Anesthesiology 2002; 96:941–6

Preparation of the Siemens KION Anesthetic Machine for Patients Susceptible to Malignant Hyperthermia

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Background: **Preparation of anesthetic machines for use with malignant hyperthermia-susceptible (MHS) patients requires that the machines be flushed with clean fresh gas. We investigated the washout of inhalational anesthetics from the KION anesthetic machine.**

Methods: **In part 1, halothane was circulated through KION anesthetic machines for either 2 or 12 h using a test lung. The times to washout halothane (to 10 parts per million [ppm]) first, from the internal circuitry and second, from the ventilator-patient cassette (without the carbon dioxide absorber) were determined at 5 and 10 l/min fresh gas flow (FGF). In part 2, the rates of washout of halothane or isoflurane from either the KION or Ohmeda Excel 210 machines were compared. The effluent gases were analyzed using calibrated Datex Capnomac Ultima (Helsinki, Finland) and a Miran LB2 Portable Ambient Air Analyzer (Foxboro, Norwalk, CT).**

Results: **Halothane was washed out of the internal circuitry of the KION within 5 min at 10 l/min FGF. Halothane was eliminated from the ventilator-patient cassette in 22 min at the same FGF. The times to reach 10 ppm concentration of halothane and isoflurane in the KION at 10 l/min FGF, 23 to 25 min, was four-fold greater than those in the Ohmeda Excel 210, 6 min.**

Conclusions: **To prepare the KION anesthetic machine for MHS patients, the machine without the carbon dioxide absorber must be flushed with 10 l/min FGF for at least 25 min to achieve 10 ppm anesthetic concentration. This FGF should be maintained throughout the anesthetic to avoid increases in anesthetic concentration in the FGF.**

TO prepare anesthetic machines for use with malignant hyperthermia-susceptible (MHS) patients, all residual inhalational anesthetic must be removed. This is usually achieved by flushing the machine with clean fresh gas.[1–3] Published guidelines for the preparation of Ohmeda Modulus 1 and 2 machines (BOC HealthCare, Madison, Wisconsin, USA), which contain no rubber components in their internal circuitry, include flushing the internal gas circuitry with 10 l/min of clean fresh gas for at least 5 min.‡ In contrast, the KION, a new anesthetic machine from Siemens Elema, Solona, Sweden, contains silicone and other rubber components within its internal circuitry that cannot be replaced. The presence of these components precludes the use of published guidelines for the preparation of other machines for MHS patients with the KION. Accordingly, we investigated the washout of inhalational anesthetics from the KION anesthetic machine with different fresh gas flows (FGF) and compared the results with data from Ohmeda machines.

Materials and Methods

This laboratory investigation was divided into two parts.

Part 1

For the purposes of this experiment, we divided conceptually the KION anesthetic machine into two circuits: internal and external. The internal circuitry was defined as those components of the machine between the fresh gas inlet and the auxiliary gas outlet (fig. 1). The external circuitry was defined by the ventilator and bellows, patient cassette, and anesthetic circuit (fig. 1). The washout of halothane from the internal and external circuitries of seven recently serviced KION anesthetic machines was determined. Two variables that might have affected the washout of halothane from the KION were investigated: the duration of priming the machine with halothane and the FGF during the washout.

Internal Circuitry. To determine the washout of halothane from the internal circuitry (table 1, part 1), the machines were primed using 1% halothane (per a calibrated Datex Capnomac Ultima, Helsinki, Finland) in air. The anesthetic mixture was circulated through a circle circuit that was closed with a Siemens test lung (part No. 80 06 832 E037E). The test lung was ventilated using the KION ventilator in a volume control mode at a tidal volume of 500 ml, a respiratory rate of 15 breaths/min and zero positive end-expiratory pressure (ZEEP) for either 2 or 12 h (table 1, part 1). After priming the machine with halothane, ventilation was discontinued, the vaporizer was closed or removed from the machine, and the carbon dioxide absorber was disconnected from the patient cassette (fig. 1). A feature of the KION includes the ability to add or remove the carbon dioxide absorber without compromising the integrity or changing the patient circuit. During the washout period, the FGF was set to either 5 or 10 l/min (table 1, part 1). To isolate the washout of halothane from the internal circuitry, effluent gas was directed through the auxiliary gas outlet (Fig. 1) and the concentration of halothane was analyzed every minute until it reached 10 ppm.[1–5]

External Circuitry. When the concentration of halothane in the internal circuitry reached 10 ppm, the

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Received from Department of Anaesthesia, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada. Submitted for publication May 9, 2001. Accepted for publication November 20, 2001. Supported in part by a grant from Siemens Elema, Markham, Ontario, Canada.

