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Carbon Monoxide Production from Desflurane, Enflurane, Halothane, Isoflurane, and Sevoflurane with Dry Soda Lime

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Background: **Previous studies in which volatile anesthetics were exposed to small amounts of dry soda lime, generally controlled at or close to ambient temperatures, have demonstrated a large carbon monoxide (CO) production from desflurane and enflurane, less from isoflurane, and none from halothane and sevoflurane. However, there is a report of increased CO hemoglobin in children who had been induced with sevoflurane that had passed through dry soda lime. Because this clinical report appears to be inconsistent with existing laboratory work, the authors investigated CO production from volatile anesthetics more realistically simulating conditions in clinical absorbers.**

Methods: **Each agent, 2.5 or 5% in 2 l/min oxygen, were passed for 2 h through a Dräger absorber canister (bottom to top) filled with dried soda lime (Drägersorb 800). CO concentrations were continuously measured at the absorber outlet. CO production was calculated. Experiments were performed in ambient air (19–20°C). The absorbent temperature was not controlled.**

Results: **Carbon monoxide production peaked initially and was highest with desflurane (507 ± 70, 656 ± 59 ml CO), followed by enflurane (460 ± 41, 475 ± 99 ml CO), isoflurane (176 ± 2.8, 227 ± 21 ml CO), sevoflurane (34 ± 1, 104 ± 4 ml CO), and halothane (22 ± 3, 20 ± 1 ml CO) (mean ± SD at 2.5 and 5%, respectively).**

Conclusions: **The absorbent temperature increased with all anesthetics but was highest for sevoflurane. The reported magnitude of CO formation from desflurane, enflurane, and isoflurane was confirmed. In contrast, a smaller but significant CO formation from sevoflurane was found, which may account for the CO hemoglobin concentrations reported in infants. With all agents, CO formation appears to be self-limited.**

CARBON monoxide (CO) poisoning is a potential life-threatening complication that may occur when volatile anesthetics have contact with anhydrous soda lime or baralyme (Chemetron Medical Divisions, Allied Health Care Products, St. Louis, MO) in an anesthetic circle. The propensity of the various volatile anesthetics to form CO and the potential mechanisms of CO formation have been investigated in elaborate experimental settings. However, there are inconsistencies between laboratory findings and clinical experience.

There are case reports of increased CO hemoglobin concentrations in two anesthetized children, where sevoflurane had contact with dry soda lime (14-yr-old girl, weight: 51 kg, CO hemoglobin: 4.4%; 2-yr-old boy, CO hemoglobin: 8.4%; both with a circle system with the fresh gas inlet upstream of the absorber canister).[1]

Laboratory investigations, however, have reported either minimal[2] or no[3] degradation of sevoflurane to form CO. Various mechanisms have been postulated to explain CO production from desflurane, enflurane, and isoflurane, but thus far none is compatible with CO production from halothane and sevoflurane.[3] In most previous laboratory investigations, volatile anesthetics were exposed to only small amounts of soda lime. Only slight temperature changes were allowed to occur, as the small absorbent containers were placed in a water bath maintained at 60°C or less.[2,4,5] With equimolar and equimac concentrations of the respective agents, CO production was highest for desflurane and enflurane and less so for isoflurane. Halothane produced almost no CO.[2,3] However, with real absorber systems, 2% isoflurane and enflurane produced the same amount of CO (CO peak, 3,500 and 3,800 ppm, respectively, with almost the identical time course),[6] Halothane produced up to 450 ppm CO.[6]

In the aforementioned clinical case reports, the investigators described surprisingly high temperatures of the soda lime— so high that they could not touch the canister. Temperatures higher than 300°C were found in animal experiments with actual anesthesia machines with sevoflurane and anhydrous baralyme[7] (Chemetron) and more than 120°C in laboratory experiments with actual absorber systems and dry soda lime.[8,9] These authors demonstrated that all modern volatile anesthetics, particularly sevoflurane, react with dry soda lime in an extremely exothermic reaction, a feature that could not be observed in laboratory studies with small amounts of soda lime[3] and where temperature was tightly controlled.[2]

In view of the questions raised by inconsistencies among laboratory investigations, and between laboratory investigations and clinical experience, we reinvestigated CO formation from anesthetic agents using a clinical

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absorber system in which temperature change was permitted.

Materials and Methods

The inhalational anesthetics and the soda lime (Drägersorb 800, composition: 2.2% KOH, 2.1% NaOH, 80.1% $Ca(OH)_2$[10]) were obtained from commercial sources. Fresh absorbent was placed in Dräger ISO absorbers (volume, 1 l; Dräger AG, Lübeck, Germany) and dried in a continuous oxygen flow ($\geq$ 12 l/min) for at least 72 h until weight remained constant. Drying was considered to be complete when there was no further weight loss ($<$ 0.05% of wet weight) for 24 h. Weight was measured with a precision balance (MC1 LC 4800 P; range, 0–1,600 g; resolution, 0.02 g; Sartorius, Göttingen, Germany). To achieve complete and homogeneous drying, the soda lime was mixed in the absorber at the time of each weighing. This may simulate a worst-case scenario. The dried absorbent was stored in an oxygen flow of 2 l/min until use, at which time weight was measured again.

