NARRATIVE REVIEW ARTICLE

CME

Carbon Dioxide Absorption During Inhalation Anesthesia: A Modern Practice

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CO_2 absorbents were introduced into anesthesia practice in 1924 and are essential when using a circle system to minimize waste by reducing fresh gas flow to allow exhaled anesthetic agents to be rebreathed. For many years, absorbent formulations consisted of calcium hydroxide combined with strong bases like sodium and potassium hydroxide. When Sevoflurane and Desflurane were introduced, the potential for toxicity (compound A and CO, respectively) due to the interaction of these agents with absorbents became apparent. Studies demonstrated that strong bases added to calcium hydroxide were the cause of the toxicity, but that by eliminating potassium hydroxide and reducing the concentration of sodium hydroxide to <2%, compound A and CO production is no longer a concern. As a result, CO_2 absorbents have been developed that contain little or no sodium hydroxide. These CO_2 absorbent formulations can be used safely to minimize anesthetic waste by reducing fresh gas flow to approach closed-circuit conditions. Although absorbent formulations have been improved, practices persist that result in unnecessary waste of both anesthetic agents and absorbents. While CO_2 absorbents may seem like a commodity item, differences in CO_2 absorbent formulations can translate into significant performance differences, and the choice of absorbent should not be based on unit price alone. A modern practice of inhalation anesthesia utilizing a circle system to greatest effect requires reducing fresh gas flow to approach closed-circuit conditions, thoughtful selection of CO_2 absorbent, and changing absorbents based on inspired CO_2. (Anesth Analg 2021;132:993–1002)

GLOSSARY

AF = autoflow; **BaOH** = barium hydroxide; **$Ca(OH)_2$** = calcium hydroxide; **$CaCl_2$** = calcium chloride; **$CaCO_3$** = calcium carbonate; **CV** = coefficient of variation; **$etCO_2$** = end-tidal CO_2; **exp** = expiratory; **F_ACO_2** = alveolar CO_2 (%); **FDA** = US Food and Drug Administration; **FGF** = fresh gas flow; **$FiCO_2$** = inspired CO_2 (%); **Freq.** = respiratory rate; **H_2O** = water; **HCO_3** = carbonic acid; **insp** = inspiratory; **KOH** = potassium hydroxide; **LiCl** = lithium chloride; **LiOH** = lithium hydroxide; **MAC** = minimum alveolar concentration; **MV** = minute ventilation; **NaOH** = sodium hydroxide; **NI** = no indicator; **PEEP** = positive end-expiratory pressure; **P_{MAX}** = maximum inspiratory pressure limit; **PPS** = inspiratory pressure support; **SD** = standard deviation; **Tco_2** = < 0.5% = time inspired CO_2 was less than 0.5%; **T_{INSP}** = inspiratory time; **V_T** = tidal volume

At this time, I happened to be engaged in the private practice of anaesthesia, using a great deal of nitrous-oxide-oxygen and buying my own gases. The saving of gas by this technique interested me.

—Ralph M. Waters, MD
Proceedings of the Royal Society of Medicine (1936)

In 1924, Ralph M. Waters[1] published an article titled, Clinical Scope and Utility of Carbon Dioxide Filtration in Inhalation Anesthesia. In that article, and subsequent publications on the topic, Waters[2,3] described his clinical use of a canister containing CO_2 absorbents for administering inhalation anesthesia. His device, the Waters Canister, facilitated rebreathing of exhaled anesthetic vapor leading to (in his words) advantages of economy because fewer inhaled drugs are used, convenience by minimizing "disagreeable odors" in the operating room, and patient welfare by conserving heat and humidity. With the introduction of CO_2 absorption into clinical practice, Waters laid the foundation for the modern practice of inhalation anesthesia, including the development of the circle breathing circuit, which is the primary method used to deliver inhalation anesthetics worldwide.[a]

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[a]The German surgeon Franz Kuhn proposed the use of a circle breathing system using potassium hydroxide to remove exhaled CO_2 as early as 1906, but he did not use it in clinical practice.

In his original articles, Waters carefully described a detailed clinical approach to what is essentially closed-circuit anesthesia, in which he attempted to eliminate waste by introducing into the breathing circuit only what the patient removes in the form of oxygen and anesthetic agents. It is a testament to his clinical skills that Waters was able to develop and use this technique safely and successfully, without the benefit of pulse oximetry or gas analysis for CO_2, oxygen, and anesthetic concentration monitoring.

Modern anesthesia practice has embraced the use of the circle breathing circuit and CO_2 absorbents to reduce the waste that can occur when delivering inhalation anesthetics. However, common practices prevent the modern anesthetist from achieving the waste reduction Waters was able to accomplish. These practices have developed in part out of concern for the potential for toxic byproducts due to the interaction between inhalation agents and CO_2 absorbents. Concern for compound A production while administering Sevoflurane has led to inherently wasteful minimum fresh gas flow (FGF) recommendations well in excess of a closed-circuit condition.[4] CO production resulting from the combination of Desflurane and desiccated absorbents has led to wasteful practices for replacing CO_2 absorbents. Managing FGF is the primary strategy for minimizing the environmental contamination from inhaled anesthetics that act as greenhouse gases and contribute to global warming.[5,6]

This article will explore the evolution of CO_2 absorbents and describe how modern CO_2 absorbents have eliminated concern for toxicity. As a result, when using a modern absorbent formulation, Sevoflurane can be administered safely under closed-circuit conditions, without concern for the minimum FGF. Similarly, absorbents need not be replaced before they are completely utilized due to concern for desiccation and CO production with Desflurane. A safe approach to selecting absorbents and using them effectively to minimize waste is described.