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‡ Malignant Hyperthermia Association of the United States. Managing malignant hyperthermia: Drugs, equipment and the antidote, Dantrolene Sodium [Web site]. Available at: http://www.mhaus.org/drugs.html. Accessed December 3, 2001.

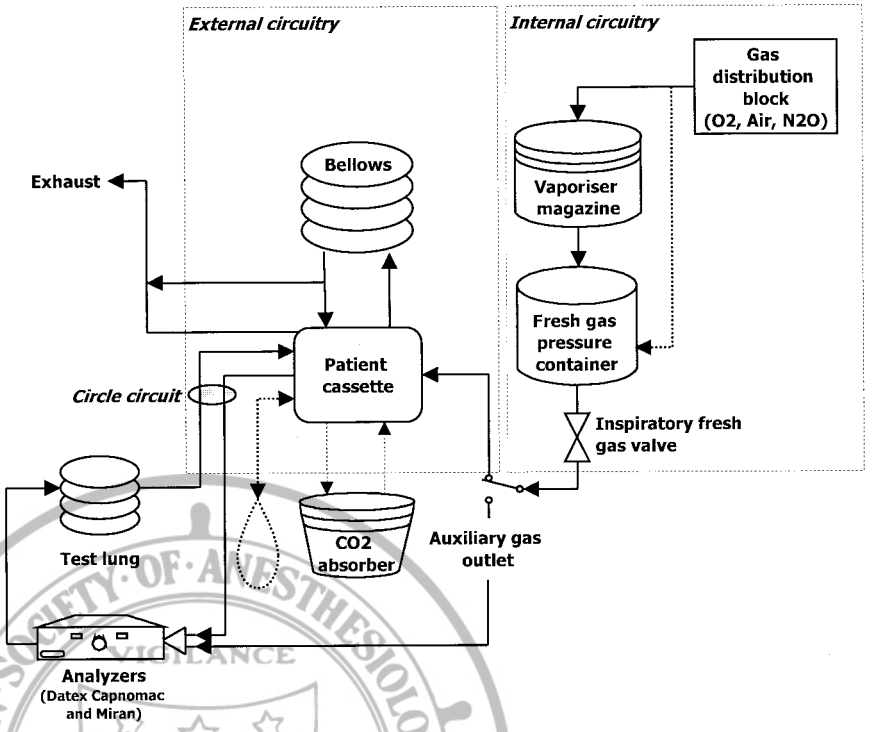

Fig 1. Simplified schematic piping diagram of the Siemens KION anesthetic machine used for the experiment. The designation of internal and external circuitries were coined exclusively for the purpose of clarifying the source of anesthetic in the washout. Fresh gas entered the KION at the gas distribution block. In *internal circuitry*, the fresh gas traversed the inspiratory fresh gas valve and was diverted through the auxiliary gas outlet to the analyzer. In *external circuitry*, fresh gas also traversed the inspiratory fresh gas valve but was directed into the ventilator/patient cassette and was analyzed after passing through the circle circuit. In both parts, the carbon dioxide absorber was removed from the circuit during the washout.

washout of halothane from the external circuit (ventilator bellows and patient cassette) was determined (table 1, part 1). To achieve this, the auxiliary gas outlet was closed and ventilation was reestablished through a circle circuit and test lung, neither of which had been exposed to inhalational anesthetics. The ventilator components and settings remained unchanged from those used during the priming with halothane. The concentration of halothane was measured every minute until the concentration reached 10 ppm (fig. 1). Each combination of KION machine, duration of priming of the machine with halothane, and FGF during the washout was repeated in triplicate.