To sample soda lime temperature, thermocouples were placed in the center of a Dräger ISO absorber 3 and 7.5 cm above the bottom of the canister. The canister was filled with a measured amount of dry soda lime that covered the upper thermocouple by 1 cm. Temperature at the two sites was recorded in 5-s intervals by a computerized data acquisition system.

The experimental procedure was similar to that previously described for investigations on sevoflurane destruction[11–13] and on heat production from the reaction of volatile anesthetics with dry soda lime.[8] Inhalational anesthetics from calibrated vaporizers at a concentration of 2.5 or 5% in a carrier gas of 2 l/min oxygen were passed through the Dräger ISO absorber filled with dry soda lime for 2 h. We chose to use equal concentrations of all anesthetics rather than clinically equivalent concentrations as we were primarily interested in the actual chemical reactions. Flow through the absorber was from bottom to top. Gas was sampled at 300 ml/min at the absorber outlet for CO determination. To remove water, the volatile anesthetics, and possible degradation products, all of which may cause cross-sensitivity, the sampled gas was passed sequentially through a 0°C (ice) cooling trap, a −79°C (dry ice) cooling trap, and an activated charcoal filter (15 ml). CO concentration was continuously determined by infrared absorption using an ANDROS 6600 OIML Class 0 bench (range, 10–100,000 ppm; resolution, 10 ppm; Andros, Berkeley, CA) as the primary method. The measured data were stored in 1-s intervals.

To confirm measurement of CO, two further methods were used. For these methods, the effluent from the IR bench was sampled. In the low range, a continuous electrochemical method was used (Dräger PAC III; range, 0–2,000 ppm; Dräger AG), which is based on the following reaction: $CO + H_2O \rightarrow CO_2 + 2H^+ + 2e^-$; $1/2O_2 + 2H^+ + 2e^- \rightarrow H_2O$).[14] Higher concentrations were validated by a chemical method using appropriate Dräger tubes based on the following reaction: $5\ CO + I_2O_5 \rightarrow I_2 + 5\ CO_2$).[15] All methods used are standard for CO measurement. IR absorption is the only continuous method available covering the required concentration range. Each method is based on a different principle. Agreement between the methods along with the use of the traps and filters make it highly unlikely that other compounds (reactants or products) affected the CO measurements.

Helium containing analyzed amounts of 100 ppm ± 5%, 1,000 ppm ± 5%, and 99,200 ppm ± 2% of CO provided by Alltech (Munich, Germany) and nitrogen containing analyzed amounts of 100 ppm ± 2% provided by Messer Griesheim (Frankfurt, Germany) were used for calibration.

Baseline CO production was determined using dry soda lime and a flow of 2 l/min oxygen with no volatile anesthetic and using fresh (wet) soda lime and a flow of 2 l/min with 5% anesthetic. The total amount of CO produced during the 2-h observation period was calculated from the gas flow through the canister, and the concentrations as measured by IR absorption. All experiments were performed in triplicate.

Additional experiments were conducted to confirm the sevoflurane results because the magnitude of the CO production was unexpected and because of the potential of a large variety of breakdown products,[9–12] some not yet identified. In these experiments we simultaneously used IR absorption, the electrochemical method, and gas chromatography. Gas chromatography used a thermal conductivity detector (Perkin Elmer Auto System, Norwalk, CT; Alltech steel column diameter: ⅛ inch, 6-foot length; packed with P/W washed molecular sive, 13 × 80/100; carrier gas, helium). Calibration was performed with the same gases used to calibrate the other instruments. In these experiments, the effluent gas from the IR bench was collected in gas-tight syringes (VICI precision sampling, Baton Rouge, LA) at 5-min intervals. In the chromatogram, the CO peak was distinctly separated from other peaks, and CO concentrations were determined in duplicate and compared with the other methods.

Statistics

A one-sided *t* test was used to compare the effect of anesthetic concentration on peak CO concentrations and the amount of CO produced with a given compound. Analysis of variance was used to assess the effect of the anesthetic agent on CO production, CO peak concentration, and temperature development at a given concentration.

Results

Drying the fresh moist soda lime produced a weight loss of 15.77 ± 0.43% (mean ± SD). An average of 755.70 ± 28.90 g dry soda lime was used per experiment.

When pure oxygen was passed through dried soda lime and when anesthetics were passed through fresh soda lime, the output of the Andros IR bench toggled in the least significant digit and the Dräger PAC III detected no CO. CO was detected with all anesthetics with dried soda lime. During all experimental conditions, the Dräger PAC and Dräger tube data agreed with the simultaneous IR data within 15% or within the intrinsic error of the methods. For this reason, only the IR data, the continuous method covering the whole range, is presented.