EVOLUTION OF CO_2 ABSORBENTS

Before exploring the details of CO_2 absorbent technology, it is useful to understand clearly how anesthetic waste can be controlled when using a circle system and the essential role of the absorbent. The circle breathing circuit has been specifically designed to reduce wasted anesthetic by facilitating the return of exhaled gases to the patient, otherwise known as rebreathing. When using a circle breathing circuit, the anesthetist controls the percentage of exhaled gas that is rebreathed by setting the FGF. When only enough fresh gas is provided to replace the losses from the circuit, 100% of the exhaled gas is rebreathed, a condition otherwise known as closed-circuit anesthesia. As fresh gas is increased above closed-circuit conditions, the rebreathed percentage decreases, and any gas flow exceeding the closed-circuit condition ultimately leaves the circuit via the scavenging system.[5] While rebreathing helps to conserve inhaled anesthetics, it can only be accomplished safely by incorporating an absorbent material to remove the exhaled CO_2 before the gas is returned to the patient.

The basic chemistry of CO_2 absorbents has not changed since the time of Waters and relies on an exothermic reaction combining CO_2 with calcium hydroxide ($Ca(OH)_2$) to form calcium carbonate ($CaCO_3$) and water (H_2O). Metal hydroxide catalysts like sodium hydroxide (NaOH), potassium hydroxide (KOH), and barium hydroxide (BaOH) are used to enhance the speed of the reaction and capacity to absorb CO_2. An example of the chemical reaction using NaOH as the catalyst is as follows:

$CO_2 + H_2O \rightarrow H_2CO_3$

$H_2CO_3 + NaOH \rightarrow NaHCO_3 + H_2O$

$NaHCO_3 + Ca(OH)_2 \rightarrow CaCO_3 + H_2O + NaOH +$ Heat

Moisture is essential to the reaction because it allows the gaseous CO_2 to form carbonic acid (HCO_3) so that it can react with the $Ca(OH)_2$.[7] Waters advocated for an absorbent containing 5% NaOH and 15%–20% H_2O. The safety of this basic formulation was unchallenged for >70 years until the introduction of Desflurane and Sevoflurane, which resulted in unintended consequences.

Strong bases such as NaOH and/or KOH added to the $Ca(OH)_2$ base enhance the absorptive capacity of $Ca(OH)_2$. As the concentration of strong base increases, the capacity of the absorbent to absorb CO_2 increases as well. In an in vitro study, Neumann et al[8] demonstrated that CO_2 appeared (indicating exhaustion of the absorbent) 12%–14% sooner when $Ca(OH)_2$ alone was compared to absorbent containing NaOH

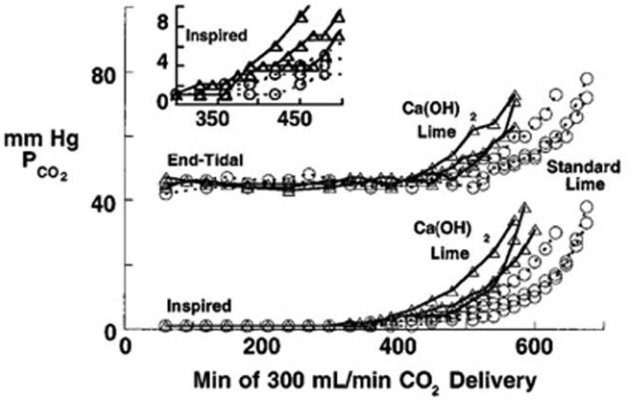

Figure 1. The difference in absorptive capacity between standard lime containing KOH and NaOH (O, dashed lines) versus $Ca(OH)_2$ alone (Δ, continuous lines). In this in vitro study, CO_2 appeared approximately 12%–14% sooner in the inspired gas with $Ca(OH)_2$ alone. From Neumann et al.[8] $Ca(OH)_2$ indicates calcium hydroxide; KOH, potassium hydroxide; NaOH, sodium hydroxide.

and KOH (Figure 1). Absorbent brands are distinguished in large part by the relative concentrations of strong base. In a study of commercially available absorbents, Stabernack et al[9] found approximately a 30% increase in time to appearance of inspired CO_2 when $Ca(OH)_2$ containing strong base was compared with $Ca(OH)_2$ alone. Of note, those authors tested lithium hydroxide (LiOH) as the primary absorbent and found nearly a 3-fold (>300%) increase in the duration of time until CO_2 absorption began to fail compared to the longest-lasting calcium-based absorbent.[9]

Desflurane and Sevoflurane were introduced in the early 1990s, offering advantages over the existing anesthetic agents, and were quickly accepted into clinical practice. The capacity for Sevoflurane to interact with absorbent material to produce compound A, which had been shown to be nephrotoxic in a rat model, was well known. Despite the lack of evidence for nephrotoxicity in humans, the initial US Food and Drug Administration (FDA)–approved labeling restricted the minimum FGF to 2 L/min to limit the amount of rebreathing and thus the concentration of compound A that could accumulate in the circuit.[4] In a review article in 2003, Baum and Woehlck[10] summarize the data, indicating that compound A is not a concern in humans. Although the initial minimum flow restriction has since been modified or even removed in many countries, wasteful practices rooted in that recommendation persist.[11] Because for most anesthetized adult patients, closed-circuit conditions require between 180 and 500 mL/min of FGF, the minimum flow recommendation guaranteed that a significant amount of anesthetic would be wasted continuously through the scavenging system. Although compound A from Sevoflurane was never identified as causing a clinical problem in humans, that was not the case with Desflurane-related byproducts. There were case reports raising patient safety concerns especially related to CO production in the presence of Desflurane.[12,13] These case reports stimulated a number of studies designed to understand the sources of these clinical problems.

Not long after the case reports began to appear, CO production was investigated in a laboratory study using absorbents commercially available at the time, specifically, Sodasorb (Molecular Products, Louisville, CO) and Baralyme (Allied Healthcare Products Inc, St Louis, MO), both of which contained NaOH and KOH.[14] Fang et al[14] studied fresh and partially and totally dried samples of soda lime (3% NaOH) and Baralyme (5.3% KOH) exposed to a continuous flow of gas containing different anesthetic agents. They found that CO production was completely dependent on the state of hydration, that is, fresh, normally hydrated samples of both absorbents did not produce CO. When testing dried absorbents, the amount of CO production depended on the type and concentration of inhalation agent used (Desflurane > Enflurane > Isoflurane > Halothane > Sevoflurane), the level of moisture, temperature, and duration of exposure. Interestingly, the author's recommendations did not focus on the presence of strong base in the absorbents because alternative choices were not available at the time. Instead, the authors recommended using fresh absorbents and keeping FGF <2–3 L/min when using Desflurane to avoid desiccation. The findings of this and other studies ultimately led to practices designed to eliminate the risk of absorbent desiccation. These practices included changing the absorbent every Monday morning or whenever fresh gas has been flowing for an undetermined amount of time. The other more important consequence has been the efforts to reformulate the absorbent chemistry to eliminate the concern for interaction with anesthetic agents.

