The color change in Amsorb results specifically from a loss of moisture and not from a chemical reaction with oxygen. We assume that the indicator dye in Amsorb changes color on drying because of the absence of strong base in this absorbent.

Anesthesiology 2002; 96: A1155

12.2 Knolle E et al

Conclusions: The absence of a color change from drying in strong-base absorbents is not connected with an increased moisture content of the absorbents compared to strong base-free absorbents. We assume that during drying the less soluble hydroxides in an absorbent like calcium hydroxide precipitate, so that the number of OH-ions decline, and the pH decreases below the dye indicators critical pH (10.3), resulting in the observed color change to violet. In absorbents containing the high water-soluble NaOH and KOH these hydroxides do hardly precipitate during drying so that the pH remains above 10.3 and the dye indicator does not change to the colored form.

Anesthesiology 2002, vol.97; no 3: A1156

12.3 Kharasch ED et al

Absorbents contain a dye that does indicate when the CO_2 scavenging capacity is exhausted, but none that indicates when drying or desiccation has occurred.

Anesthesiology, V 91, No 5, Nov 1999

12.4 Knolle E et al

With Amsorb layered at the out-flow, it changed color when the mean water content of the samples was reduced to 8.8%, and carbon monoxide formation was detected to varying degrees.

The authors assume that the indicator dye in Amsorb changes color on drying because of the absence of strong base in this absorbent.

Clinical Implications
Adding an Amsorb layer to strong base-containing absorbents at the fresh gas inflow of carbon dioxide-absorbent canisters appears to allow the reliable early detection
of moisture decrease in the absorbent by exploiting Amsorb's property of changing color when drying. With this method, absorbent dehydration is detected before CO formation in the absorbent occurs. This could provide a greater margin of patient safety when strong base-containing absorbents are used.

Anesthesiology, V 97, No 2, Aug 2002

IS LESS K - OK?

13.1	Rolly G et al
13.2	Versichelen LFM et al
13.3	Knolle E et al
13.4	Kharasch ED et al
13.5	Higuchi et al

IS LESS K - OK?

13.1 G Rolly et al

Discussion: Using Amsorb and Sevoflurane in closed circuit conditions, no Comp A is formed in excess of that normally present in Sevoflurane. In contrast Sofnolime produced even higher Comp A values than reported with classical Sodasorb (2). The results prove that it is not sufficient to remove the reactive KOH, but also NaOH to prevent Comp A formation. No important canister temp. diff. is seen between AM and Sofn, suggesting that a "lime" temp. diff. is not an element for non Comp A formation. Our results suggest that Sevoflurance can be safely used with Amsorb in closed circuit conditions.

Notes from ASA Meeting Oct 17 2000 Moscone Convention Center, Room A, A571

13.2 Versichelen LFM et al

With KOH-free (but sodium hydroxide [NaOH]-containing) soda limes even higher compound A concentrations are recorded than with standard Sodasorb. Only by eliminating KOH as well as NaOH from the absorbent (Amsorb and lithium hydroxide) is no compound A produced.

In conclusion, our results show strongly that a working hypothesis of only eliminating KOH from soda lime to reduce the production of compound A with sevoflurane administration is not supportable because two different brands of KOH-free soda lime not only produced compound A, but also produced compound A in even higher quantities than the classic Sodasorb.

Anesthesiology, V 95, No 3, Sep 2001

13.3 Knolle E et al

But only the complete lack of both potassium and sodium hydroxide in soda lime composition (Amsorb) prevents CO formation.

ASA Abstract 2000 A1236

13.4 Kharasch et al

Thus, dehydrated absorbents containing strong base (KOH, NaOH) consistently degrade desflurane and isoflurane to toxic concentrations of CO, whereas Amsorb® caused no detectable CO formation, did not increase COHb concentrations, and did not decrease O2Hb 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.

Anesthesiology, V96, No 1, Jan 2002

13.5 Higuchi et al

Moreover, sevoflurane was not degraded at all using Amsorb®, which contains neither KOH nor NaOH. Consequently, these results suggest that the degradation of sevoflurane to Compound A is directly related to the presence of monovalent hydroxide bases.

In summary, sevoflurane degradation to Compound A is decreased by decreasing the concentration of monovalent bases in the carbon dioxide absorbent (Drägersorb 800 Plus® and Medisorb®) and is virtually eliminated in the absence of these bases (Amsorb®).

Anesth Analg 2000;91:434-9

ETHICS

14.1	Kharasch ED et al
14.2	J Baum and H Van Aken
14.3	Ebert TJ et al
14.4	Higuchi et al
14.5	Olympio M A et al

14.1 Kharasch ED et al

Amsorb® caused minimal if any CO formation, minimal compound A formation regardless of absorbent hydration, and the least amount of sevoflurane degradation. An absorbent like Amsorb®, 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).

These are the first in vivo results that demonstrate greater potential safety, vis-à-vis CO formation and toxicity, of absorbents lacking strong base.

The current investigation, using a clinically relevant animal model, demonstrates that Amsorb® 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®, there seems to be less need to replace Amsorb® at arbitrary time intervals or to discard Amsorb® that has become desiccated before exhaustion of CO_2 scavenging capacity.

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

Anesthesiology, V 96, No 1, Jan 2002

14.2 J Baum and H Van Aken

If sevoflurane is the preferred volatile agent, even in longer lasting cases and with low-flow anaesthetic techniques, the use of calcium hydroxide lime should be obligatory.

European Journal of Anaesthesiology, 17, 597-600

14.3 Ebert TJ et al

Amsorb® is an effective CO_2 absorbent and does not degrade sevoflurane to Compound A. There was no evidence of CO formation with desflurane, isoflurane, or enflurane but for ethical reasons we did not dessicate the absorbent to enhance CO formation. Use of an absorbent that does not cause anesthetic breakdown in clinical practice should add an additional margin of safety to the practice of anesthesia.

ASA Meeting 2000 Abstract A90

14.4 Higuchi et al

Widespread use of absorbents without monovalent bases will decrease or eliminate concerns regarding Compound A toxicity from sevoflurane and carbon monoxide toxicity from desflurane, enflurance, or isoflurane.

Anesth Analg 2000;91:434-9

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NEWSLETTER

The Official Journal of the Anesthesia Patient Safety Foundation

Volume 20, No. 2, 25-44 Circulation 75,648 Summer 2005

Carbon Dioxide Absorbent Desiccation Safety Conference Convened by APSF

by Michael A. Olympio, MD

There is increasing evidence that exposure of volatile anesthetics to desiccated carbon dioxide absorbents may result in exothermic reactions leading to fires in anesthetic breathing circuits and production of toxic products (e.g., carbon monoxide, compound A, methanol, formaldehyde). Although fires have only been reported in association with sevoflurane exposed to desiccated Baralyme® (Allied Healthcare/Chemetron, withdrawn from the market), there is significant evidence that potentially toxic products can be produced upon exposure of volatile anesthetics to other desiccated absorbents containing strong bases, particularly potassium and sodium hydroxide. In some cases this may lead to sub-clinical carbon monoxide exposure.

In view of these continued anesthesia patient safety concerns, the Anesthesia Patient Safety Foundation invited medical experts and industry representatives (manufacturers of carbon dioxide absorbents, anesthesia machines, and volatile anesthetics) to attend a conference entitled *Carbon Dioxide Absorbent Desiccation: APSF Conference on Safety Considerations* on April 27, 2005, in Chicago, IL. In addition to medical experts and industry representatives (Table 1), APSF invited several organizations, including the American Society of Anesthesiologists and the American Association of Nurse Anesthetists to send observers to the conference (Table 2). The conference was funded by the Anesthesia Patient Safety Foundation with the support of unrestricted educational grants from the 10 industry cosponsors.

The format of the conference included formal presentations by the 4 medical experts as well as presentations by representatives of industry. Following reports generated from small group break-out sessions there was general discussion among all attendees and development of a consensus statement to reflect the stated goal of the conference, which was ***"to develop a consensus statement to share with anesthesia professionals on the use of carbon dioxide absorbents so as to reduce the risk of adverse interactions with volatile anesthetic drugs."***

Left to right, Drs. Dorsch, Olympio, Kharasch, Woehlck, Stoelting, and Eger speak at the APSF Conference on Safety Considerations of Carbon Dioxide Absorbents on July 27, 2005, in Chicago, IL.

Summary of Expert Medical and Industry Representative Presentations

Jerry A. Dorsch, MD, speaking on *Anesthesia Machine Characteristics That Promote Absorbent Desiccation:*

The retrograde flow of fresh gas through the absorber can desiccate the absorbent. This may be affected by a number of factors, including the design of the anesthesia breathing system, the presence or absence of the reservoir bag, whether the APL valve is open or closed, the relative resistance through the components of the breathing circuit, the fresh gas flow rate, I:E ratio, use of heat and moisture exchangers, and scavenger suction. With conventional breathing system design, removing the bag, opening the APL valve, and occluding the Y-piece all enhance retrograde flow and desiccation. The effects of these maneuvers in newer, more modern machines are variable, complex, and may have the opposite effect. Furthermore, we do not know of published data that describe the flow of gas under these various conditions. Unfortunately, the flow of gas in these breathing systems has not been well studied.

Evan D. Kharasch, MD, PhD, speaking on *Heat, Fire, and Smoke: Shining Light on the Issue of Carbon Dioxide Absorbents and Anesthetic Degradation:*

The chemical breakdown to compound A can occur in moist, as well as desiccated absorbent, but the potential for highly exothermic reactions and

See "Absorbents," Page 27

Inside:

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Consensus Statement Agreed Upon

"Absorbents," From Preceding Page

One absorbent provides a graded and permanent colorimetric indicator of both expected desiccation and exhaustion (Amsorb® Plus, Armstrong Medical Ltd.), while another (Spherasorb®, Intersurgical Ltd.) contains a substance that delays the total desiccation of the absorbent. Reducing by-products to negligible levels does not require strong-base-free absorbents.

The incidence of patient exposure to carbon monoxide is unknown. ECRI, Abbott Laboratories, and other investigators have already published recommendations to minimize the risk of unintended desiccation of absorbents. Anesthesia machine manufacturers are aware that fresh gas flow through modern and unique breathing circuits may promote desiccation of absorbent in different ways. Clinicians are directed to those resources for detailed information.

Monitoring absorbent temperature is one potentially useful adjunct, but the critical location of the probe and the quantity of heat that is worrisome have not been clearly identified. Temperature is elevated during normal carbon dioxide absorption reactions, and varies widely throughout the absorbent. Furthermore, carbon monoxide can still be produced at temperatures that might otherwise be associated with normal absorption. Relative humidity of the gas flowing out of the absorbent may be directly related to, and therefore indicate, its moisture content. Simple (home) devices to measure carbon monoxide are disrupted in the presence of volatile agents, but more sophisticated monitors are available. Some desiccated absorbents will continue to absorb carbon dioxide; therefore, the presence of an acceptable capnographic waveform should not be taken as confirmation that the breathing gas is free from carbon monoxide. Alternatively, an elevated baseline of inspired carbon dioxide on the capnogram should alert the clinician to the possibility of desiccation and/or exhaustion.

Consensus Statement

At the conclusion of this conference, attendees were asked to again consider the goal of the conference, ***"to develop a consensus statement to share with anesthesia professionals on the use of carbon dioxide absorbents so as to reduce the risk of adverse interactions with volatile anesthetic drugs,"*** and make appropriate recommendations. Based on those responses, the APSF drew the following conclusions:

The APSF recommends use of carbon dioxide absorbents whose composition is such that exposure to volatile anesthetics does not result in significant degradation of the volatile anesthetic.