When anesthetic agent was passed through dry soda lime, the time course and rate of CO production and the time course of temperature changes differed markedly between the agents (figs. 1–5). The soda lime temperature increase appeared first at the lower sensor and subsequently at the upper sensor, following the direction of gas flow. The time courses of temperature changes at the two sensors were distinctly separated from each other. With all compounds except desflurane and enflurane, a temperature increase at the upper sensor did not begin to appear until the temperature at the lower sensor had passed its maximum. The time course of the temperatures indicates zonal heat production linked to an exothermic process passing gradually upward through the absorber. The time lag between the appearance of the first and second temperature maximum differed from agent to agent and was taken as a measure of the velocity of the reactive zone moving through the absorber. For all compounds, the time lag was shorter at the higher concentration. Analysis of variance confirmed the influence of the agent on heat production at the respective concentrations. For both concentrations and sensor locations, peak temperatures were dependent on agent in the following order (from highest to lowest): sevoflurane > isoflurane ≥ halothane ≥ enflurane > desflurane (for statistics see table 1).

Measurable amounts of CO were found immediately after the contact of desflurane, enflurane, or isoflurane with the anhydrous soda lime but only after a delay with sevoflurane. The CO concentration from halothane was too small to allow detailed analysis of the concentration curves. During the 2-h observation period, CO production with all agents returned to approximately zero. With desflurane, enflurane, and isoflurane, CO production appears to occur in two phases, which may partly overlap. CO concentrations of the investigated agents generally passed their first maximum before maximal temperature was reached at the lower sensor. A second later peak was clearly seen with desflurane, and less so with isoflurane and enflurane. Figures 1–3 illustrate the time courses of the CO concentrations and the temperatures with these agents at 2.5% and 5%.

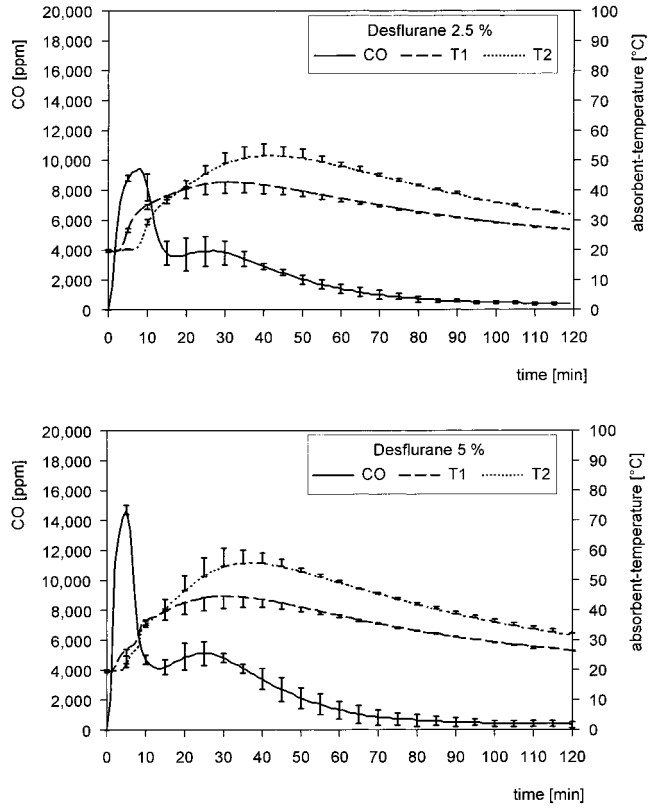

Fig. 1. Desflurane 2.5% (*top*) and 5% (*bottom*) in 2 l/min oxygen flowing through dry soda lime; time course of carbon monoxide (CO) concentration (left ordinate, solid line, positive and negative SD bars; 1% = 10,000 ppm) at the absorber outlet and temperature in the center of the absorber canister 3 cm (T1, right ordinate, dashed line, negative SD bars) and 7.5 cm (T2, right ordinate, dotted line, positive SD bars) above the bottom. SD bars plotted only every 5 min. Each point is the mean of three studies. At both concentrations, the temperature increase at the upper sensor lags that at the lower sensor, indicating a moving zone of heat production. The lag is greater at 2.5%. Temperature increase with desflurane is not as fast as with the other compounds. CO production is calculated from the area under the concentration curve. CO production is biphasic. The CO concentration passed its initial maximum when the temperature just started to increase at the upper sensor. CO production shows a second increase with its maximum distinctly separated from the first, when temperature exceeded 40°C at both sensors.

With sevoflurane, the time course of CO production was different (fig. 5). CO was only detected after a delay, coincident with or after the temperature at the lower sensor began to increase. CO production increased to its maximum while temperature was still increasing at the lower sensor. It remained almost constant, with only a gradual subsequent decrease, and ceased when temperature reached its maximum at the upper sensor.