Absorbent chemistry has evolved significantly since 1995 and represents the first major changes in CO_2 absorbents since the introduction into clinical practice by Waters in 1924. Initial studies confirmed the requirement for desiccated absorbent and Desflurane to produce significant CO and identified that the type and concentration of strong base was directly related to the amount of CO produced. Specifically, KOH produced more CO than NaOH, and reducing the NaOH concentration to <2% reduced the amount of CO produced[8] (Figure 2). Since the study by Neumann et al,[8] other studies have confirmed the relationship between the concentration of strong base and the amount of CO produced. Stabernack et al[9] desiccated 8 commercially available absorbents to

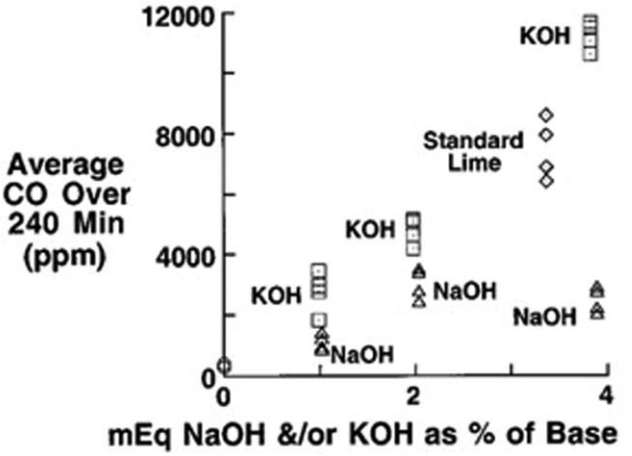

Figure 2. The impact of increasing concentrations of strong base on the amount of CO produced by Desflurane in the presence of desiccated absorbents. □ KOH, Δ, NaOH, and ◇ both KOH and NaOH. Each marker represents the average CO over 240 min (determined from the area under the curve) for each of 4 experiments. KOH produces more CO than NaOH and limiting the concentration of NaOH to <2% reduces the CO produced dramatically. From Neumann et al.[8] KOH indicates potassium hydroxide; NaOH, sodium hydroxide.

study their potential to produce CO: 7 using $Ca(OH)_2$ and 1 using LiOH as the primary absorbent. These authors found that $Ca(OH)_2$ alone or LiOH virtually eliminated CO production. The lowest concentration of strong base studied was KOH 0.1% in $Ca(OH)_2$, and peak CO was <10,000 ppm versus nearly 40,000 ppm for soda lime containing 3% NaOH.[9] Keijzer et al[15] studied 6 commercially available absorbents in desiccated form, comparing 2 containing both KOH and NaOH to 3 made of $Ca(OH)_2$ alone and 1 with LiOH. They confirmed that CO production requires the presence of strong base and was absent when using LiOH as the primary absorbent.[15] These studies confirmed that both the presence of strong base and desiccation of the absorbent material were required for CO to be produced in the presence of Desflurane, but this was not the only interaction of concern.

Compound A was another concern during this time as it was well known that Sevoflurane interacted with CO_2 absorbents to produce this potentially nephrotoxic compound. Some of the studies investigating the factors leading to CO production also examined how those factors influenced the production of compound A.[8,9,16,17] Neumann et al[8] compared normally hydrated "standard" lime (KOH + NaOH) to hydrated $Ca(OH)_2$ without strong base for the potential to produce compound A. Peak compound A levels with standard lime significantly but only slightly exceeded those with $Ca(OH)_2$ alone at 21.6 vs 20.3 ppm.[8] Higuchi et al[16] studied 4 absorbents, Dräegersorb 800 (2% NaOH, 3% KOH; Draeger Medical, Lubeck, Germany), Dräegersorb 800+ (2% NaOH, 0.003% KOH; Draeger Medical, Lubeck, Germany), Medisorb (1% NaOH, 0.003% KOH; CareFusion, Helsinki, Finland), and Amsorb (Armstrong Medical, Londonderry, UK) for the potential to produce compound A. Amsorb produced the least compound A consistent with the baseline concentration of compound A in the drug. Medisorb produced significantly less compound A than the other 2 containing strong base but still contained some KOH.[16] Versichelen et al[17] concluded that both KOH and NaOH needed to be removed to eliminate compound A production, but of note, those authors did not study any absorbent with NaOH <2% in the absence of KOH. Stabernack et al[9] studied commercially available absorbents and found that the presence of NaOH and KOH increased the compound A levels, although the total compound A measured was <30 ppm. For perspective, compound A toxicity in animal studies was observed for concentrations exceeding 100 ppm and has never been observed in humans. $Ca(OH)_2$ and LiOH without strong base produced very little compound A.[9]

Absorbents without any strong base were developed and introduced commercially in the late 1990s and early 2000s. At the same time, it was well known that the presence of strong base enhanced the absorptive capacity of $Ca(OH)_2$. The challenge to the chemists was to develop absorbent formulations that maximized absorbent capacity while eliminating any significant potential to produce CO in the presence of Desflurane when desiccated, or compound A in the presence of Sevoflurane.

One of the first absorbents studied containing $Ca(OH)_2$ alone was Amsorb.[18] The goal of that formulation was to eliminate the strong bases, NaOH and KOH, and the production of CO and compound A. Instead of strong base, Amsorb uses calcium chloride ($CaCl_2$) as a humectant to maintain the moisture content in the absorbent. Murray et al[18] compared Amsorb to 2 other commercially available absorbents, Intersorb (3% NaOH; Intersurgical, Berkshire, UK) and Dräegersorb (3% NaOH), to understand the relative potential of these absorbents to produce CO in the presence of inhalation agents when dried, compound A in the presence of Sevoflurane, and also the capacity to absorb CO_2. Peak CO concentrations approached 600 ppm for Intersorb and Dräegersorb versus 1–3 ppm for Amsorb depending on the inhalation agent tested. When exposed to Sevoflurane, compound A concentrations with Amsorb were equivalent to those found in the drug normally at <3 ppm, whereas the mean concentrations were 30–35 ppm for the other absorbents. The Amsorb formulation eliminated CO and compound A production, but CO_2 absorption capacity was reduced at 102 versus 120 and 115 L/kg for Intersorb and Dräegersorb, respectively.