The APSF further recommends that there should be institutional, hospital, and/or departmental policies regarding steps to prevent desiccation of the carbon dioxide absorbent should they choose conventional carbon dioxide absorbents that may degrade volatile anesthetics when absorbent desiccation occurs.

In such circumstances of using absorbents that may degrade volatile anesthetics, conference attendees generally agreed that users could take the following steps, consistent with ECRI recommendations:

1. Turn off all gas flow when the machine is not in use.
2. Change the absorbent regularly, on Monday morning for instance.
3. Change absorbent whenever the color change indicates exhaustion.
4. Change all absorbent, not just 1 canister in a 2-canister system.
5. Change absorbent when uncertain of the state of hydration, such as if the fresh gas flow has been left on for an extensive or indeterminate time period.
6. If compact canisters are used, consider changing them more frequently.

There was also support for the APSF to create an "Expert Task Force" to define further the characteristics of carbon dioxide absorbents that do not significantly degrade volatile anesthetics.

Dr. Olympio is Professor of Anesthesiology, former Director and Founder of the Patient Simulation Laboratory, and former Vice Chair for Education for the Department of Anesthesiology at Wake Forest University School of Medicine in Winston-Salem, NC. He is also Chair of the APSF Committee on Technology and serves on the APSF Executive Board as well.

Table 1. Invited Medical Experts, APSF, and Industry Representatives

Medical Experts	
Jerry A. Dorsch, MD Jacksonville, FL	Edmond I Eger, II, MD Professor of Anesthesiology University of California, San Francisco, CA
Evan D. Kharasch, MD, PhD Professor of Anesthesiology University of Washington School of Medicine Seattle, WA	Harvey J. Woehlck, MD Professor of Anesthesiology Medical College of Wisconsin Milwaukee, WI
Anesthesia Patient Safety Foundation	
Robert C. Morell, MD Editor, *APSF Newsletter*	Michael A. Olympio, MD Chair, APSF Committee on Technology Co-moderator of Conference
George A. Schapiro Executive Vice President	Robert K. Stoelting, MD President Co-moderator of Conference
Industry Representatives	
Drug and Equipment Manufacturers Randall D. Ostroff, MD *(Abbott Laboratories)* Raul A. Trillo, Jr., MD *(Baxter Healthcare)* Christoph Manegold *(Datascope)* Juergen-Ralf Lange *(Dräger Medical)* Michael Mitton, CRNA *(GE Healthcare)*	***Carbon Dioxide Absorbent Manufacturers*** Dr. Ciarán Magee *(Armstrong Medical, Ltd.)* Dr. Michael Clarke *(Molecular Products, Ltd.)* Mike Holder *(Intersurgical, Ltd.)* Eldon P. Rosentrater *(Allied Healthcare)* Jeffrey H. Mack *(W.R. Grace)*

Recommended References

1. Holak EJ, Mei DA, Dunning MB III, et al. Carbon monoxide production from sevoflurane breakdown: modeling of exposures under clinical conditions. *Anesth Analg* 2003;96:757-64.
2. Olympio MA, Morell RC. Canister fires become a hot safety concern. *APSF Newsletter* 2003-04;18:45, 47-8.
3. Fatheree RS, Leighton BL. Acute respiratory distress syndrome after an exothermic Baralyme-sevoflurane reaction. *Anesthesiology* 2004;101:531-3.
4. Wu J, Previte JP, Adler E, et al. Spontaneous ignition, explosion, and fire with sevoflurane and barium hydroxide lime. *Anesthesiology* 2004;101:534-7.

See "Absorbents," Next Page

Editor's Note: *There is not uniform agreement among experts as to the specific types and amounts of degradation products that may form when volatile anesthetics are exposed to desiccated absorbents that contain significant amounts of KOH and NaOH. Hence, no specific conclusions can be drawn from this conference about the relative contribution of any specific degradation product or circuit material [including plastics] as a combustible fuel in a high heat, oxygen-enriched environment.*

APSF Newsletter Summer 2005, vol. 20, No. 2, pp. 25, 27-29

SOLUTION

15.1	Kharasch ED
15.2	Baxter PJ et al
15.3	Moon RE
15.4	Woehlck HJ

SOLUTION

15.1 Kharasch ED

This apparent solution (Amsorb®) to anesthetic degradation is elegant in its simplicity.

An effective CO_2 absorbent that does not degrade anesthetics is not yet available in the United States. If and when it does reach the market, it could, and should, change the way clinicians deliver inhalation anesthesia, both domestically and worldwide.

Anesthesiology, V 91, No 5, Nov 1999

Should we change our volatile agent ?

15.2 Baxter PJ et al

Anesthetic development and the search for an "ideal" anesthetic agent continue. A previous investigation identified structural features that predispose halogenated compounds to metabolism and metabolism-based toxicity and proposed methods for designing safer chemicals by avoiding these elements. [42] Similarly, the current investigation identifies structural features that predispose halogenated anesthetics to CO_2 absorbent-catalyzed degradation to CO, and a possible mechanism of CO formation. Safer anesthetics can be designed by avoiding structural features that facilitate CO formation.

Anesthesiology 1998*; vol. 89; pp929-941*

15.3 Moon RE

Soda Lime Contamination

Although the soda lime in semi-closed circuits has been implicated in the pathogenesis of " phenomenon, the mechanism is still not understood and is under active investigation. Formulation does not appear to be important, since both Sodasorb and Baralyme have been in use during the cases collected from the three institutions mentioned above. Analysis of fresh and used Sodasorb samples has revealed traces of formate in some used samples, particularly in ones associated with CO poisoning. Since CO can readily be generated from formate, one has to suspect a possible link. Formic acid is endogenously generated and trace quantities in exhaled gas could be trapped in soda lime, providing a source for CO production.

Because of its episodic nature, the elucidation of the cause of this rare but potentially fatal phenomenon has been difficult to establish. Since it has not (as yet) been reproducible in the laboratory, it is likely to be in part due to interaction between soda lime and some component of exhaled gas from patients. Carbon monoxide poisoning cannot be detected using standard anesthesia monitors. The guidelines for prevention, listed in the text, appear to be effective. Treatment of CO poisoning should include removal from the source, administration of 100% 02 and if neurological symptoms or signs exist, hyperbaric oxygen.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

15.4 Woehlck HJ

Because only one or two chemicals that constitute the absorbent can generate CO when desiccated,[2] can the quantity and composition of alkaline materials be changed to enhance safety while maintaining adequate CO_2 absorbing qualities?

Anesthesiology 1999;90:353-359

ECONOMIC ARGUMENT

16.1	J Baum & H Van Aken
16.2	Kharasch ED et al
16.3	Stabernack et al
16.4	Lentz RE
16.5	Woehlck HJ
16.6	Murray JM et al
16.7	Abbott Labs - Sevoflurane
16.8	ECRI Hazard Report
16.9	Cobos II F V et al
16.10	O Ahmed, S Mannion

ECONOMIC ARGUMENT

16.1 J Baum and H Van Aken

Of course, routine use of higher gas flow rates will decrease the costs per hour for absorbents, although the knock-on added costs of volatile agents will exceed these savings considerably. Thus, the additional cost resulting from the use of calcium hydroxide lime is really quite low when related to the potential improvement in patient safety, which may be gained by the use of an absorbent being completely inert with respect to all volatile agents.

European Journal of Anaesthesiology, 17, 597-600

16.2 Kharasch et al

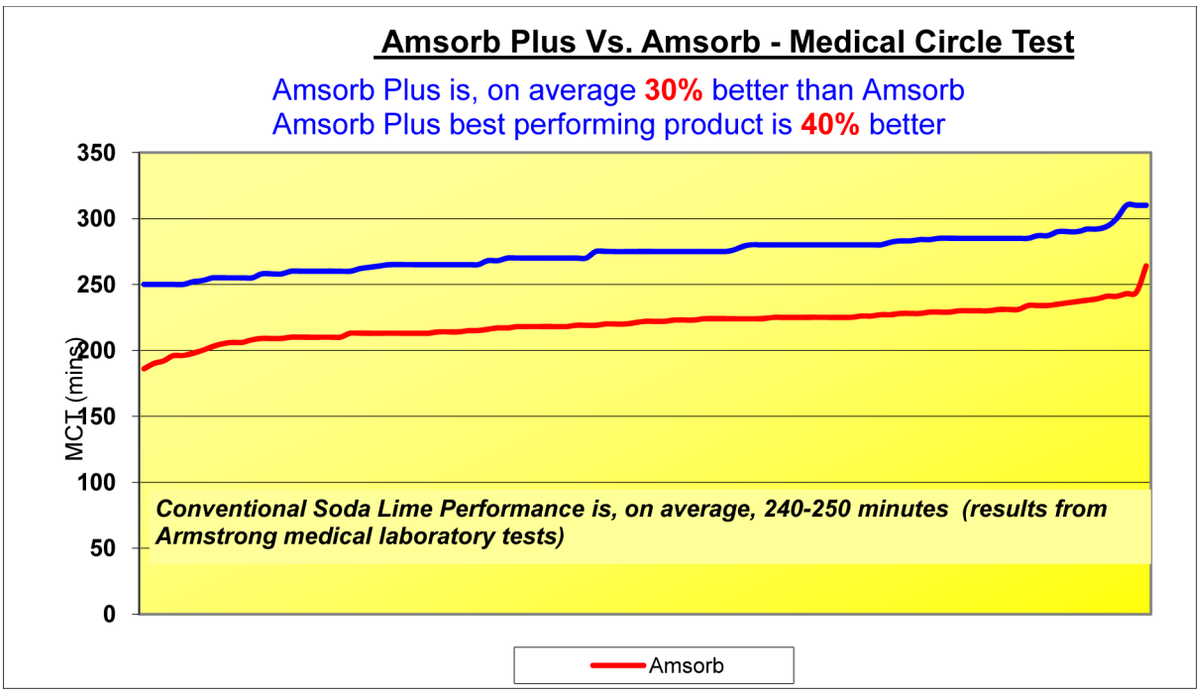
The current investigation, using a clinically relevant animal model, demonstrates that Amsorb® caused minimal if any CO formation and the least amount of sevoflurane degradation. These findings suggest that the use of an absorbent that does not cause anesthetic degradation and formation of toxic products may have benefit with respect to patient safety, inhalation induction, and anesthetic consumption (cost). Because these benefits occur with both fresh and dehydrated Amsorb®, there seems to be less need to replace Amsorb® at arbitrary time intervals or to discard Amsorb® that has become desiccated before exhaustion of CO_2 scavenging capacity.