At equal anesthetic concentrations, the amount of CO produced was dependent on agent in the following order (from highest to lowest): desflurane ≥ enflurane > isoflurane ≥ sevoflurane ≥ halothane. For peak concen-

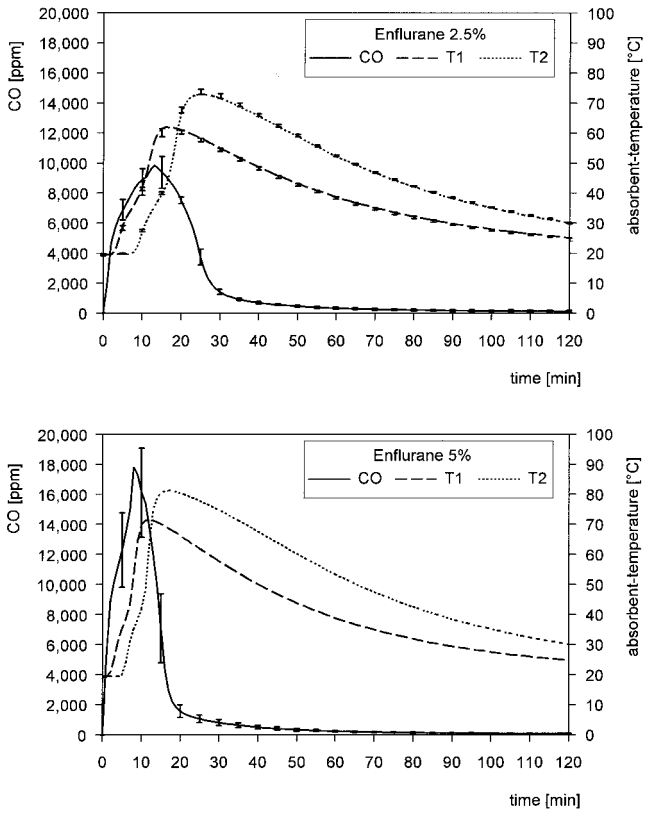

Fig. 2. Enflurane 2.5% (*top*) and 5% (*bottom*) in 2 l/min oxygen flowing through dry soda; scaling and legend as in figure 1. The time courses and peak values of carbon monoxide (CO) concentration and temperature development differ considerably, although the same amount of CO is formed at the two enflurane concentrations. The shape of concentration time course suggests that the initial maximum is dependent on more than one process.

trations of CO, the ranking was slightly different: enflurane ≥ desflurane > isoflurane > sevoflurane ≥ halothane. Statistical analysis confirmed significant differences ($P < 0.05$) in CO production between most agents at 2.5% as well as at 5%. At 2.5%, no difference could be estimated between desflurane *versus* enflurane ($P = 0.652$) and halothane *versus* sevoflurane ($P = 0.99$). At 5%, the differences between halothane *versus* sevoflurane ($P = 0.477$) and isoflurane *versus* sevoflurane ($P = 0.162$) failed to reach statistical significance.

Doubling the agent concentration from 2.5 to 5% caused a statistically significant increase in CO peak concentration for all agents ($P < 0.05$). However, doubling of the agent concentration did not lead to systematic changes in total CO production. It did not differ with enflurane and halothane; the 30% change with isoflurane failed to reach statistical significance ($P = 0.064$). The increases with desflurane (approximately 30%) and sevoflurane (approximately 300%) reached statistical significance ($P < 0.05$). Doubling the agent concentration caused less than a 10°C increase in peak temperature at the upper sensor, except for sevoflurane, when the peak temperature increase from 105 to 133°C. Peak temperatures at both sensors, CO peak concentrations, and the amounts of CO produced are summarized in table 1.

The 5% sevoflurane experiment was repeated with the addition of gas chromatography measurements to provide additional confirmation of the significant production of CO. Figure 6 shows the time course of CO production as measured simultaneously by gas chromatography, IR, and the electrochemical Dräger PAC III, confirming the results described above.

Discussion

This investigation of the production of CO by the degradation of anesthetics in the presence of desiccated soda lime (Drägersorb 800) differs from previous investigations. In our attempt to better emulate the situation in clinically used absorber systems, we: (1) used a clinical absorber with a large amount of soda lime; (2) used a continuous gas flow; (3) allowed the soda lime temperature to increase during the reaction; and (4) followed the reaction for a long period of time. It should not be surprising that some of our findings differ from those of previous investigators who used different conditions.