LiOH was evaluated as an alternative to $Ca(OH)_2$ and found to not interact with anesthetic agents to produce either compound A or CO and provide an even better absorbent capacity. Stabernack et al[9] evaluated LiOH at 2 different temperatures and found that it did not produce compound A or CO. Even better, the lithium absorbent capacity was more than 200% greater than any of the calcium-based absorbents tested.[9] Keijzer et al[15] confirmed that LiOH did not produce CO but commented that its caustic nature prevented it from being used in clinical practice. SpiraLith (Micropore Inc, Elkton, MD) was initially introduced as an LiOH absorbent eliminating concerns for caustic injury by embedding the LiOH on a solid polymer matrix rather than using granules. Hendrickx et al[19] and Omer et al[20] have done comparative testing of SpiraLith against a variety of $Ca(OH)_2$-based absorbent canisters using 2 different anesthesia machines and confirmed the increased absorptive capacity of LiOH in a controlled laboratory model. Unfortunately, the cost of lithium has become too prohibitive in recent years to be used as a medical absorbent. Lithium chloride (LiCl) continues to be used in LithoLyme (Allied Healthcare Products Inc, St Louis, MO) as a catalyst added to $Ca(OH)_2$.

The evolution of absorbent formulations demonstrates the process of finding the optimal absorbent chemistry. The primary approach has been to reduce or eliminate the strong base to maximize absorption and eliminate the potential for toxic interactions with inhalation anesthetics.

WHAT ABSORBENT FORMULATIONS MAXIMIZE ABSORPTIVE CAPACITY WHILE ELIMINATING CONCERN FOR EXPOSURE TO CO AND COMPOUND A?

Comparisons of the most recently developed absorbent formulations that have minimized or eliminated NaOH help us to understand the formulation that maximizes absorption and eliminates patient risk from CO and compound A. Kharasch et al[21] performed the only in vivo study using a pig model to determine the CO production and resulting carboxyhemoglobin levels when Desflurane, Isoflurane, and Sevoflurane were administered using 4 different absorbents in fresh or dried forms. The absorbents studied were Baralyme, soda lime, new soda lime, and Amsorb. Both Baralyme and soda lime contained KOH. New soda lime eliminated KOH but used 2.5% NaOH and Amsorb had no strong base. Not surprisingly, Desflurane produced the most CO in the presence of dried absorbents especially with Baralyme. When using Amsorb and new soda lime, the levels of CO in inspired gas and the resulting carboxyhemoglobin were virtually the same and changed very little from baseline. Amsorb did not produce compound A in the presence of Sevoflurane, while the other absorbents resulted in 20–40 ppm of compound A.

More recent studies have directly compared Dräegersorb Free (NaOH < 2%; Draeger Medical, Lubeck, Germany) and Amsorb Plus (Armstrong Medical, Londonderry, UK), both engineered to minimize interaction with anesthetic agents while preserving maximum absorption capacity. Dräegersorb Free includes a minimal amount of strong base, while Amsorb Plus uses engineered granule size and shape to maximize absorption. Kobayashi et al[22] studied compound A production with 4 absorbents—Dräegersorb Free (2% NaOH), Sodasorb II (2.5% KOH, 2.5% NaOH; Molecular Products, Louisville, CO), Amsorb, and Amsorb Plus. They found that only Sodasorb II produced compound A. For the other absorbents, compound A concentrations were not significantly different from baseline (Figure 3). Struys et al[23] directly compared Amsorb and Dräegersorb Free to determine the relative absorptive capacity and potential to produce compound A with Sevoflurane and CO with Desflurane when absorbents were dried. Dräegersorb Free lasted nearly 20% longer to the inspiratory CO_2 target than Amsorb. Compound A production was <1 ppm for both absorbents albeit slightly higher (0.25 ppm) with Dräegersorb Free. No detectable CO was found with either absorbent.[23]

The optimal chemical formulation to maintain absorbent capacity without potential for toxic interactions with anesthetic agents eliminates KOH but includes NAOH <2%. Knolle et al[24] directly measured the absorptive capacity in liters of CO_2 per 100 g of absorbent of several absorbents in a laboratory setting. For each sample tested, the same mass of absorbent (30 g) was placed in glass tubes and exposed to a gas mixture containing 5.1% CO_2 until the concentration of CO_2 leaving the tube was 0.5%. The total amount of CO_2 the material was exposed to could then be calculated. The absorbents were divided into 3 groups, where group 1 contained both KOH and NaOH, group 2 contained only NaOH, and group 3 had no strong base. The groups with the strong base had the longest durations and greatest absorptive capacity with nearly a 2-fold difference in some cases (Table 1).

SpiraLith Ca (Micropore Inc, Elkton, MD) is the newer version of a nongranular solid polymer $Ca(OH)_2$-based absorbent that replaced SpiraLith,