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

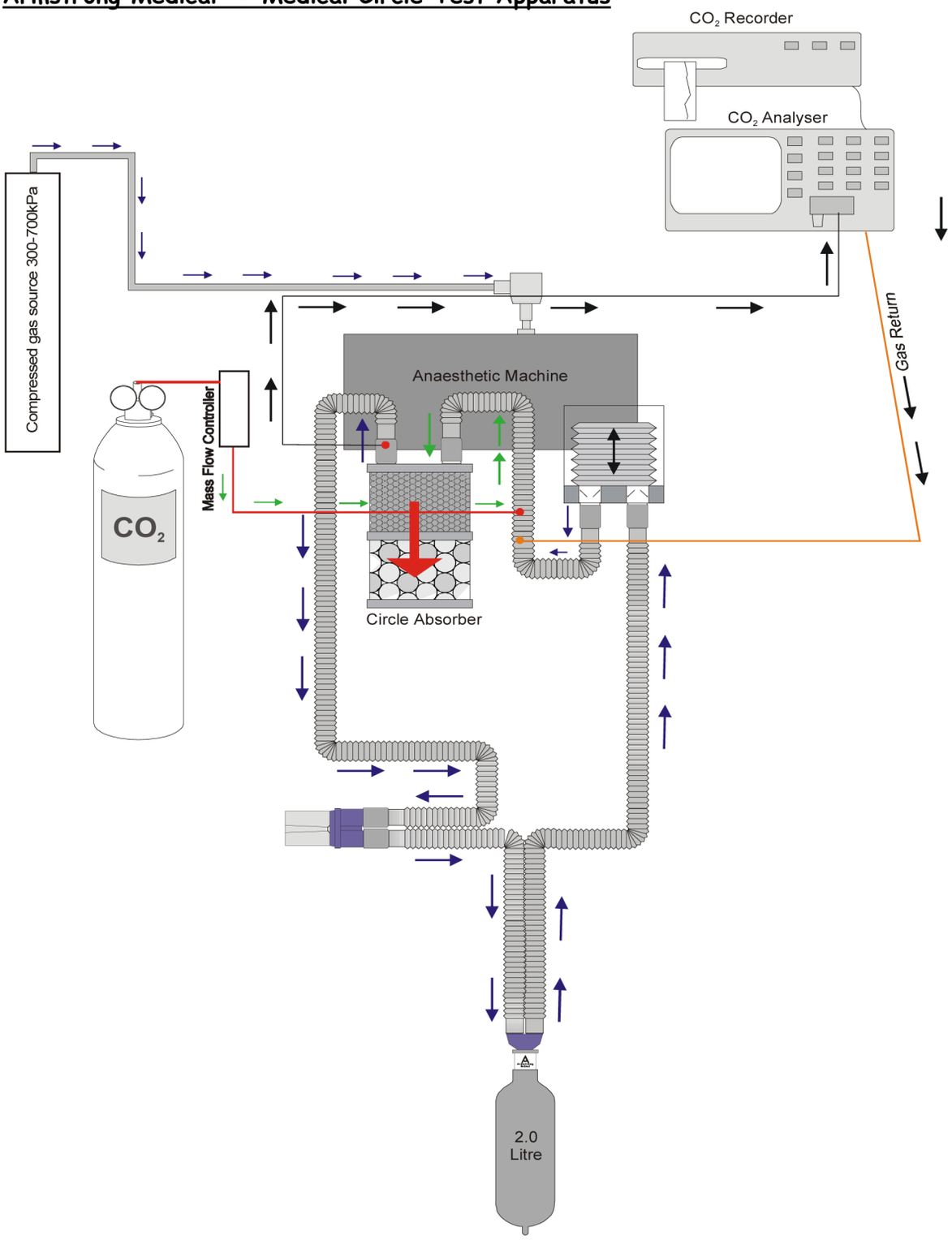
Anesthesiology, V 96, No 1, Jan 2002

16.3 Stabernack et al

Since submission of this report, Murray et al. (5) have described the development and properties of Amsorb®. Our results confirm their findings for desflurane and sevoflurane suggesting that Amsorb® causes minimal or absent production of CO and Compound A by the degradation of these anesthetics. Similarly, they and we found that Amsorb® was modestly less efficient in



Armstrong Medical - Medical Circle Test Apparatus



The decreased destruction, and thus, cost of anesthetic also might recommend the use of either Amsorb® or LiOH relative to other absorbents.

The final clinical choice of absorbent may be dictated by the premium placed by the manufacturers of Amsorb® and LiOH.

Anesth Analg 2000;90:1428-35

16.4 Lentz RE

The US FDA Center for Disease Control recommendations regarding this subject matter are as follows:

* All soda lime that has been dormant in the anesthesia machine for more than 24 hours should be changed, and dated.

* In addition to changing the soda lime, the anesthesia machine should also be flushed continuously with 100% 02 for at least one minute prior to the first case of the day.

Anesthesia Patient Safety Foundation Newsletter Vol 9, No 2, 13-24 Summer 1994

16.5 Woehlck HJ

Relatively expensive monitoring may become cost-effective if balanced against the potential cost of absorbent in the absence of monitoring for anesthetic breakdown to CO.

Anesthesiology 1999;90:353-359

16.6 Murray JM et al

From a patient-safety perspective, widespread adoption of a non-destructive CO_2 absorbent should be axiomatic. Assuming a reasonable and only marginally increased cost over currently used absorbents, economic arguments against a non-destructive absorbent should be moot: it represents a minute portion of total perioperative costs and might even be more cost-effective after considering medicolegal implications, potentially revised gas flow rates, and the need to replace desiccated absorbents.

Anesthesiology, V 91, No 5, Nov 1999

16.7 Abbott Labs

Sevoflurane – Responsive, reliable and affordable anaesthesia

Cost of sevoflurane (£ per min) for induction

Sevoflurane %						
	8.00	0.94	1.17	1.41	1.64	1.87
	7.00	0.81	1.01	1.22	1.42	1.62
	6.00	0.69	0.86	1.03	1.20	1.38
	5.00	0.57	0.71	0.85	0.99	1.13
	4.00	0.45	0.56	0.67	0.79	0.89
		4.00	**5.00**	**6.00**	**7.00**	**8.00**
		Fresh gas flow (litres per min)				

Source: Calculation based on formula set out in Thwaites et al, 1997[2]

Cost of sevoflurane (£ per hour) for maintenance

Sevoflurane %						
	8.00	0.94	1.17	1.41	1.64	1.87
	7.00	0.81	1.01	1.22	1.42	1.62
	6.00	0.69	0.86	1.03	1.20	1.38
	5.00	0.57	0.71	0.85	0.99	1.13
	4.00	0.45	0.56	0.67	0.79	0.89
		4.00	**5.00**	**6.00**	**7.00**	**8.00**
		Fresh gas flow (litres per min)				

Source: Calculation based on formula set out in Thwaites et al, 1997[2]

December 2000 – HXSEV20000158

Costs of sevoflurane

sevoflurane %	cost of sevoflurane £ per hour (for maintenance)					
4.0%	£2.02	£3.37	£6.73	£13.46	£20.20	£27.00
3.0%	£1.50	£2.50	£5.00	£9.99	£14.99	£19.99
2.0%	£0.99	£2.65	£3.30	£6.59	£9.89	£13.19
1.0%	£0.49	£0.82	£1.63	£3.36	£4.90	£6.53
0.5%	£0.24	£0.41	£0.82	£1.62	£2.44	£3.25
	0.30	0.50	1.00	2.00	3.00	4.00
	fresh gas flow rate (L/min)					

Source: Thwaites et al Br. J Anaesth 1997; 78:356-361

key: medium-to-high flow anaesthesia; low flow anaesthesia

Costs of AMSORB PLUS

price/jerican	cost of AMSORB PLUS £ per kg per hour					
£30.00	£3.33	£1.67	£0.67	£0.28	£0.17	£0.10
£28.00	£3.11	£1.56	£0.62	£0.26	£0.16	£0.09
£26.00	£2.89	£1.44	£0.58	£0.24	£0.14	£0.08
£24.00	£2.67	£1.33	£0.53	£0.22	£0.13	£0.08
£22.00	£2.44	£1.22	£0.49	£0.20	£0.12	£0.07
	0.30	0.50	1.00	2.00	3.00	4.00
	fresh gas flow rate (L/min)					

key: medium-to-high flow anaesthesia; low flow anaesthesia

Comsumption (g) of AMSORB PLUS

	consumption of AMSORB PLUS (g) per hour					
	500	200	100	40	25	14
	0.30	0.50	1.00	2.00	3.00	4.00
	fresh gas flow rate (L/min)					

key: medium-to-high flow anaesthesia; low flow anaesthesia

16.8 ECRI - Health Devices AlertsTM

December 11, 1998 **Number 1998-A50**

ANESTHESIA UNIT ABSORBERS, CARBON DIOXIDE (10-140)

ANESTHESIA UNIT CARBON DIOXIDE ABSORBENTS (17-509)

Devices (1) Anesthesia Unit Carbon Dioxide Absorbents; (2) Anesthesia Unit Carbon Dioxide Absorbers; (3) Semi-closed Circle Anesthesia Systems

Problems: ECRI has investigated several incidents of patient exposure to carbon monoxide (CO); a patient injury resulted in one of the incidents. CO is produced when halogenated anesthetic agents contact commonly used CO2 absorbents that have become excessively dry due to medical gas flow during lengthy periods (eg, overnight, over a weekend) of anesthesia machine inactivity.

Action Needed: (Note; Refer to the original report, cited below, for the rationale behind the following recommendations.) ECRI recommends the following: (1) Alert anesthesia and other appropriate personnel to the problem and to the referenced document. (2) Ensure that medical gas is turned off when an anesthesia machine will not be promptly used for another procedure. At the end of each day, verify that the gas is off for all machines. (3) Before performing a pre-use check for the first case of the day, determine if there is any flow of medical gas. If there is, replace the absorbent material in both absorbent canisters before using the machine. Identify and address the cause of the gas flow. If you have any questions regarding these recommendations, contact ECRI at (610) 825-6000

Source: ECRI Carbon Monoxide exposure during inhalation anesthesia; the interaction between halogenated anesthetic agents and carbon dioxide absorbers [hazard report]. Health Devices 1998 Nov, 27 (11): 402-4

Accession No.: A3649

ANESTHESIA UNITS (10-134)

See: Accession No. A3649, this issue

DIALYZERS, HEMODIALYSIS (11-232)

See: Accession No. A3651, this issue

ECRI PROBLEM REPORTING SYSTEM

HAZARD REPORT

Carbon Monoxide Exposures during inhalation Anesthesia: The interaction between Halogenated Anesthetic Agents and Carbon Dioxide Absorbents

Anesthesia Unit Absorbers, Carbon Dioxide (10-140)
Anesthesia Unit Carbon Dioxide Absorbents (17-509)
Anesthesia Units (10-134)

Problem

ECRI has investigated several incidents of patient exposure to carbon monoxide (CO) during the administration of inhalation anesthetics through semi-closed circle anesthesia systems. In each case, after ruling out other possible sources of CO, we concluded that dangerous levels of the gas were generated within the anesthesia system under the conditions present during the incidents. These conditions included the presence of excessively dry carbon dioxide (CO_2) absorbent in an anesthesia system being used to deliver halogenated anesthetic agents for the first case of the day.

Similar incidents have been reported in the literature, with one common characteristic being the timing of the exposures. Many incidents have occurred during Monday morning cases, and all appear to be associated with the first delivery of an anesthetic after a lengthy period (eg, overnight, over a weekend) of anesthesia machine inactivity.

Background

The Dangers of Carbon Monoxide Exposure

Carbon monoxide is very toxic, even in low concentrations. Once in the blood, CO binds tightly with hemoglobin, forming carboxyhemoglobin and diminishing the ability of hemoglobin to transport and release oxygen. The level of CO exposure will be a function of both the inhaled concentration and the exposure duration. The specific effect on the patient will very depending on the patient's cardiovascular condition and the level of oxygen administered before and during administration of the anesthetic.

Circle Anesthesia Systems and Carbon Dioxide Absorbers

To understand how CO exposures can occur, readers will need a basic understanding of circle anesthesia systems and the role of CO_2 absorbers within these systems. Inhalation anesthetics are usually administered through semi-closed circle anesthesia systems, although closed circle systems are sometimes used. In either type of circle anesthesia system, some portion of the gas exhaled by the patient is re-circulated through the system and back to the patient, thus conserving medical gases, vaporous anesthetics and expired water vapor.