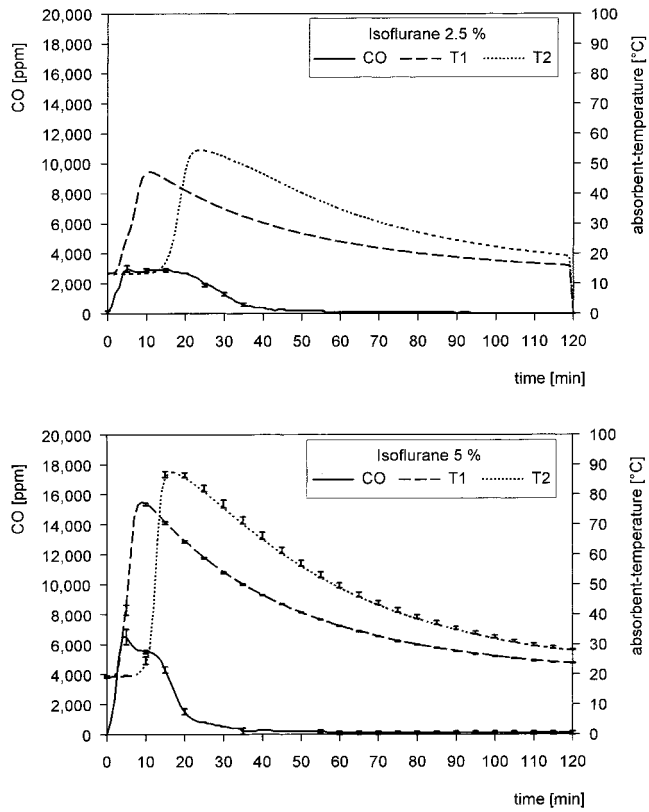

Fig. 3. Isoflurane 2.5% (*top*) and 5% (*bottom*) in 2 l/min oxygen flowing through dry soda lime; scaling and legend as in figure 1. Carbon monoxide (CO) concentration–time curve shows an initial peak (more pronounced at 5%) and is maintained at a high level. The ultimate decrease does not occur until temperature has reached its maximum at the upper sensor.

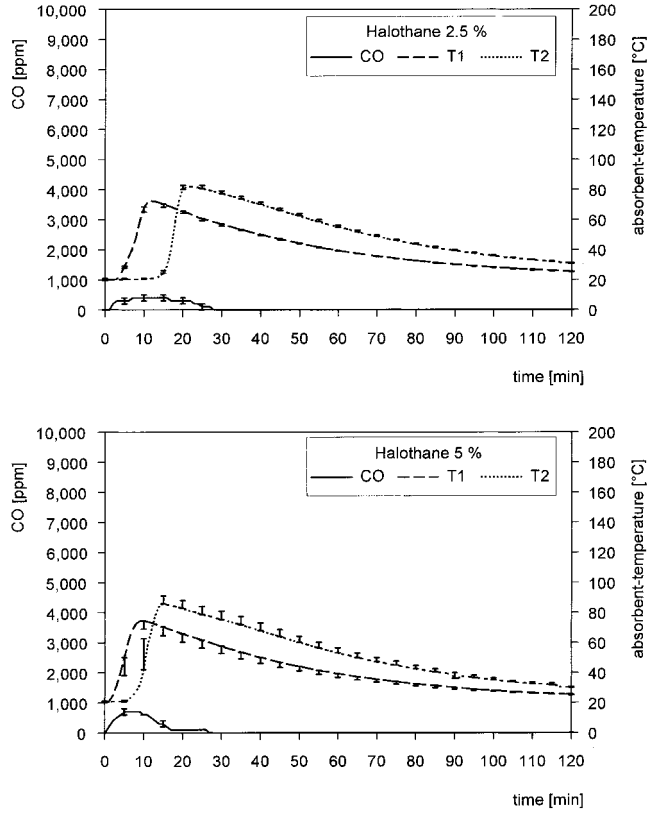

Fig. 4. Halothane 2.5% (*top*) and 5% (*bottom*) in 2 l/min oxygen flowing through dry soda lime; legend corresponds to figure 1, scaling differs from figures 1–3. Range of carbon monoxide (CO) concentration (left ordinate) is reduced from 2 to 1% (0.1% = 1,000 ppm); temperature (right ordinate) is increased to 200°C. CO formation starts gradually at the time the temperature increases and ceases when temperature reaches the upper layer of the soda lime.

We did confirm the findings of previous investigators that desflurane, enflurane, and isoflurane react with desiccated soda lime to produce large quantities of CO. We compared the compounds at equal concentrations, covering the inspiratory concentration range used during induction or rapid wash-in. It is only the desflurane concentrations are at the lower end of the clinical used range. At 10% desflurane, 767 ml CO was measured in the same setting.[16] This does not compromise the impact of this investigation. However, in contrast to previous investigators,[2,3] we also demonstrated sufficient CO production from sevoflurane to explain recent clinical reports of increased CO hemoglobin concentrations in children after mask induction or initial wash-in with this anesthetic.[1] We also confirmed CO production from halothane in the range previously described by Strauß *et al.*[6] but not seen in recent reports.[3]

It is of note that CO production eventually ceases despite the continued flow of the anesthetic. After 2 h of flowing dry anesthetic gases through desiccated soda lime, we found that the CO concentration decreased to zero or near zero in all cases. This implies that some substance or reaction site in the soda lime required for a continued reaction was being used up. The fact that the zone of temperature increase appears to move in the same direction of the gas flow lends additional credence to this notion, as does a recent preliminary report[17] that demonstrated that total CO production is linearly dependent on the amount of desiccated soda lime. If the total CO produced is at least partly dependent on the absorbent mass, the very large absorber systems commonly used in North America may have the disadvantage of having the potential to produce particularly large amounts of CO.