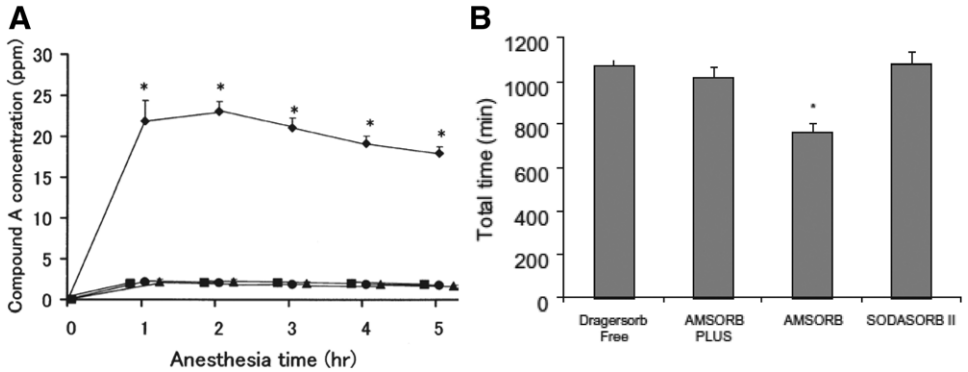

Figure 3. Compound A production (A) and absorptive capacity (B) for 4 different absorbents reported as mean ± SD for 3 runs. ◊ Sodasorb II, ○ Amsorb Plus, □ Amsorb, and Δ Dräegersorb Free. By limiting the NaOH to <2%, Dräegersorb Free does not produce compound A yet preserves the maximum absorptive capacity. From Kobayashi et al.[22] KOH indicates potassium hydroxide; NaOH, sodium hydroxide; SD, standard deviation.

Table 1. Eight Different Uniform Samples of CO_2 Absorbents Were Tested in Test Tubes to Determine Absorptive Capacity and Duration of Action by Exposing the Absorbents to a Standardized Flow of CO_2

Characteristics of CO_2 Absorption in Untreated Samples								
	Sample (Brand)							
	Group 1 (KOH + NaOH)		Group 2 (NaOH Only)			Group 3 (No Strong Base Added)		
Variable	A (Baralyme)	B (Drägersorb 800)	C (Drägersorb 800 Plus)	D (Intersorb)	E (Spherasorb)	F (LoFloSorb)	G (Superia)	H (Amsorb)
T_{CO_2} < 0.5% (h:min)	3:41 ± 0:19	5:53 ± 0:30	5:53 ± 0:20	5:04 ± 0:27	5:21 ± 0:19	3:00 ± 0:06	5:23 ± 0:06	3:09 ± 0:12
Absorption capacity (L/100 g)	9.1 ± 0.8	14.5 ± 1.3	14.6 ± 0.8	12.6 ± 1.1	13.3 ± 0.8	7.3 ± 0.3	13.4 ± 0.3	7.8 ± 0.5

Each trial ended when the effluent CO_2 concentration was 0.5%. Group 1 contained both KOH and NaOH, group 2 only NaOH, and group 3 no strong base. Five samples of each absorbent were tested in groups 1 and 2. For group 3, 4 samples were tested. Data are reported as mean ± SD. Note that in general, the capacity for CO_2 absorption and duration of action were diminished in the absence of strong base. Adapted from Knolle et al.[24]

Abbreviations: KOH, potassium hydroxide; NaOH, sodium hydroxide; SD, standard deviation; T_{CO_2}, < 0.5% = time inspired CO_2 was less than 0.5%.

Table 2. Sixteen Different CO_2 Absorbents Were Tested Using a Circle System and Test Lung to Determine Duration of Action as Measured by Time to an Inspired CO_2 of 0.5%

Brand (Manufacturer)	Macro Shape	NaOH (%)	Micro Shape	Weight Fresh Product in Compact Bloc (g)	Density (g/100 mL)	Volume Fresh Product in Compact Bloc (mL)	CO_2 Flow (mL/min)	$F_ACO_2 - FiCO_2$ (%)	Time per 100 mL of Product for $FiCO_2$ to Reach 0.5%	
									min	CV (%)
LoFloSorb (Intersurgical, Berkshire, UK)	Granular	0	Spheres	461 (5)	67 (0)	687 (7)	160 (3)	4.4 (0.1)	50 (2)	5
Amsorb Plus (Armstrong Medical, Londonderry, UK)	Granular	0	Broken cylinders	449 (11)	65 (1)	688 (16)	160 (2)	4.3 (0.1)	56 (3)	6
LithoLyme (Allied Healthcare Products Inc, St Louis, MO)	Granular	0/LiCl	Broken cylinders	464 (17)	67 (0)	691 (26)	161 (1)	4.3 (0.1)	59 (3)	5
SoLo (Molecular Products, Essex, UK)	Granular	<1	Broken fragments	452 (16)	64 (1)	707 (30)	160 (1)	4.3 (0.1)	61 (5)	8
SodaSorb LF (Molecular Products)	Granular	<1	Broken cylinders	529 (4)	73 (1)	730 (15)	161 (1)	4.1 (0.1)	66 (2)	4
Drägersorb Free (Draeger Medical, Lubeck, Germany)	Granular	0.5–2	Hemisphere	544 (9)	77 (0)	709 (12)	160 (1)	4.3 (0.2)	69 (2)	4
Spherasorb (Intersurgical)	Granular	1.5	Spheres	517 (14)	75 (0)	686 (18)	161 (2)	4.3 (0.2)	70 (1)	1
AtraSorb (Atrasorb Pharma Sao Roque, Brazil)	Granular	2.5–3.0	Bullet	584 (14)	80 (0)	726 (18)	160 (3)	4.3 (0.1)	72 (1)	2
Sofnolime (Molecular Products)	Granular	< 3	Broken fragments	561 (9)	78 (0)	721 (12)	161 (1)	4.2 (0.3)	77 (2)	3
SodaSorb (Molecular Products)	Granular	< 4	Broken cylinders	586 (14)	85 (1)	690 (21)	161 (2)	4.3 (0.1)	78 (4)	5
Intersorb Plus (Intersurgical)	Granular	3	Broken cylinders	564 (29)	80 (1)	701 (32)	158 (0)	4.2 (0.1)	88 (6)	6
Medisorb (CareFusion, Helsinki, Finland)	Granular	1–2	Broken fragments	544 (6)	77 (1)	711 (10)	161 (1)	4.2 (0.1)	88 (4)	5
FLOW-i (Molecular Products; distributed by Getinge, Solna, Sweden in proprietary container)	Granular	< 3	Broken fragments	559 (9)	79 (2)	704 (26)	160 (2)	4.2 (0.1)	90 (2)	2
Drägersorb 800 (Draeger Medical)	Granular	2	Hemisphere	578 (4)	82 (0)	702 (5)	160 (2)	4.3 (0.1)	91 (1)	1
SpiraLith Ca with indicator[a] (Micropore Inc, Elkton, MD)	Cartridge	<1	Preformed channels	824 (11)[b]	88 (1)	933 (0)[c]	160 (1)	4.5 (0.1)	95 (1)	1
SpiraLith Ca NI[a] (Micropore Inc)	Cartridge	<1	Preformed channels	815 (7)[b]	87 (1)	933 (0)[c]	161 (1)	4.3 (0.2)	100 (1)	1