To prevent dangerous levels of CO_2 from accumulating in the re-circulating gas mixture, anesthesia machines that employ circle systems include an integral CO_2 absorber to remove the CO_2 exhaled by the patient. These absorbers typically consist of two stacked canisters containing granular absorbent materials that chemically neutralize CO_2 as the exhaled gas passes through. Commonly used absorbent materials include soda lime (eg Sodasorb) and barium hydroxide lime (eg Baralyme). When the ability of these materials to neutralise CO_2 becomes exhausted the absorbent is replaced. For most absorbents, the current basis for determining when replacement is needed is the change in color of a pH indicator impregnated in the absorbent material.

Discussion

Although the exact chemical mechanism by which CO can generated is not clear, published studies have indicated that a reaction between halogenated anesthetic agents and commonly used CO_2 absorbents can produce CO if the CO_2 absorbent is excessively dry. Drying out of the absorbent material can occur when (1) an anesthesia machine has been sitting idle, such as over a weekend, and (2) there is a continuous flow of medical gas (which is very dry) through the CO_2 absorber. When dry, the absorbent becomes highly reactive in the presence of certain halogenated agents, resulting in the production of CO as the agent flows through the machine's CO_2 absorber. Desflurane (Suprane) appears to be the most reactive of the halogenated anesthetic agents, although other agents – particularly enflurane and Isoflurane – have also been reported to produce CO. The reaction between the agent and the absorbent material can continue for many minutes.

Complicating matters is the fact that identifying patient exposure to CO when it does occur can be difficult because carboxyhemoglobin levels are not monitored during anesthesia. Monitoring devices such as pulse oximeters and blood gas analysers are not intended to detect carboxyhemoglobin; in fact, pulse oximeters will usually detect carboxyhemoglobin as oxyhemoglobin. Similarly, medical mass spectrometers are not configured to detect CO. And while whole blood co-oximeters can distinguish carboxyhemoglobin from oxyhemoglobin, these devices require a fresh blood sample and cannot provide real-time monitoring. As a result, CO exposure may go undiscovered unless patient morbidity leads to a comprehensive clinical and device investigation.

In the cases investigated by ECRI, anesthetists identified all the incidents of CO exposure indirectly. For example, in the incident that resulted in an injury, the patient's pulse oximetry readings had become erratic, but the heart rate and ECG waveform remained normal. After the same results were obtained using another pulse oximeter (of the same model) and a new probe, blood was drawn for a blood gas analysis, which revealed a high partial pressure of oxygen (PaO_2>600mm Hg). Suspecting a problem with the anesthesia machine, the staff switched to a different machine. The blood sample was then analysed by co-oximetry, which revealed a carboxyhemoglobin level of 60% to 70% (values that grossly exceed normal levels); thus, the cause of the patient's condition was determined to be CO exposure.

One further complication is that it can be difficult to determine when CO exposure is likely to occur because there appears to be no readily available, convenient, or reliable means of monitoring moisture within an absorber or of re-hydrating absorbent that has dried out. Thus, to prevent the conditions under which CO can be produced from developing, users will need to ensure that the absorbent does not dry out. To do this, they need to ensure that the flow of medical gas is discontinued whenever an anesthesia machine is not in use on a patient; it is particularly important that the gas flow be stopped at the end of the workday.

Conclusions
It should be stressed that the reactions that produce CO within an anesthesia system do not occur while the machine is idle; rather, they occur only when agent vapor flows through the absorber. Therefore, flushing the breathing circuit with fresh gas before use (such as during a pre-use check) will not prevent or relieve the problem. It should also be stressed that CO exposures are unlikely to be detected intraoperatively; thus, healthcare facilities need to ensure that the conditions under which CO can be produced during inhalation anesthesia do not occur. Specifically, users must be sure to discontinue the flow of medical gas whenever an anesthesia machine will not be promptly used on another patient. ECRI recommends that the absorbent material in both canisters of an absorber be replaced whenever there is reason to believe that a machine has been left idle with gas flowing for an undetermined time. Fresh absorbent materials are sufficiently hydrated and normally remain hydrated by exhaled water vapor in the circle system, thereby preventing reaction with halogenated agents.

There is still much to be learned both chemically and clinically about the phenomenon of CO production associated with the interaction of halogenated anesthetic agents and CO_2 absorbent materials. ECRI will continue to assess relevant new findings in the medical literature and to evaluate changes in anesthesia monitoring and delivery systems. Given the present technology and knowledge of the problem, all efforts to prevent CO exposure must be directed at detecting and protecting against unintended medical gas flow when anesthesia systems are not in use.

Recommendations
1) Alert anesthesia and other appropriate personnel to the problem and to our report.
2) Ensure that medical gas is turned off when an anesthesia machine will not be promptly used for another procedure. At the end of every day, verify that the gas is off for all machines.
3) Before performing a pre-use check for the first case of a day, determine if there is any flow of medical gas. If there is, replace the absorbent material in both absorbent canisters before using the machine. Identify and address the cause of the gas flow.

Health Devices - November 1998 – Vol. 27, No. 11

16.9 Cobos et al

Analysis of Discarded Soda Lime; Economic & Practice Implications

Background: Although the theoretical and practical maximum absorption of CO2 by soda lime are known, how closely either are being approached in clinical practice has not been studied. Because soda lime in our ORs is routinely changed by technical support personnel, who are understandably concerned about leaving exhausted sodalime in the cannisters, we hypothesized that a significant portion of our institution's soda lime was likely being discarded prior to exhausting its clinical usefulness. Sodalime is not inexpensive. There are newer, even more costly CO2 absorption materials now available. If the dye in these newer materials is more permanent, and therefore results in less wastage of still useful absorbant, we wondered if the cost differential might not be so great with use of the newer materials. Our first step in investigating this was to determine how much of our discarded sodalime was in fact still usable.

Methods: Samples of discarded soda lime were obtained from the OR waste containers. To avoid response bias, which might otherwise have altered how soda lime was used intraoperatively or when it was discarded, samples were always obtained without the knowledge of any personnel involved in anesthesia patient care. Operating room administration was informed of our study and fully approved. Samples were obtained by donning latex gloves, reaching into the waste containers and obtaining a handful of the used soda lime. Then the glove was turned inside out and the soda lime sealed in air-tight plastic bags. In a laboratory, samples of approximately 10 grams were enclosed in 15 ml containers and exposed to 5% CO2 in O2 using a constant flow rate of 7.5 ml/min. A Nelcor CO2 analyzer was used to detect CO2 emerging from the containers. When 1% CO2 was detected, we considered the sodalime to be exhausted. The time at which this occured was recorded for each sample. Two samples of new soda lime were analyzed as controls. To calculate the remaining percentage of usable soda lime, the CO2 absorption capacity of each sample was divided by the average of the two controls. 95% confidence intervals for unused capacity were calculated using Students's two tailed t statistic.

Results: The usable absorption capacity remaining in the samples ranged from 13.5% to 73.3%, with a mean of 44.8% (95% CI 20.4% to 69.2%; p = 0.002).

Conclusion: Our data demonstrate that a substantial portion of our discarded soda lime remained usable. In our samples, which varied considerably, between 13.5% and 73.3% of full capacity remained unused. Analyzing for costs, utilizing soda lime to an unused capacity of 10%, instead of 45% (keeping a safety reserve) could result a savings of $0.35 per dollar spent. We believe cost savings can be achieved by directing efforts toward reducing wastage of still useful soda lime.

Waste Soda Lime Analysis		
Sample	Minutes to Exhaustion	% Capacity Remaining
1	5.23	13.5
2	27.9	72.1
3	21.35	55.2
4	28.35	73.3
5	9.75	25.2
6	23.13	59.8
7	5.55	14.4
Mean		44.79
Standard Deviation		26.4
p-value		0.0020
95% CI		20.4 to 69.2

Controls - New Soda Lime	
Sample	Minutes to Exhaustion
1	44.6
2	32.75
Mean	38.68

Anesthesiology 2004; 101: A567

16.10 O Ahmed, S Mannion

Results and Discussion:

The total costs over each four week period were €4375.69 and €3150.94 for soda lime and Amsorb® respectively. Reduced cost during Amsorb® period were due to 1) less sevoflurane consumption 2) fewer Amsorb® changes because of reliable colour change, and 3) cheaper domestic waste disposal of Amsorb® as it is inert.

Conclusion

We demonstrated Amsorb® to be a cost efficient alternative to soda lime in everyday clinical practice.

Cost comparison between soda lime and Amsorb®.

	Soda lime	**Amsorb®**	**P-Value**
Number of GAs	231 patients	236 patients	
Product used and cost	34 canisters	14 canisters	0.006 (number of canisters)
	€505.24 (€14.86/canister)	€296.38 (€21.17/canister)	
Sevoflurane bottles (250mls) and cost	35 bottles	26 bottles	0.22 (number of bottles)
	€3839.85 (€109.71/bottle)	€2852.46 (€109.71/bottle)	
Waste and cost	34 kilograms	14 kilograms	0.006 (kgs)
	€30.6 (€0.9/kg*)	€2.1 (€0.15/kg^)	
Total cost (4 weeks)	**€4375.69**	**€3150.94**	

*Sodalime is disposed in healthcare waste ^Amsorb® is disposed in domestic waste

European Journal of Anaesthesiology June 2011-volume 28-issue-P12-13

LOW FLOW

17.1	Frink EJ et al
17.2	Kharasch ED et al
17.3	Moon RE et al

LOW FLOW

17.1 Frink EJ et al

The production of sevoflurane degradation products was evaluated using a low-flow anesthetic technique in patients receiving sevoflurane anesthesia in excess of 3 h.

Concentrations of compound A increased during the first 4 h of anesthesia with soda lime and baralyme and declined between 4 and 5 h when baralyme was used. Mean maximum inhalation concentration of compound A using baralyme was
20.28 +/- 8.6 ppm (mean +/- SEM) compared to 8.16 +/- 2.67 ppm obtained with soda lime, a difference that did not reach statistical significance. A single patient achieved a maximal concentration of 60.78 ppm during low-flow.

Exhalation concentrations of compound A were less than inhalation concentrations, suggesting patient uptake.

Anesthesiology 1992; vol. 77; pp1064-1069

17.2 Kharasch ED et al

Additional factors that influence formation of compound A include absorbent water content and temperature, CO2 production, and fresh gas flow rates, with greater formation of compound A at lower flows.[17]

As a result of concerns over the renal effects of compound A formation and the influence of fresh gas flow rates, and concerns over CO formation and the critical role of absorbent water on CO production, the Food and Drug Administration has made specific recommendations regarding product labeling.

Anesthesiology, V 91, No 5, Nov 1999

17.3 Moon RE et al

Although high fresh gas flows appear to have placed a part in reducing the likelihood of CO poisoning, the additional cost of anesthetics is substantial. At Duke Medical Center recently, the policy has been changed to remove the restriction on fresh gas flow rate, while continuing to monitor weekend CO levels. If the distribution of CO levels does not indicate greater numbers of machines with dangerous CO concentrations it may be possible to remove this most costly of the three 1990 guidelines.