With desflurane, a concentration increase from 2.5 to 5% led to an increase of peak CO concentration of 65%, whereas the amount of CO produced increased only by 30%. A similar change in CO production was found with isoflurane, but the increase in CO peak concentration was 125%. In the case of enflurane, the same amount was produced despite an increase of the peak of 85%. Thus, we found no correlation between peak concentration and the amount of CO produced. In contrast to previous work with baralyme[2] (Chemetron), we also have no evidence for a linear relation between either peak concentration or CO formation and anesthetic con-

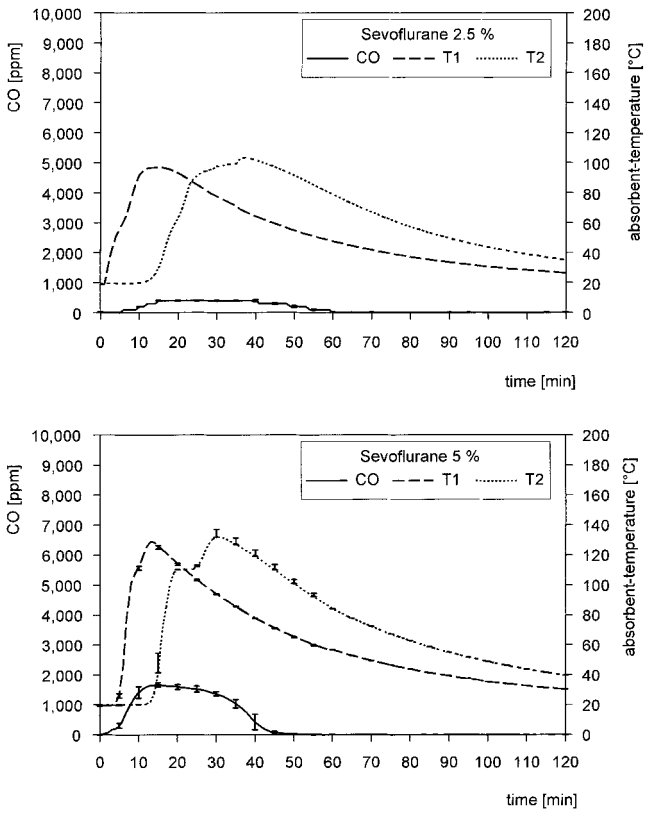

Fig. 5. Sevoflurane 2.5% (*top*) and 5% (*bottom*) in 2 l/min oxygen flowing through dry soda lime; legend corresponds to figure 1, scaling corresponds to figure 4. Carbon monoxide (CO) concentration increases at or after the temperature increases and reaches its maximum when temperature reaches its maximum at the lower sensor. CO production shows a gradual decay while the heat zone moves upward. It ceases when heat reaches its maximum at the upper sensor.

Table 1. Peak Temperatures and CO Production

Agent	Concentration	T_1 (°C)	T_2 (°C)	dt (min)	CO_a (ml)	CO_p (ppm)	t_{COp} (min)
Desflurane	2.5%	42.7 ± 3.4^{E,H,I,S}	51.8 ± 3.7^{E,H,I,S}	12.6 ± 2.8	507 ± 70.0^{H,I,S}	8,996 ± 673^{H,I,S}	6.9 ± 0.63
	5%^{a,p}	46.9 ± 2.1^{E,H,I,S}	58.1 ± 2.3^{E,H,I,S}	3.9 ± 0.3	656 ± 59.6^{E,H,I,S}	14,793 ± 310^{H,I,S}	4.8 ± 0.36
Enflurane	2.5%	62.0 ± 1.5^{D,H,I,S}	72.9 ± 1.6^{D,H,I,S}	7.3 ± 0.8	460 ± 41.6^{H,I,S}	10,106 ± 1,604^{H,I,S}	11.4 ± 2.31
	5%*^{p}	73.5 ± 2.1^{D,S}	81.7 ± 0.4^{D,S}	5.1 ± 0.8	475 ± 99.2^{D,H,I,S}	18,486 ± 3,178^{H,I,S}	8.2 ± 0.24
Halothane	2.5%	72.6 ± 2.5^{D,E,S}	82.2 ± 2.5^{D,E,S}	10.0 ± 0.2	22 ± 3.5^{D,E,I}	423 ± 76^{D,E,I}	8.8 ± 0.83
	5%^{p}	75.3 ± 5.6^{D,S}	86.9 ± 5.7^{D,S}	5.6 ± 0.2	20 ± 1.4^{D,E,I}	730 ± 45^{D,E,I}	7.0 ± 0.79
Isoflurane	2.5%*	70.8 ± 1.1^{D,E,S}	81.9 ± 0.7^{D,E,S}	12.5 ± 0.9	176 ± 2.8^{D,E,H,S}	3,080 ± 183^{D,E,H,S}	5.7 ± 0.66
	5%^{p}	77.4 ± 0.6^{D,S}	87.9 ± 0.5^{D,S}	7.7 ± 1.2	227 ± 21.1^{D,E,H}	6,983 ± 223^{D,E,H,S}	4.6 ± 0.27
Sevoflurane	2.5%*	101.3 ± 1.3^{D,E,H,I}	104.9 ± 0.1^{D,E,H,I}	21.7 ± 1.4	34 ± 1.4^{D,E,I}	426 ± 11^{D,E,I}	21.0 ± 1.27
	5%^{a,p}	129.3 ± 3.1^{D,E,H,I}	132.5 ± 4.6^{D,E,H,I}	16.1 ± 0.9	104 ± 4.2^{D,E}	1,600 ± 317^{D,E,I}	17.3 ± 2.59