Note that in general, the longer duration of action per standardized volume of product was associated with increasing concentration of NaOH. The exception is SpiraLith CA, which has the same chemistry as Dräegersorb Free, but a duration of action nearly 30% greater. The CO_2 flow and $F_ACO_2 - FiCO_2$ difference did not differ between products (P = .774 and .052, respectively). Time (min) per 100 mL of product for $FiCO_2$ to reach 0.5% did differ among the different products.From Jiang et al.[28]

Abbreviations: CV, coefficient of variation; F_ACO_2, alveolar CO_2 (%); $FiCO_2$, inspired CO_2 (%); LiCl, lithium chloride; NAOH, sodium hydroxide; NI, no indicator.

Time (min) per 100 mL of product for $FiCO_2$ to reach 0.5% did differ among the different products.

[a]Tested in custom-made refillable plastic container different from that used to test granular products—see text for details.

[b]Does not include weight of plastic core nor wrap around cartridge.

[c]Does not include volume of plastic core (67 mL).

the LiOH absorbent product. This technology utilizes a similar chemistry to Dräegersorb Free, but the lime is embedded on a solid polymer (nongranular) sheet. The official safety data sheet indicates that Dräegersorb Free has an NaOH concentration between 0.5% and 2%, whereas NaOH is <1% for SpiraLith Ca.[25,26] This chemistry is designed to maximize the absorptive capacity while eliminating concerns for CO or compound A production. Further, the SpiraLith Ca solid polymer approach is designed to maximize the exposure of exhaled gas to the active absorbent material and eliminate the channeling associated with granules, both of which help to maximize absorbent utilization. Granule properties (shape and size) are engineered to influence the absorptive capacity of absorbents.[27] There are no published studies specifically looking at the gas flows through SpiraLith. SpiraLith is unique as a nongranular absorbent, and the engineering intended to maximize absorbent capacity is proprietary. Studies comparing absorptive capacity for absorbents with similar chemistry but different morphology provide insight into the impact of the solid polymer design.

SpiraLith Ca has been compared in an in vitro study to a number of granular absorbents to determine the relative absorbent capacities of currently available granular formulations.[28] This study tested the "efficiency" of 16 different absorbents in vitro under low-flow conditions. Efficiency was defined as the time to appearance of an inspired CO_2 of 0.5% in the breathing system and normalized to 100 mL of absorbent to facilitate comparison. The normalized efficiency ranged from 50 min/100 mL of absorbent for Amsorb to 100 min/100 mL for SpiraLith Ca. SpiraLith Ca and Dräegersorb Free have similar chemistries in limiting the concentration of NaOH to <2%, but the time to an inspired CO_2 of 0.5% was 40% longer for SpiraLith Ca than Dräegersorb Free, attesting to the added efficiency of the solid polymer packaging (Table 2).

MAXIMIZING ABSORBENT PERFORMANCE

CO_2 absorbent is absolutely required to facilitate safe rebreathing of exhaled gases in a circle anesthesia system. As a consumable item, these absorbents are purchased, adding cost to patient care, along with increasing the waste stream, and contributing to the problem of medical waste disposal. It makes sense therefore to develop strategies that maximize the absorbent performance. In essence, maximizing performance can be defined as absorbing the most CO_2 per mass of absorbent at the least cost. The goal of maximizing performance can be achieved by a combination of thoughtful absorbent selection and following clinical practices that ensure maximal utilization before the absorbent is discarded.

We have already reviewed the data which indicate that the optimal absorbent chemistry seeks to both maximize absorptive capacity and eliminate concerns for toxicity from CO or compound A. $Ca(OH)_2$ combined with NaOH <2% is the sweet spot for maximizing absorption and eliminating toxicity concerns. Data indicate that a solid polymer absorbent increases absorptive capacity relative to currently available granular forms. $Ca(OH)_2$ alone eliminates toxicity concerns at the cost of at least a 20%–30% reduction in absorptive capacity. Thus, from a cost perspective, $Ca(OH)_2$ alone could be a good choice if it is at least 20%–30% less expensive than the products containing NaOH <2%, but it will still generate an increased volume of waste for disposal because more product will be required to absorb the same amount of CO_2.

Minimizing absorbent waste likely depends at least as much on clinical practice as it does on selecting the absorbent material. Absorbents are commonly exchanged for new material when the indicator, typically ethyl violet, changes color. Unfortunately, there is no standard clinical practice designed to maximize absorbent utilization before the material is discarded, and as a result, much useful CO_2 absorbent is likely being discarded. Further, when using granular absorbents, potentially useful absorbent material is virtually always wasted due to channeling of gases through the path of least resistance, bypassing active absorbent material.

An alternative to using the indicator to guide when to change the absorbent is to monitor inspired CO_2 and change the absorbent when the inspired CO_2 level reaches around 5 torr or 0.05% (Figure 4). The effect of this modest increase in inspired CO_2 concentration on the end-expired CO_2 concentration is clinically inconsequential for the majority of the patients yet guarantees maximal utilization of the purchased material before it is discarded. Fortunately, because capnography is a monitoring standard when inhaled anesthetics are administered, the inspired CO_2 is routinely monitored, making it feasible to change the material based on inspired CO_2 measurement. Changing absorbent based on the inspired CO_2 concentration may require performing the change during an anesthetic. Many anesthesia delivery systems offer an option for an absorbent canister that can be changed during an anesthetic without creating a leak in the system. This option, while it may add some cost to the workstation, is desirable because it allows for maximal utilization of absorbent.