Anesthesia Safety Foundation Newsletter 1994; vol. 09; pp13-14

LONGEVITY

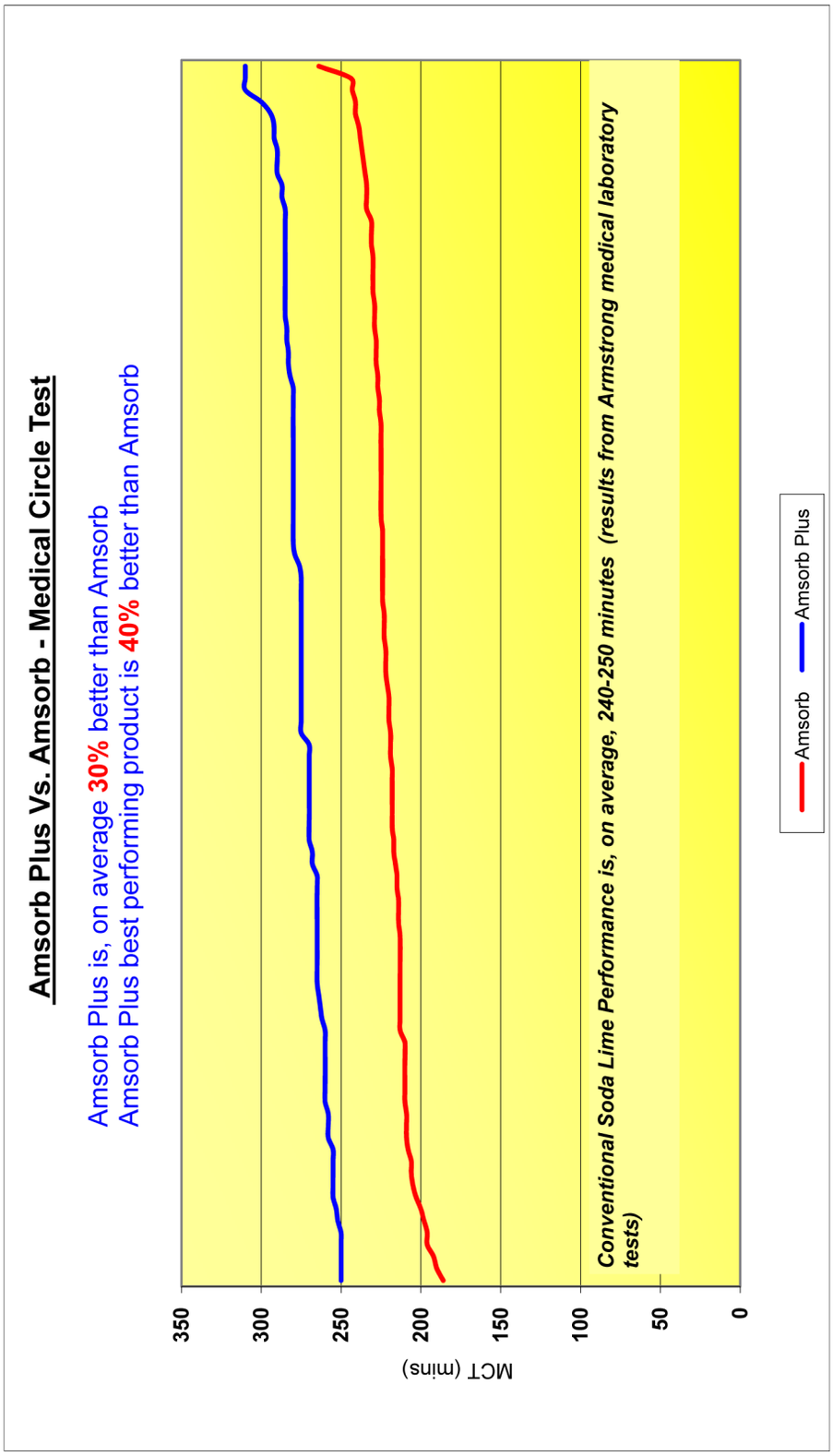
18.1	Higuchi H et al
18.2	Magee CD et al
18.3	Kobayashi S et al

LONGEVITY

18.1 Higuchi H et al

In summary, the CO2 absorption capacity of Amsorb is half that of soda lime under clinical low-flow (1 l/min) anesthesia with either a small or large canister. Further study with a larger amount of absorbent, which is used in clinical practice, is required regarding the longevity of Amsorb and soda lime.

Anesth Analg 2001; 93:221-5



Armstrong Medical - Medical Circle Test Apparatus

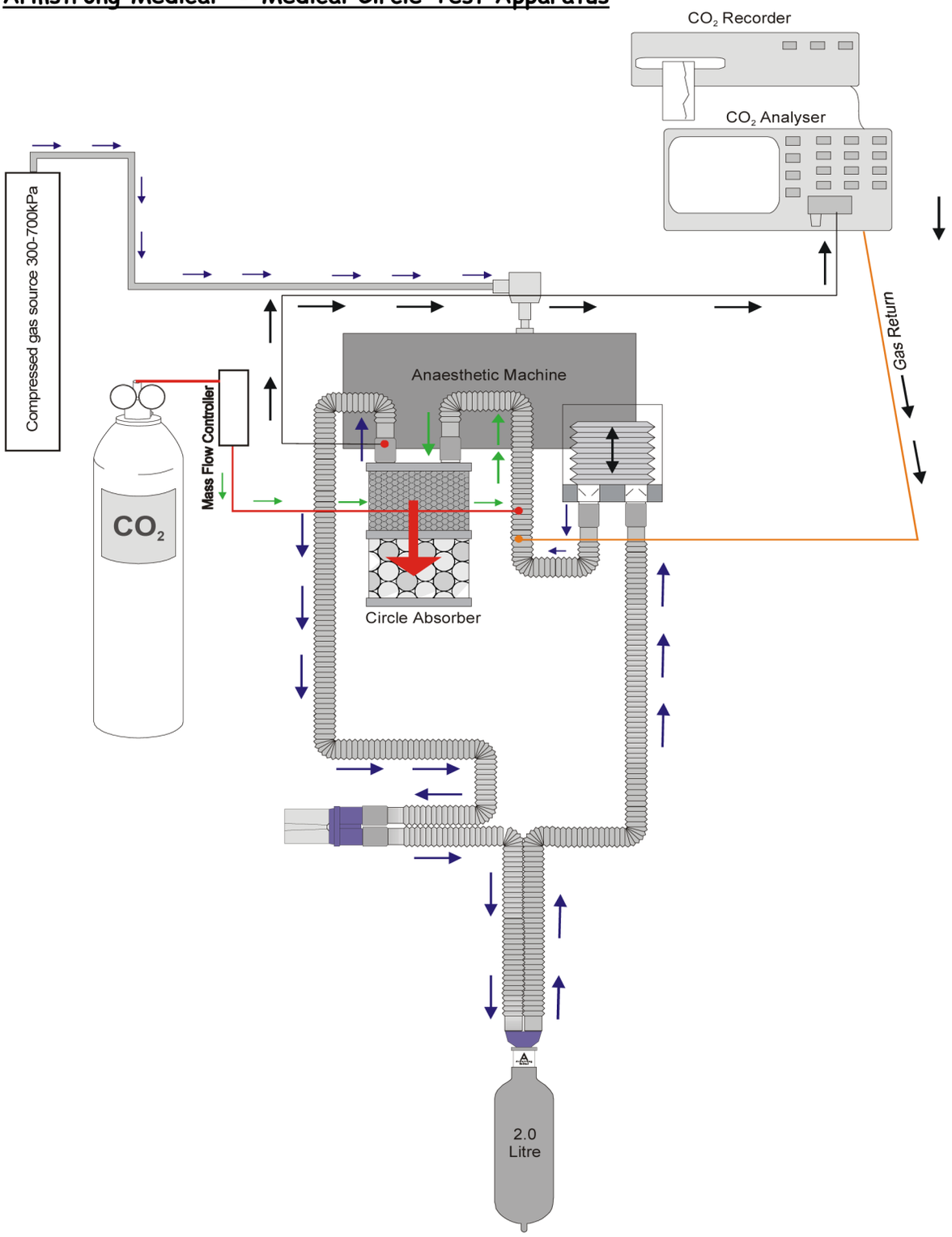


Table 4.

Sevoflurane 8%	Adsorption: Total time to equilibrium (min) to 90% of vapouriser setting	Adsorption: Total vapour volume loss to 40 min (%)
AMSORB PLUS, fresh	8	
LoFloSorb, fresh	28	
Medisorb, fresh	14	
AMSORB PLUS, partially-desiccated	23	
LoFloSorb, partially-desiccated	37	
Medisorb, partially-desiccated	31	
AMSORB PLUS, fresh desiccated	22	19
LoFloSorb, fresh desiccated	80	39
Medisorb, fresh desiccated	41	29

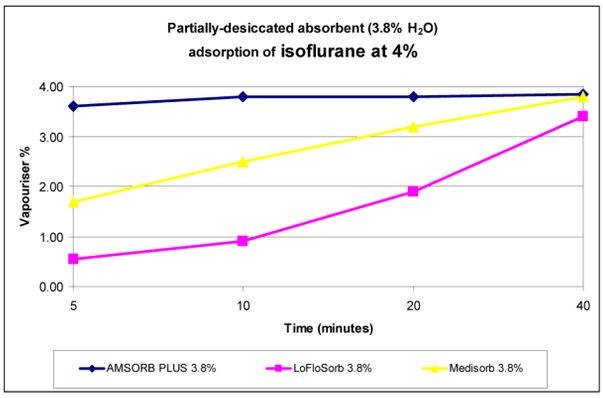


Table 5.

Isoflurane 4%	Adsorption: Total time to equilibrium (min) to 90% of vapouriser setting	Adsorption: Total vapour volume loss to 40 min (%)
AMSORB PLUS, fresh	6	
LoFloSorb, fresh	21	
Medisorb, fresh	20	
AMSORB PLUS, partially-desiccated	5	
LoFloSorb, partially-desiccated	48	
Medisorb, partially-desiccated	31	
AMSORB PLUS, fresh desiccated	5	3
LoFloSorb, fresh desiccated	62	48
Medisorb, fresh desiccated	32	19

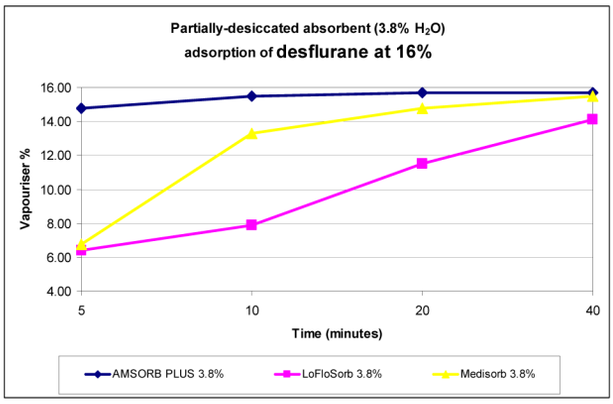
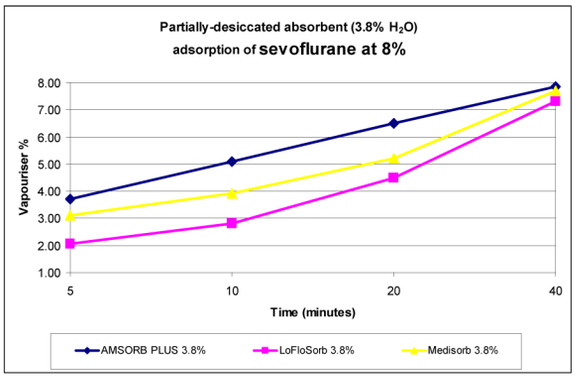


Table 6.

Desflurane 16%	Adsorption: Total time to equilibrium (min) to 90% of vapouriser setting	Adsorption: Total vapour volume loss to 40 min (%)
AMSORB PLUS, fresh	5	
LoFloSorb, fresh	19	
Medisorb, fresh	17	
AMSORB PLUS, partially-desiccated	3	
LoFloSorb, partially-desiccated	43	
Medisorb, partially-desiccated	13	
AMSORB PLUS, fresh desiccated	6	5
LoFloSorb, fresh desiccated	26	23
Medisorb, fresh desiccated	23	15



CO_2 Absorption Capacity

CO_2 absorption capacity in fresh or partially-desiccated absorbent was greatest with AMSORB PLUS and least with LoFloSorb (see tables 7-9). CO_2 absorption capacity was not influenced by choice of anaesthetic agent but was affected by absorbent hydration levels. Fresh AMSORB PLUS, on average, has 45% more absorption capacity than LoFloSorb, presumably due to the absence of any absorption catalyst within the LoFloSorb formulation. Fresh AMSORB PLUS, on average, has 27% more absorption capacity than Medisorb. More striking results were found for partially-desiccated absorbents, where AMSORB PLUS had almost 10 times more absorption capacity than LoFloSorb, when CO_2 absorption resumed. CO_2 absorption activity in fresh-desiccated absorbent was greatest with Medisorb and least with LoFloSorb and AMSORB PLUS. Of the fresh-desiccated absorbents, only Medisorb demonstrated notable CO_2 absorption activity.