Maximum temperatures at the lower (T_1) and upper (T_2) probe and time lag (dt) between the temperature maximums (mean ± SD) and amount of carbon monoxide production (CO_a), peak concentration (CO_p), and time to reach peak concentration (t_{COp}). Temperature: At 2.5%, temperatures for T_1 and T_2 differed significantly ($P < 0.05$) between all anesthetics except halothane *versus* isoflurane. At 5%, no statistical difference among enflurane, halothane, and isoflurane could be estimated for T_1 and T_2. Values are given as mean ± SD. CO: Significant difference ($P < 0.05$) in CO amount or CO peak concentration between trials with 2.5% or 5% of the given agent is indicated in the concentration column by ^{a} or ^{p}. Statistically significant differences ($P < 0.05$) between the agents at the same concentration estimated by analysis of variance are indicated with the initials of the respective agent in superscript (^{D,E,H,I,S}).

* Temperature file of one trial lost.

centration during our conditions. In fact, CO concentrations determined in an open system appear not to be a good measure for the toxic risk. According to our experimental experience, they can easily be modulated by gas flow and anesthetic concentration in a given setting. Moreover, the concentration time course measured in an open system cannot be taken as an indication of the inspiratory concentration in an anesthetic circle even when gas flow and the amount of lime are in an appropriate ratio. As CO production ceased, we were able to calculate the amount of CO produced, which we believe is a better indicator of the potential for toxicity than peak concentrations.

In many previous studies on anesthetic degradation, temperature was maintained more or less constant. In our studies, the soda lime temperature was allowed to change, and it increased with all agents and at both concentrations tested. However, the temperature increase with sevoflurane was far greater than with any of the other agents. The peak temperature observed with sevoflurane often exceeded 120°C. We postulate that such a temperature increase facilitates the degradation of sevoflurane to CO in these laboratory experiments and in the clinic. Most chemical reactions proceed at a higher rate at increased temperatures, and it is reasonable to believe that the degradation of all of the anesthetic agents were affected by the temperature changes. This seems to be the rationale for previous investigators who used a range of temperatures. However, the effects of exothermic reactions, which themselves increase soda lime temperature, were not taken into account. Thus, temperature clamping on a lower level may limit chemical reactions. For desflurane, the initial CO production preceded the initial temperature changes. The CO production peaked and then began to decrease. However, there was a second increase in CO production approximately 20 min later that coincided with and may have been caused by the increase in soda lime temperature. The data from isoflurane suggest a similar phenomenon, although the late-stage CO production was merely evidenced by a plateau in the CO concentration. This phenomenon is also suggested in the case of enflurane, where the CO concentration curve has a shoulder. The time lag between the initial prompt and large CO production and the temperature increase is of note. It is doubtful that the temperature increase was primarily caused by whatever chemical reactions caused the initial formation of CO; subsequent reactions may well have been responsible.

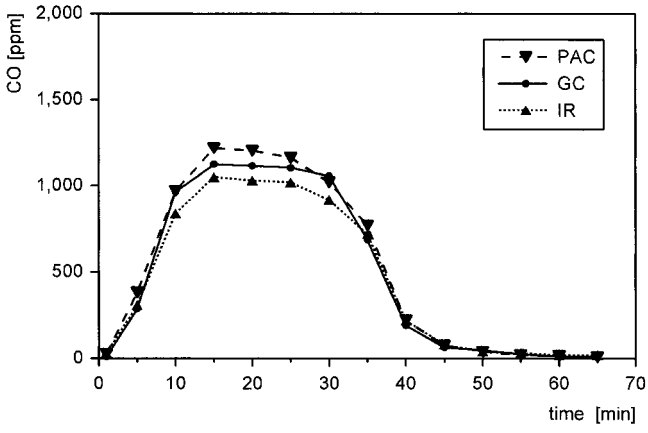

Fig. 6. Data from an experiment with 5% sevoflurane in 2 l/min oxygen using gas chromatography to confirm our results. Carbon monoxide (CO) concentrations were determined every 5 min by the three methods. All three methods are in good accordance. Gas chromatography results, average of duplicate measurements (solid line), were slightly higher than the IR results (dotted line), but slightly lower than electrochemical results (dashed line). IR = infrared.