There are a couple of caveats to using the technique of changing absorbent based on inspired CO_2 safely and successfully. Exhausted CO_2 absorbent is the most common, but not only, cause of a horizontal elevation of the capnogram indicating inspired CO_2. Incompetent valves, especially expiratory valves,

Figure 4. A, Example of inspired CO_2 during low-flow anesthesia with exhausted absorbent. B, FGF increased to exceed minute ventilation and create an open circuit resulting in elimination of inspired CO_2. AF indicates autoflow; $etCO_2$, end-tidal CO_2; exp, expiratory; FGF, fresh gas flow; $FiCO_2$, inspired CO_2 (%); Freq., respiratory rate; Insp, inspiratory; MAC, minimum alveolar concentration; MV, minute ventilation; PEEP, positive end-expiratory pressure; P_{MAX}, maximum inspiratory pressure limit; P_{PS}, inspiratory pressure support; T_{INSP}, inspiratory time; and V_T, tidal volume.

will also cause a horizontal elevation of inspired CO_2. In both these scenarios, increasing FGF above minute ventilation will return inspired CO_2 to baseline. Other causes of inspired CO_2 that are not sensitive to changes in FGF include too much apparatus dead space, especially when CO_2 is measured on the patient side of the dead space, and rapid respiratory rates combined with small tidal volumes, as seen in pediatric patients. Because an incompetent expiratory valve is a rare occurrence, it is reasonable to identify the need to change the absorbent by increasing FGF and looking for a change in inspired CO_2. A high inspired CO_2 alarm may help alert the clinician that canister change is required.

Another potential problem associated with changing an absorbent canister during an anesthetic is the potential to introduce an unintended leak in the circuit after inserting the new absorbent canister. Checking for a circuit leak is part of the preanesthetic checkout procedure and can be performed either

manually or by an automated process. Changing an absorbent canister during a procedure bypasses the leak test, and there are reports of leaks being introduced due to damaged canisters.[29] Unfortunately, no manufacturer to date has developed a method for leak testing absorbent canisters before they are placed in service. Loss of volume in the breathing circuit by collapse of the reservoir bag or bellows is evidence of leaks after a canister has been changed during a procedure.

A critique of low-flow or closed-circuit techniques is that inhaled anesthetic waste may be reduced, but absorbent utilization is increased. Are the inhaled anesthetic savings justified when one considers the increased cost of CO_2 absorbents? Feldman et al[30] addressed this question using a mathematical model to compare the anesthetic cost savings as flows are reduced to the increased absorbent costs. The model included a parameter for absorbent efficiency defined as amount of CO_2 absorbed per gram of absorbent. The authors found that for the more expensive anesthetics Sevoflurane and Desflurane, anesthetic costs fall more rapidly than absorbent costs increase when flows are reduced. Therefore, lowering FGF always reduced cost when using these agents. For the least expensive anesthetic, Isoflurane, absorbent costs increased slightly more than inhaled anesthetic costs decreased but the difference was small. Maximizing the absorbent efficiency was important and helped to minimize the absorbent costs. While this study provided insight into the financial considerations of reducing FGF and increasing absorbent usage, the environmental implications require further study. Reducing FGF is desirable to reduce the green house impact of the anesthetics, but absorbents have their own life cycle impact on the environment that requires further investigation.

The majority of data on CO_2 absorbents, especially more modern formulations, are based on in vitro data. There are little to no data examining the performance of absorbents during use in the operating room. Clinical trials comparing absorbents typically focus on the length of time between changing absorbents, yet this is a flawed method of comparison because many factors influence how long a given canister will last, most importantly the FGF used for each case and the related degree of rebreathing. Another factor is the amount of CO_2 produced by each patient. Clinical performance of canisters will also depend on the practices used to guide replacement. We do not know how much absorbent is wasted when the indicator color is used to guide replacement and inspired CO_2 is still zero.

Besides honing our practice to maximally exploit the CO_2 absorption capacity of safe $Ca(OH)_2$-based products, the search for alternative methods of CO_2 absorption should continue. A new approach to absorbent technology (Memsorb, DMF Medical, Halifax, Nova Scotia, Canada) currently under development does not rely on a chemical reaction to eliminate exhaled CO_2 and offers the potential to eliminate both concern about toxic interactions with inhaled anesthetics and the waste associated with a disposable absorbent product.[31]

SUMMARY

Nearly 100 years ago, Waters introduced CO_2 absorbents and the ability to minimize waste when administering inhaled anesthetics by reducing FGF to closed-circuit conditions. The introduction of Sevoflurane and Desflurane which could degrade into compound A and CO production, respectively, entrenched wasteful practices for inhaled anesthetic delivery and absorbent use. Fortunately, several advances have made it possible to reduce FGF safely to closed-circuit conditions and minimize the waste associated with inhaled anesthetic delivery. Modern absorbent formulations that limit or eliminate strong base have made it possible to safely reduce FGF to closed-circuit conditions without concern for toxic byproducts. Modern anesthesia workstations that provide capnography, and the ability to change CO_2 absorbents in the middle of an anesthetic, support a clinical practice of changing absorbent based on the appearance of inspired CO_2 so that the absorbent does not enter the waste stream until it has been maximally utilized. New formulations such as the solid polymer approach engineered to ensure uniform distribution of exhaled gas in the absorbent further help to eliminate channeling and minimize the absorbent material that is discarded unused.

Waste and environmental pollution associated with inhaled anesthetic delivery can be minimized by reducing FGF to closed-circuit conditions, by selecting absorbent products that are safe and effective at low FGFs, and adopting clinical practices that ensure absorbent is used to the greatest extent possible before it is discarded.