Table 7.

Absorbent	Duration (min)	Average total CO_2 absorption (L/kg)
AMSORB PLUS fresh 14.6% H_2O	691	134
Medisorb fresh 15.8% H_2O	510	99
LoFloSorb fresh 14.6% H_2O	385	74

Table 8.

Absorbent	Duration (min)	Total CO_2 absorption (L/kg)
AMSORB PLUS partially-desiccated 3.8% H_2O	505	97
Medisorb partially-desiccated 3.8% H_2O	445	85
LoFloSorb partially-desiccated 3.8% H_2O	55	10

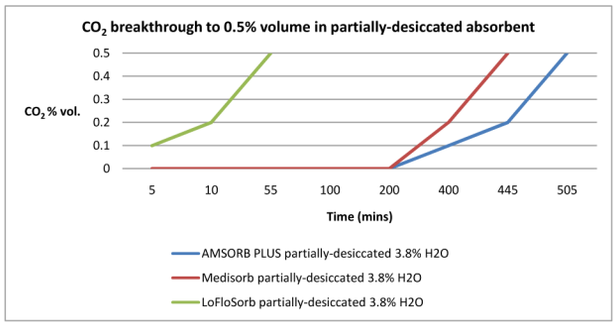
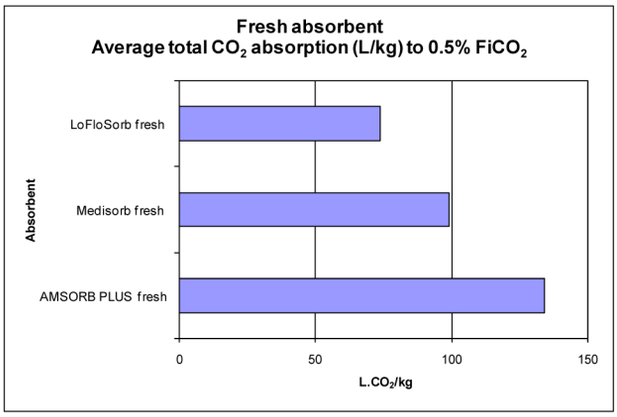
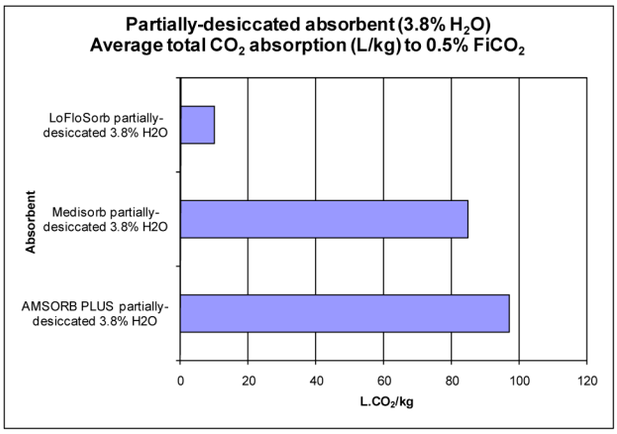
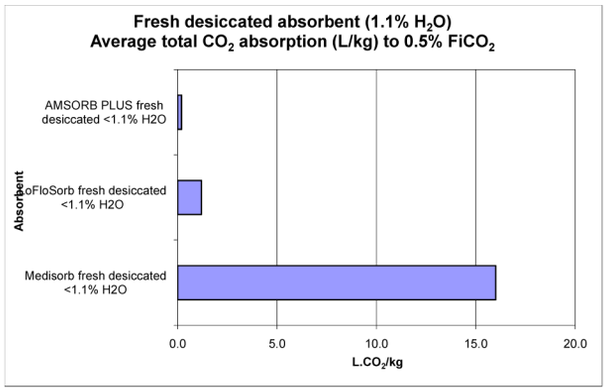


Table 9.

Absorbent	Duration (min)	Total CO_2 absorption (L/kg)
Medisorb fresh desiccated <1.1% H_2O	85	16.0
LoFloSorb fresh desiccated <1.1% H_2O	7	1.2
AMSORB PLUS fresh desiccated <1.1% H_2O	1	0.2







Temperature

Analysis of peak temperature and time to peak temperature confirmed that temperature elevation, beyond the typical observation of peak temperature in the range 36°C to 44°C during absorption of CO_2 with a hydrated absorbent, was statistically significant in fresh-desiccated Medisorb only (peak of 74°C after 90 minutes) and was consistent with simultaneous production of CO. Peak temperatures below 36°C were consistent with zero or minimal CO_2 absorption activity in fresh-desiccated AMSORB PLUS and LoFloSorb. This would support the assertion that attainment of temperatures above 36°C in these absorbents is related to CO_2 absorption activity, for which at least partial absorbent hydration is required, rather than any heat created by breakdown of anaesthetic agent by these absorbents, given that the levels of breakdown to CO with LoFloSorb are less, relative to levels produced by NaOH-containing absorbents.

Methods

AMSORB PLUS and LoFloSorb were tested in their fresh state, partially-desiccated state and fresh-desiccated state, when in contact with varying percentages of isoflurane, sevoflurane and desflurane in a clinical simulation model. Individual 1.0kg ±20g samples of both materials were chosen from batches of absorbent available in a number of European and USA hospitals. Medisorb (GE Healthcare, Helsinki, Finland) was used as the control in tests.

Conditioning of Samples

Samples were tested in their fresh state or conditioned, as appropriate. All tests were completed in triplicate and data averaged. Samples of absorbent in their fresh state were checked for moisture content, viable lime content and bulk density and placed in sealed vessels as 1.0kg ±20g batches, awaiting testing. Material, to create 1.0kg ±20g fresh-desiccated samples, was prepared from fresh absorbent samples with known moisture content and viable lime

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Amsorb Plus and Drägersorb Free, two new-generation carbon dioxide absorbents that produce a low compound A concentration while providing sufficient CO_2 absorption capacity in simulated sevoflurane anesthesia

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Abstract
Purpose. The properties of two new-generation CO_2 absorbents, Amsorb Plus (Armstrong Medical, Coleraine, UK) and Drägersorb Free (Dräger, Lübeck, Germany), were compared with those of Amsorb (Armstrong Medical) and Sodasorb II (W.R. Grace, Lexington, MA, USA).
Methods. The concentration of compound A produced by each absorbent was determined in a low-flow circuit containing sevoflurane, and the CO_2 absorption capacity of the absorbent was measured. The circuit contained 1000 g of each absorbent and had a fresh gas (O_2) flow rate of 1 l·min^{-1} containing 2% sevoflurane. CO_2 was delivered to the circuit at a flow rate of 200 ml·min^{-1}.
Results. The maximum concentrations of compound A were 2.2 ± 0.0, 2.3 ± 0.3, 2.2 ± 0.2, and 23.5 ± 1.5 ppm (mean ± SD) for Amsorb Plus, Drägersorb Free, Amsorb, and Sodasorb II, respectively. The maximum concentration of compound A for Sodasorb II was significantly higher than those for the other absorbents ($P < 0.01$). The CO_2 absorption capacities (time taken to reach an inspiratory CO_2 level of 2 mmHg) were 1023 ± 48, 1074 ± 36, 767 ± 41, and 1084 ± 54 min, respectively, and the capacity of Amsorb was significantly lower than that of the other absorbents ($P < 0.01$).
Conclusion. The new-generation carbon dioxide absorbents, Amsorb Plus and Drägersorb Free, produce a low concentration of compound A in the circuit while showing sufficient CO_2 absorption capacity.

Key words CO_2 absorbent · Compound A · CO_2 absorption capacity · Sevoflurane · Low-flow anesthesia

Introduction

Classical carbon dioxide (CO_2) absorbents degrade sevoflurane to 2-fluoromethyl-2-difluoro-1-(trifluoromethyl) vinyl ether (compound A) [1]. Although the toxicity of compound A is debatable [2–11], a CO_2 absorbent with reduced reactivity with sevoflurane is preferable for clinical use. In 1999, Amsorb (Armstrong Medical), the first absorbent to generate only small amounts of compound A, was released. However, in addition to this unique property, Amsorb has been reported to have a reduced capacity for CO_2 absorption, with a capacity of only 40% to 90% of that of standard sodalime [12–15]. Recently, two new-generation carbon dioxide absorbents, Amsorb Plus (Armstrong Medical) and Drägersorb Free (Dräger, Lübeck, Germany) have been released. Amsorb Plus is an advanced version of Amsorb. The manufacturers have announced that Amsorb Plus and Drägersorb Free generate small amounts of compound A from sevoflurane in a circle absorber and also have sufficient CO_2 absorption capacity. In the present study, we determined compound A concentrations in a low-flow circuit containing sevoflurane in the presence of each absorbent, and we simultaneously measured the CO_2 absorption capacity of the absorbent, in order to compare the properties of Amsorb Plus and Drägersorb Free with those of Amsorb and Sodasorb II.

Materials and methods

An Aestiva 3000 anesthesia system (Ohmeda, Madison, WI, USA) was used throughout this study. A 3-l latex bag connected to the Y-piece of the circuit acted as an artificial lung, and CO_2 was delivered at a flow rate of 200 ml·min^{-1} into the distal part of the bag. The artificial lung was ventilated 10 times·min^{-1} with a measured expired tidal volume of 500 ml. The anesthesia system was equilibrated on line for 30 min with a fresh gas (100% oxygen) flow rate of 6 l·min^{-1} in the absence of the CO_2 absorbent. After the preparation period, 1000 g of fresh absorbent (Amsorb Plus, Drägersorb Free, Amsorb, or

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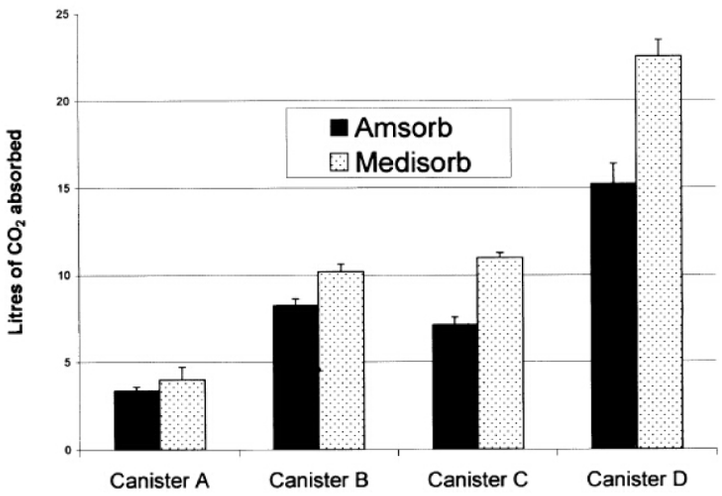
CANISTER DESIGN

19.1 Bedi A et al

CANISTER DESIGN



r design.

Figure 5 The amount of CO_2 absorbed (litres) per 100g absorbent within each different canister system ($n = 3$), before CO_2 levels exceeded 0.5% in the 'inspiratory' limb of the *in vitro* breathing circuit. Bars (error bars) are mean (SD).