It would probably be naive to assume that all of our data can be explained by an initial exothermic reaction, which then causes an increase in temperature that then enhances the same reaction. In fact, there is no reason to

assume that the same reactions predominate at ambient and elevated temperatures or even that only chemical reactions are occurring. The case of sevoflurane is of particular interest as the temperature increase appears to precede the production of CO. This is particularly evident at 2.5% sevoflurane. It appears likely that there is an initial exothermic reaction that does not itself produce CO. A different reaction, probably requiring an elevated temperature, would then be responsible for the actual formation of CO either from sevoflurane or from its degradation of products from an earlier chemical reaction. However, the initial reaction need not be chemical. It could be the exothermic physical adsorption of sevoflurane onto desiccated soda lime, as postulated by early investigators who hypothesized that removal of water from soda lime left it with molecular sieve-like properties.[18]

Commenting on the experiments of Fang *et al.*,[2] Callan[19] pointed out that minute CO production with halothane and sevoflurane was only observed in experiments in which dry limes were maintained at 60°C, a temperature that she stated was not clinically relevant. Our study, as well as previous laboratory reports[8,13] and animal trails,[7] have demonstrated that heat production during sevoflurane degradation on dry limes is sufficient to produce even higher temperatures. Nevertheless, Callan's observation supports our hypotheses. It is further supported by preliminary data on the interaction of hexafluoroisopropanol, a postulated intermediate of sevoflurane degradation,[20] with dry soda lime (Sodasorb; Grace, Epernon, France).[21] In a setting similar to this study, in which evaporated hexafluoroisopropanol was completely absorbed by the dry lime, no CO and no temperature change were observed. However, 500–1,500 ppm of CO was measured at the outlet, when the absorbent was heated in a water bath to 70°C, which demonstrates that the degradation of hexafluoroisopropanol to CO requires a higher temperature level.

Our experimental conditions differed widely from those in and earlier study by Fang,[2] where the anesthetics were fed at a carrier gas flow of 12.5 ml/min through 21 g of dry soda lime and temperature was clamped at various levels (range, 20–60°C), and from studies where soda lime was placed in a flask in which anesthetic agents were evaporated.[3,5] Results may differ because, in a clinical absorber, with a realistic gas flow there is a zone of reaction that progresses in time, allowing free temperature development and fresh soda lime to come in contact with the anesthetic agents and its degradation products. Actual clinical conditions are even more complex than our experimental conditions because bidirectional flow may occur through the absorber.

It has been generally assumed that CO production from sevoflurane is of no clinical relevance[2] or does not even exist.[3] We found that CO production from 5% sevoflurane was 104 ml, while that from 5% desflurane was 656 ml. However, clinical relevance is dependent on several factors, including the partial pressure of CO compared with the partial pressure of oxygen, the amount of CO that can be delivered to the alveolar compartment, the volume of distribution for CO (mainly the blood volume), the time of exposure, and other factors determining patient uptake.[22] Even small amounts of CO can become relevant when they accumulate in the circle during "low" or "minimal flow" techniques. However, CO, with its 220- to 300-fold affinity, binds to the same sites on the hemoglobin molecule as oxygen. The amount of CO linked to hemoglobin can easily be determined by the equations known for oxygen content. Thus, at a hemoglobin of 15 g/dl, 100 ml CO taken up by 1 l of blood will cause a CO hemoglobin of 50%. An uptake of merely 12–20 ml of CO would be enough to cause the 8.4% CO hemoglobin that was reported in a 2-yr-old child.[1] Even less would be needed in anemic or smaller patients.

Other investigations[8,9,13] have confirmed that a large temperature increase occurs when sevoflurane is allowed to come in contact with dry soda lime in clinical cases[1] or desiccated baralyme in animal trials.[7] There is even evidence that small quantities of CO may even be formed when sevoflurane flows through moist soda lime in the presence of carbon dioxide.[23] CO production from sevoflurane and halothane has only been detected in experimental settings in which the anesthetic was flowing through heated soda lime[2] or temperature was allowed to increase.[6] Thus, in both laboratory experiments that emulated clinical conditions and in the clinic, there is adequate reason to believe that one cannot completely avoid the hazards of CO by using sevoflurane. It would seem prudent to regard the potential for CO formation to be a general property of all modern volatile anesthetics contacting dry commonly used limes and to always take adequate precautions to insure that soda lime is not allowed to become desiccated.

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