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Name: Jan Hendrickx, MD, PhD.
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REFERENCES

1. Waters RM. Clinical scope and utility of carbon dioxide filtration in inhalation anesthesia. *Anesth Analg*. 1924;3:20–22.
2. Waters RM. Advantages and technique of carbon dioxide filtration with inhalation anesthesia. *Curr Res Anesth Analg*. 1926;5:160–162.
3. Waters RM. Carbon Dioxide absorption from anæsthetic atmospheres: (Section of Anæsthetics). *Proc R Soc Med*. 1936;30:11–22.
4. AbbVie Inc. Ultane® (Sevoflurane) Label. Published 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020478s030lbl.pdf. Accessed January 20, 2020.
5. Feldman JM. Managing fresh gas flow to reduce environmental contamination. *Anesth Analg*. 2012;114:1093–1101.
6. Sulbaek Anderson MP, Nielsen OJ, Karpichev B, Wallington TJ, Sander SP. Atmospheric chemistry of isoflurane, desflurane and sevoflurane: kinetics and mechanisms of reactions with chlorine atoms and OH radicals and global warming potentials. *J Phys Chem*. 2011;116:5806–5820.
7. Walker SG, et al. Breathing circuits. In: Ehrenwerth J, *et al*. ed. *Anesthesia Equipment*. 2nd ed. Philadelphia, PA: Elsevier Saunders; 2013.
8. Neumann MA, Laster MJ, Weiskopf RB, et al. The elimination of sodium and potassium hydroxides from desiccated soda lime diminishes degradation of desflurane to carbon monoxide and sevoflurane to compound A but does not compromise carbon dioxide absorption. *Anesth Analg*. 1999;89:768–773.
9. Stabernack CR, Brown R, Laster MJ, Dudziak R, Eger EI. Absorbents differ enormously in their capacity to produce compound A and carbon monoxide. *Anesth Analg*. 2000;90:1428–1435.
10. Baum JA, Woehlck HJ. Interaction of inhalational anaesthetics with CO2 absorbents. *Best Pract Res Clin Anaesthesiol*. 2003;17:63–76.
11. Kennedy RR, Hendrickx JF, Feldman JM. There are no dragons: low-flow anaesthesia with sevoflurane is safe. *Anaesth Intensive Care*. 2019;47:223–225.
12. Lentz RE. CO Poisoning During Anesthesia Poses Puzzles: New Agent Used in Florida Case. *APSF Newsletter*. Summer 1994;9. Available at: https://www.apsf.org/article/co-poisoningduring-anesthesia-poses-puzzles-new-agent-used-in-florida-case/. Accessed January 11, 2020.
13. Moon RE. Cause of CO poisoning, relation to halogenated agents still not clear. *APSF Newsletter*. Summer 1994;9. Available at: https://www.apsf.org/article/cause-of-co-poisoningrelation-to-halogenated-agents-still-not-clear/. Accessed January 11, 2020.
14. Fang ZX, Eger EI II, Laster MJ, Chortkoff BS, Kandel L, Ionescu P. Carbon monoxide production from degradation of desflurane, enflurane, isoflurane, halothane, and sevoflurane by soda lime and Baralyme. *Anesth Analg*. 1995;80:1187–1193.
15. Keijzer C, Perez RS, de Lange JJ. Carbon monoxide production from desflurane and six types of carbon dioxide absorbents in a patient model. *Acta Anaesthesiol Scand*. 2005;49:815–818.
16. Higuchi H, Adachi Y, Arimura S, Kanno M, Satoh T. Compound A concentrations during low-flow sevoflurane anesthesia correlate directly with the concentration of monovalent bases in carbon dioxide absorbents. *Anesth Analg*. 2000;91:434–439.
17. Versichelen LFM, Bouche M-PLA, Rolly G, 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;95:750–755.
18. Murray JM, Renfrew CW, Bedi A, McCrystal CB, Jones DS, Fee JP. Amsorb A new carbon dioxide absorbent for use in anesthetic breathing systems. *Anesthesiology*. 1999;9l:l342–1348.
19. Hendrickx JF, De Ridder SP, Dehouwer A, Carette R, De Cooman S, De Wolf AM. In vitro performance of prefilled CO_2 absorbers with the Aisys®. *J Clin Monit Comput*. 2016;30:193–202.
20. Omer M, Hendrickx JFA, De Ridder S, et al. In vitro performance of prefilled CO_2 absorbers with the Zeus®. *J Clin Monit Comput*. 2018;32:799–806.
21. Kharasch ED, Powers KM, Artru AA. Comparison of Amsorb, sodalime, and Baralyme degradation of volatile anesthetics and formation of carbon monoxide and compound a in swine in vivo. *Anesthesiology*. 2002;96:173–182.
22. Kobayashi S, Bito H, Morita K, Katoh T, Sato S. 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. *J Anesth*. 2004;18:277–281.
23. Struys MM, Bouche MP, Rolly G, et al. Production of compound A and carbon monoxide in circle systems: an in vitro comparison of two carbon dioxide absorbents. *Anaesthesia*. 2004;59:584–589.
24. Knolle E, Heinze G, Gilly H. Small carbon monoxide formation in absorbents does not correlate with small carbon dioxide absorption. *Anesth Analg*. 2002;95:650–655.
25. Micropore, Inc. Safety Data Sheet, SpiraLith® Ca. Published March 26, 2019. Available at: https://spiralithusa.com/wp-content/uploads/2019/03/SAFETY-DATA-SHEET-CaOH2-Medical.pdf. Accessed January 9, 2020.
26. Draeger Medical. Safety Data Sheet, Draegersorb® Free. Published October 1, 2001. Available at: https://www.medline.com/media/catalog/Docs/MSDS/MSD_SDSD71242.pdf. Accessed January 9, 2020.
27. Isa MC, Yusoff NHN, Yati MSD, et al. Characterisation of carbon dioxide absorbent material for enclosed space applications. *Defence S T Technical Bulletin*. 2012;5:1–10.
28. Jiang Y, Bashraheel MK, Liu H, et al. In vitro efficiency of 16 different $Ca(OH)_2$ based CO_2 absorbent brands. *J Clin Monit Comput*. 2019;33:1081–1087.
29. Kuruma Y, Kita Y, Fujii S. Exchanging the CLIC absorber in the middle of surgery. *APSF Newsletter*. 2013;27:64–65.
30. Feldman JM, Lo C, Hendrickx J. Estimating the impact of carbon dioxide absorbent performance differences on absorbent cost during low-flow anesthesia. *Anesth Analg*. 2020;130:374–381.
31. DMF Medical Inc. Next-generation CO_2 removal for anesthesia circuits. Published 2016. Available at: https://www.dmfmedical.com/the-technology.html. Accessed January 20, 2020.