Canister A: ADU (Datex-Ohmeda, Helsinki, Finland)
Canister B: ThermH2Osorb canister (Raincoat Corporation, Louisville, KY, USA)
Canister C: The absorbent canister from a Draeger Julian anaesthetic machine (Draeger Medizintechnik GmbH, Germany
Canister D: Canister from an Ohmeda Modulus anaesthetic machine (Datex-Ohmeda, Helsinki, Finland)

Anaesthesia 2000, 56, pages 1-6

COMPETITORS

20.1	Knolle E et al
20.2	Knolle E et al
20.3	Schuler HG et al

20.1 Knolle E et al

In the first experimental series, no CO formation was measured in the Amsorb (Sample H) when 0.5% isoflurane was directed through them. For all the other tested absorbents (A–G), there were reproducible CO concentration curves (Fig. 1). The corresponding calculated values of CO formation (CO and COMean) differed significantly among the absorbents (Table 2)

Table 2. Characteristics of CO Formation During Passage of 0.5% Isoflurane

	Sample (brand)									
		Group 1			Group 2			Group 3		
Variable	A Baralyme	B Dragersorb 800	A-B	C Dragersorb 800 Plus	D Intersorb	E Spherasorb	C-E	F LoFloSorb	G Superia	H (Amsorb)	F-H
CO (mL)	223 ± 6	140 ± 12	181 ± 45	66±3	73 ± 3	49 ± 4	63 ± 11	8 ± 2	3 ± 2	0	4 ± 4
CO_{Mean}(ppm)	730 ± 20	458 ± 39	594 ± 146	218 ± 9	239 ± 10	162 ± 13	206 ± 35	26 ± 5	9 ± 5	0	12 ± 12
CO_{Max}(ppm)	875 ± 34	737 ± 49	806 ± 83	620 ± 17	548 ± 23	281 ± 18	483 ±152	38 ± 8	13 ± 7	-	25 ± 15
T_{COMax}(min)	24 ± 2	18 ± 1	21 ± 4	10 ± 1	12 ± 1	23 ± 1	15 ± 7	50 ± 2	25 ± 1	-	37 ± 13
$Temp_{Baseline}$(°C)	24.8±0.5	27.3 ± 1.2	26.1±1.6	26.3 ± 0.7	25.9±0.3	25.4 ± 0.2	25.9±0.6	24.8 ± 0.2	25.8 ± 0.3	26.2 ± 0.3	25.6±0.7
$Temp_{Max}$(°C)	27.7±4.2	32.0 ± 0.8	29.8±3.6	27.8 ± 0.6	27.4±0.12	26.9 ± 0.2	27.4±0.5	24.9 ± 0.2	26.2 ± 0.5	26.3 ± 0.3	25.8±0.8
$Temp_{Mean}$(°C)	25.4±1.1	28.7 ± 0.4	27.0±1.9	27.2 ± 0.5	26.6±0.05	25.9 ± 0.1	26.6±0.6	24.5 ± 0.1	25.9 ± 0.3	26.1 ± 0.2	25.5±0.8
ISO_{Loss}(%)	63 ± 1	36 ± 1	50 ± 15	26 ± 3	31 ± 1	50 ± 2	36 ± 11	89 ± 5	41 ± 2	20 ± 4	50 ± 15
$T_{ISO<0.4\%}$(min)	>60	38 ± 2		16 ± 2	20 ± 0	33 ± 1		>60	26 ± 4	15 ± 3	
$T_{ISO<0.4\%}$(min) (fresh soda lime)	<1, <1	1, 1		1, 1	<1, 1	1, 2		2, 2	1, 1	1, 1	

The largest isoflurane loss (89% ± 5%) took place in LoFloSorb, but the level of CO formation in this absorbent was among the smallest.

When the inlet isoflurane concentration was increased to 4% from 0.5%, the mean CO formation with LoFloSorb was approximately twofold larger, but with Superia, CO formation was approximately the same. Amsorb produced no CO. The differences in CO formation and CO_{Mean} among the three absorbents were significant.

Anesth Analg 2002;95:650-5

20.2 Knolle E et al

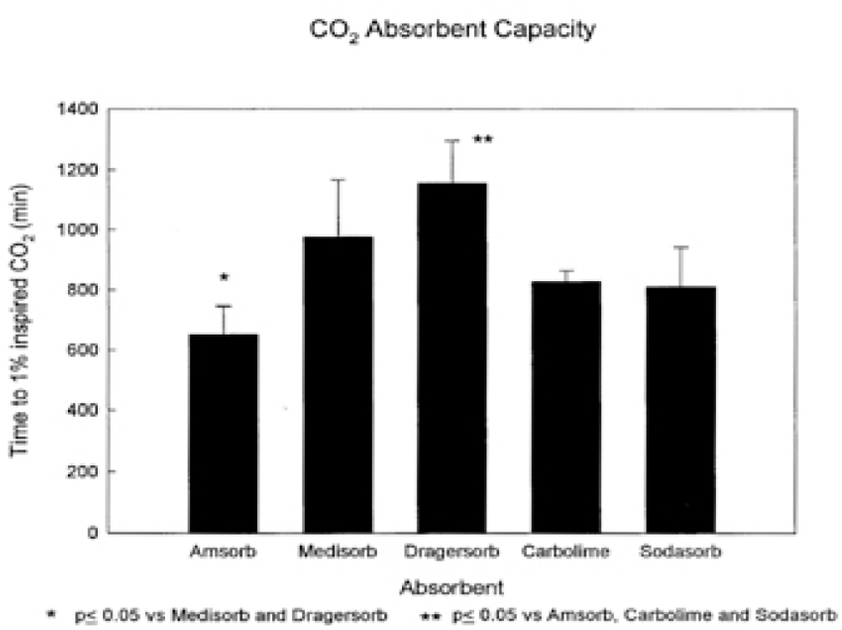
Table 2. Water Content and Carbon Monoxide (CO) Formation in Absorbents when Drying was indicated by Amsorb Layered at the Fresh Gas Outflow

	Intersorb	Spherasorb	Baralyme	Dragersorb 800	Dragersorb 800plus
Initial water content (%)	14.2	11.8	13.4	15.3	15.8
Drying period to colour change T_{colour} [h]	9, 12	6, 4	4, 4	4, 6	12, 12
Water content [%] at T_{colour}	7.8, 6.1	7.4, 8.6	10.4, 10.5	12.2, 10.8	7.1, 7.3
CO_{max} [ppm] after T_{colour}	102	36	19	25	194
Co_{total} [ml] after T_{colour}	6.6	4.1	2.5	1.8	8.4
Complete drying period T_D [h]	96	72	136	72	72
CO_{max} [ppm] after T_D	460	201	767	719	483
Co_{total} [ml] after T_D	49.6	32.2	170.3	125.4	36.1

Experimental series B: two samples (540 g) each of five different strong-base absorbents were covered with a layer of Amsorb (60 g) and dried with oxygen directed through them from the bottom at a flow of 5 l/min until a color change in Amsorb was detectable (T_{color}). Half of each pair of samples was then dried completely (T_D). Isoflurane (0.5%) was added to the oxygen flow for 60 min both in the samples dried to T_{color} and those dried to T_D, and the maximum CO concentration (CO_{max}) at the outflow and the amount of CO formed (CO_{total}) were determined for both drying times.

Anesthesiology, V 97, No 2, Aug 2002

20.3 Schuler HG et al



Anesthesiology 2001; Vol 95;A510. Abstract from ASA 2001, New Orleans

REFERENCES

	Clinical Reference Bibliography For Soda Limes, Baralyme, AMSORB® and AMSORB® PLUS	Hyperlink to File where possible	Image/Graph	Accompanying Notes where applicable	DRAGERSORB 800	DRAEGERSORB 800 +	DRAGERSORB FREE	MEDISORB	SPHERASORB	LOFLOSORB	SODASORB	BARALYME	WAKOLIME	CARBOLIME	SOFNOLIME	INTERSORB	INTERSORB PLUS	AMSORB	AMSORB PLUS	OTHER
1	**Barth** *et al*. Barium Hydroxide Lime Turns Yellow After Desiccation. Anaes. Analg. 2005; vol. 101; pp. 748-752	Barth et al 2005										Y								Y
2	**Baum J** *et al.* Calcium hydroxide lime – a new carbon dioxide absorbent: a rationale for judicious use of different absorbents. European Jn. of Anaesthesiology 2000; vol. 17; pp597-600	Baum et al 2000				Y			Y			Y			Y			Y		Y
3	**Baum J** *et al* Interaction of inhalational anaesthetics with CO_2 absorbents. Best Practice and Research Clinical Anaesthesiology 2003; vol.17; no. 1; pp63-76	Baum et al 2003				Y	Y		Y	Y		Y			Y			Y		Y
4	**Bedi A**. Real problems with some CO2 absorbents. Presentation at Austrian International Congress 2004.	Bedi A 2004						Y			Y	Y						Y		Y
5	**Bedi A** *et al.* The In Vitro Degradation of Sevoflurane to Formaldehyde Following Exposure to CO_2 Absorbents. Poster Presentation. The Queen's University of Belfast, Northern Ireland	Bedi et al																		Y
6	**Bedi A** *et al*. The *in vitro* performance of carbon dioxide absorbents with and without strong alkali. Anaesthesia 2001; vol. 56; pp. 1-6	Bedi et al 2001						Y										Y		Y
7	**Bedi** *et al.* The In Vitro Degradation of Sevoflurane to Formaldehyde Following Exposure to CO_2 Absorbents. Anesthesiology 2001; vol. 95; A-1190. Abstract from ASA 2001, New Orleans	Bedi et al ASA2001						Y			Y							Y		
8	**Castro BA** *et al*. Explosion within an Anesthesia Machine: Baralyme®, High Fresh Gas Flows and Sevoflurane Concentration. Anesthesiology 2004; vol.101; pp537-539	Castro et al 2004										Y								
9	**Cobos II F V** *et al*. Analysis of Discarded Soda Lime; Economic and Practice Implications. Anesthesiology 2004; vol. 101; A-567. Abstract from ASA 2004, Las Vegas	Cobos II, F V et al 2004																		Y
10	**Coppens** *et al.* The mechanisms of carbon monoxide production by inhalational agents. Anaesthesia 2006; vol. 61; pp. 462-468	Coppens et al 2006			Y		Y					Y			Y			Y	Y	Y
11	**Cummings K**. LETTER. Carbon Dioxide Rebreathing Due To Unrecognised Amsorb Plus Exhaustion. Anesthesia & Analgesia 2007; vol. 105; p. 289	Cummings 2007.pdf																	Y	
12	**D'Eramo CD**. AMSORB®: safety and absorptive capacity during low-flow anaesthesia. Preliminary clinical experience. Universitá di Parma 2001	D'Eramo C et al 2001				Y						Y						Y		
13	**Di Filippo A** *et al.* Sevoflurane low-flow anaesthesia: best strategy to reduce Compound A concentration. Acta Anaesthesiologica Scandinavica, 2002; vol. 46; pp 1017-1020	Di Filippo et al 2002				Y												Y		Y
14	**Di Filippo A** *et al.* AMSORB reduces the compound A production in vitro and clinical results. Applied Cardiopulmonary Pathophysiology 2000; vol.9; no. 2; pp103-106	Di Filippo et al 2000.doc																Y		Y
15	Ebert TJ et al. A New Carbon Dioxide Absorbent Devoid of Anesthetic Breakdown. Anesthesiology 2000; vol 93; A-90. Abstract from ASA 2000, San Francisco	Ebert et al 2000	Ebert et al image															Y		Y
16	**Higuchi** *et al.* Compound A Concentrations During Low-Flow Sevoflurane Anesthesia Correlate Directly with the Concentration of Monovalent Bases in Carbon Dioxide Absorbents. Anesthesia & Analgesia 2000; vol. 91; pp434-439	Higuchi et al 2000			Y	Y		Y										Y		
17	**Higuchi** *et al.* The Carbon Dioxide Absorption Capacity of Amsorb® is Half That of Soda Lime. Anaesthesia & Analgesia 2001; vol. 93; pp221-225	Higuchi et al 2001						Y			Y							Y		
18	**Junzheng WU** *et al.* Spontaneous Ignition, Explosion, and Fire with Sevoflurane and Barium Hydroxide Lime. Anesthesiology 2004; vol.101; pp534-537	Juzheng Wu et al 2004											Y					Y		
19	**Keijzer C** *et al.* Compound A and carbon monoxide production from sevoflurane and seven different types of carbon dioxide absorbent in a patient model. Acta Anaesthesiologica Scandinavica 2007; vol 51; pp31-37	Keijzer et al 2007			Y			Y	Y	Y								Y		
20	**Keijzer C** *et al*. Carbon monoxide production from desflurane and six types of carbon dioxide absorbents in a patient model. Acta Anaesthesiologica Scandinavica 2005; vol. 49; pp. 815-818	Keijzer C et al 2005.pdf		Keijzer et al 2005.doc				Y	Y	Y								Y		Y
21	**Kharasch ED** *et al.* In reply to LETTER: Amsorb® Causes No Less Carbon Monoxide Formation than Either "New" or "Classic" Sodalime. (**Lemmens H.** Anesthesiology 2002; vol. 97; no. 4; pp 1038)	Kharasch et al 2002						Y										Y		Y
22	**Kharasch ED** *et al.* Comparison of Amsorb®, Sodalime and Baralyme® Degradation of Volatile Anesthetics and Formation of Carbon Monoxide and Compound A in Swine In Vivo. Anesthesiology 2002; vol. 96 pp173-182	Kharasch et al 2002										Y						Y		Y
23	**Kharasch ED** *et al.* Comparison of Amsorb®, Sodalime, and Baralyme® Degradation of Desflurane and Isoflurane and on Formation of Carbon Monoxide in Swine In Vivo. Anesthesiology 2001; vol. 95; A-1125. Abstract from ASA 2001, New Orleans	Kharasch et al ASA 2001										Y						Y		Y
24	**Kharasch ED** *et al.* Comparison of Amsorb®, Sodalime, and Baralyme® Degradation of Sevoflurane and on Formation of Compound A in Swine In Vivo. Anesthesiology 2001; vol. 95; A-1124. Abstract from ASA 2001, New Orleans	Kharasch et al2 ASA 2001										Y						Y		Y
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33	**Kobayashi S** *et al.* Compound A Concentration in the Circle Absorber System during Low Flow Sevoflurane Anesthesia Comparison between Drägersorb Free®, Amsorb® and Sodasorb II® J. Clin. Anesth., Vol. 15, Feb. 2003	Kobayashi S et al 2003						Y										Y		Y
34	**Kobayashi S** *et al.* Compound A Concentration and CO_2 Absorption Using Amsorb® during Low-Flow Sevoflurane Anesthesia a Comparison of Amsorb® and Standard Soda Lime. Anesthesiology 2002; vol. 96; A-82. Abstract from ASA 2002, Orlando	Kobayashi S et al 2002									Y							Y		Y
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	Clinical Reference Bibliography For Soda Limes, Baralyme, AMSORB® and AMSORB® PLUS	Hyperlink to File where possible	Image/Graph	Accompanying Notes where applicable	DRAGERSORB 800	DRAEGERSORB 800 +	DRAGERSORB FREE	MEDISORB	SPHERASORB	LOFLOSORB	SODASORB	BARALYME	WAKOLIME	CARBOLIME	SOFNOLIME	INTERSORB	INTERSORB PLUS	AMSORB	AMSORB PLUS	OTHER
36	**Laster M** *et al.* Fires from the Interaction of Anesthetics with Desiccated Absorbent. Anesth. Analg. 2004; vol. 99; pp. 769-774	Laster M et al 2004		Laster et al 2004								Y								
37	**Lemmens H**. LETTER: Amsorb® Causes No Less Carbon Monoxide Formation than Either "New" or "Classic" Sodalime. Anesthesiology 2002; vol. 97; no. 4; pp 1038	Lemmens H 2002										Y						Y		Y
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40	**Mchaourab A** *et al.* Lack of Degradation of Sevoflurane by a New Carbon Dioxide Absorbent in Humans. Anesthesiology 2001; vol. 94; pp1007-9	Mchaourab et al 2001										Y						Y		
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42	**Murray JM** *et al.* LETTER in reply to: Warning: Carbon Dioxide Absorption Capacity of Amsorb Was Unexpectedly Low in Low-Flow Anesthesia. (**Ueyama H** *et al.* Anesthesiology 2000; vol. 93; pp1560)	Ueyama et al Murray in reply 2000				Y		Y										Y		
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48	**Renfrew C** *et al.* A New Approach to Carbon Dioxide Absorbents. ACTA Anaesthesiologica Scandanavica 1998; vol. 42; pp58-60	Renfrew C et al 1998																		Y
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55	**Versichelen LFM**. New Generation CO_2 Absorbents, Conference Notes, ALFA Congress 2002, Pisa, Italy	Versichelen 2002			Y	Y		Y	Y	Y	Y	Y			Y			Y		Y
56	**Versichelen LFM** *et al.* Only Carbon Dioxide Absorbents Free of Both NaOH and KOH Do Not Generate Compound A during In Vitro Closed-system Sevoflurane. Anesthesiology 2001; vol. 95; pp750-755	Versichelen et al 2001.pdf			Y	Y		Y			Y		Y		Y			Y		Y
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61	**Yamakage M** *et al.* Performance of four carbon dioxide absorbents in experimental and clinical settings. Anaesthesia 2009; vol. 64; pp287-292	Yamakage et al 2009						Y			Y								Y	Y
	References to Published Papers Specifically on Degradation of Volatile Anaesthetic Agents by Sodium- and/or Potassium Hydroxide-based Carbon Dioxide Absorbents.																			
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104	**Bedford RF** *et al.* The Renal Safety of Sevoflurane. Anesthesia & Analgesia 2000; vol. 90; pp505-508	Bedford et al 2000										Y						Y		Y
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106	**Bedi** *et al.* Postoperative nausea and vomiting following 8% sevoflurane anaesthesia. Anaesthesia 2000; vol. 55; pp55-56	Bedi et al 2000																		
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	Clinical Reference Bibliography For Soda Limes, Baralyme, AMSORB® and AMSORB® PLUS	Hyperlink to File where possible	Image/Graph	Accompanying Notes where applicable	DRAGERSORB 800	DRAEGERSORB 800 +	DRAGERSORB FREE	MEDISORB	SPHERASORB	LOFLOSORB	SODASORB	BARALYME	WAKOLIME	CARBOLIME	SOFNOLIME	INTERSORB	INTERSORB PLUS	AMSORB	AMSORB PLUS	OTHER
109	**Bito H** *et al.* Degradation products of sevoflurane during low-flow anaesthesia. British Journal of Anaestheisa 1995; vol. 74(1); pp56-59	Bito et al 1995																		Y
110	**Bito H** *et al.* Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime. British Journal of Anaesthesia 1995; vol. 74(6); pp667-669	Bito et al 1995 (2)									Y	Y								Y
111	**Bito H** *et al.* Effects of Low-Flow Sevoflurane Anesthesia on Renal Function: Comparison with High-Flow Sevoflurane Anesthesia and Low-Flow Isoflurane Anesthesia. Anesthesiology 1997; vol. 86(6); pp1231-1237	Bito et al 1997										Y								Y
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113	**Bito H** *et al.* Long-Duration, low flow sevoflurane anaesthesia using two carbon dioxide absorbents: Quantification of degradation products in the circuit. Anesthesiology 1994; vol. 81; pp340-345	Bito et al 1994 (2)										Y								Y
114	**Bonome C** *et al.* Low-flow Anesthesia and Reduced Animal Size Increase Carboxyhemoglobin Levels in Swine During Desflurane and Isoflurane Breakdown in Dried Soda Lime. Anesthesia & Analgesia 1999; vol. 89; pp909-16	Bonome et al 1999			Y							Y								
115	**Bouche M P** *et al.* No Compound A Formation with Superia® During Minimal -Flow Sevoflurane Anaesthesia: A Comparison of Sofnolime®. Anaesthesia & Analgesia 2002; vol. 95; pp1680-1685	Bouche M P et al 2002									Y				Y			Y		Y
116	**Brown BR Jr** *et al.* Sevoflurane Breakdown in Soda Lime. Anesthesia & Analgesia 1991; vol. 73(5); pp670-671																			
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121	**Chang Kil Park**. Effect of the Elimination of CO_2 Absorbtion Canister on the Rate of Recovery from General Anesthesia. Anesthesiology 2001; vol 95; A-101. Abstract ASA 2001, New Orleans	Park ASA 2001	Park ASA 2001									Y								
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124	**Conzen P F** *et al.* Low-flow Sevoflurane Compared with Low-flow Isoflurane Anesthesia in Patients with Stable Renal Insufficiency Anesthesiology 2002; vol. 97(3); pp578-584	Conzen P T et al 2002										Y								Y
125	**Conzen P** *et al.* Sensitive Markers of Renal Injury after Low-Flow-Sevoflurane and Isoflurane in Patients with Preexisting Renal Insufficiency. Anesthesiology 2000;vol 93; A-. Abstract from ASA 2000, San Francisco	Conzen P et al																		Y
126	**Cunningham DD** *et al.* Sevoflurane degradation to compound A in anaesthesia breathing systems. British Journal of Anaesthesia 1996; vol. 77; pp537-543	Cunningham DD et al 1996									Y									Y
127	**Czerner S** *et al.* Sevoflurane Low-Flow-Anesthesia in Patients with Renal Insufficiency: A Multi-Center, Randomized, Comparative Study. Anesthesiology 2000;vol 93; A-. Abstract from ASA 2000, San Francisco	Czerner et al ASA 2000										Y								Y
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130	**ECRI Hazard Report.** Anaesthesia Unit Absorbers, Carbon Dioxide. Vol. 24; No. 6; Nov. 2003	ECRI 2003(2)										Y								Y
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133	**Eger EI 2nd** *et al.* Circuit absorption of halothane, isoflurane, and sevoflurane. Anesthesia & Analgesia 1998; vol. 86; pp1070-1074	Eger et al 1998																		Y
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	Clinical Reference Bibliography For Soda Limes, Baralyme, AMSORB® and AMSORB® PLUS	Hyperlink to File where possible	Image/Graph	Accompanying Notes where applicable	DRAGERSORB 800	DRAEGERSORB 800 +	DRAGERSORB FREE	MEDISORB	SPHERASORB	LOFLOSORB	SODASORB	BARALYME	WAKOLIME	CARBOLIME	SOFNOLIME	INTERSORB	INTERSORB PLUS	AMSORB	AMSORB PLUS	OTHER
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155	**Frink EJ Jr** *et al.* Sevoflurane degradation product concentrations with soda lime during prolonged anesthesia. Journal of Clinical Anesthesia 1994; vol. 6(3); pp239-242	Frink EJ et al 1994																		Y
156	**Frink EJ Jr** *et al.* Compound A Concentrations during Sevoflurane Anesthesia in Children. Anesthesiology 1996; vol. 84(3); pp566-571	Frink EJ et al 1996									Y	Y								Y
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