Part 2

The washout profiles of halothane and isoflurane were determined in two types of anesthetic machines, KION (4 machines) and Ohmeda Excel 210 (BOC HealthCare, Madison, Wisconsin, USA) with Air-Shields Ventimeter® Controller II ventilator (Air-Shields Vickers, Hatboro, Pennsylvania, USA) (two machines) during controlled ventilation of a test lung using a circle circuit. All machines were recently serviced. Two variables were evaluated (table 1, part 2): the type of anesthetic machine and the type of anesthetic. The machines were primed with either 1% halothane or 1.5% isoflurane (per the Datex Capnomac Ultima) in air. The anesthetic mixture was circulated for 2 h through a circle circuit that was closed with a test lung. The test lung was ventilated throughout part 2 using either a KION ventilator in volume control mode at a tidal volume of 500 ml, a respiratory rate of 15 breaths/min and ZEEP or an Air-Shields Ventimeter® ventilator with similar ventilator settings.

Table 1. Summary of Experimental Design

				Washout	
Part 1	Anesthetic Machine	Anesthetic Agent	Duration of Exposure	Internal Circuitry	External Circuitry
	KION	1% halothane	2 h	5 l/min	5 l/min
	KION	1% halothane	2 h	10 l/min	10 l/min
	KION	1% halothane	12 h	5 l/min	5 l/min
Part 2				High FGF	Low FGF
	KION	1% halothane	2 h	10 l/min	5 l/min
	Ohmeda	1% halothane	2 h	10 l/min	5 l/min
	KION	1.5% isoflurane	2 h	10 l/min	5 l/min

FGF = fresh gas flow.

Table 2. Pharmacokinetic-derived Variables

	Y	K	Half-life (min)	Time to 10 ppm (min)	Y	K	Half-life (min)	Time to 10 ppm (min)
Part 1	Internal Circuitry				External Circuitry			
A. 2 h ventilation, 5 l/min washout	9,936 ± 191	1.26 ± 0.06	0.55	8–12	493 ± 16	0.13 ± 0.01	5.19	59–75
B. 2 h ventilation, 10 l/min washout	10,002 ± 240	1.87 ± 0.15	0.37	5	418 ± 7	0.47 ± 0.02	1.48	13–22
C. 12 h ventilation, 5 l/min washout	9,400 ± 186	1.21 ± 0.06	0.57	10–16	494 ± 11	0.15 ± 0.01	4.72	71–84
Part 2	High FGF (10 l/min)				Low FGF (5 l/min)			
A. KION, 1% halothane	9,986 ± 61	1.66 ± 0.03	0.42	17–23	34.9 ± 0.89	0.04 ± 0.002	17.2	26–34
B. Ohmeda, 1% halothane	9,999 ± 69	2.03 ± 0.05	0.34	5–6	20.6 ± 1.00	0.09 ± 0.01	7.6	6–9
C. KION, 1.5% isoflurane	14,985 ± 49	1.66 ± 0.02	0.42	22–25	32.4 ± 0.39	0.03 ± 0.001	26.2	35–41

Values for Y and K are mean ± standard error, and for Time to 10 ppm, (range). $r^2 \geq 0.98$ for all curves, except Part 1(A) external circuitry, 0.89; and Part 1(C) external circuitry, 0.93.

FGF = fresh gas flow; ppm = parts per million.

After priming the anesthetic machine with the designated anesthetic, the vaporizer was closed or removed from the machine, the carbon dioxide absorber was removed from the circuit and the circle circuit and test lung were replaced with components that had never been exposed to anesthetics. During the washout, the FGF was initially set to 10 l/min (high FGF). The concentration of halothane or isoflurane was analyzed every minute until it reached 10 ppm (fig. 3). The FGF was then decreased to 5 l/min (low FGF) to simulate clinically relevant flows during anesthesia, and the anesthetic concentration continued to be recorded until it reached 10 ppm once again.

For both parts of this experiment, concentrations of halothane and isoflurane were measured continuously with both a calibrated Datex Capnomac Ultima (Helsinki, Finland) and a calibrated Miran LB2 Portable Ambient Air Analyzer (Foxboro, Norwalk, CT, USA).

Statistical Analysis

Anesthetic concentration-time profiles were fitted to an exponential decay equation:

Halothane or isoflurane concentration [ppm] = $Y \times e^{(-k \times \text{Time [min]})}$, where Y and k are parameters, using nonlinear least squares regression. Half-lives ($T_{1/2}$) were computed using the expression: $T_{1/2} = 0.69/k$.

The effects of the duration of priming with halothane and FGF during the washout in part 1, and of the type of anesthetic machine and inhalational anesthetic in part 2, on the time to reach 10 ppm and the peak anesthetic

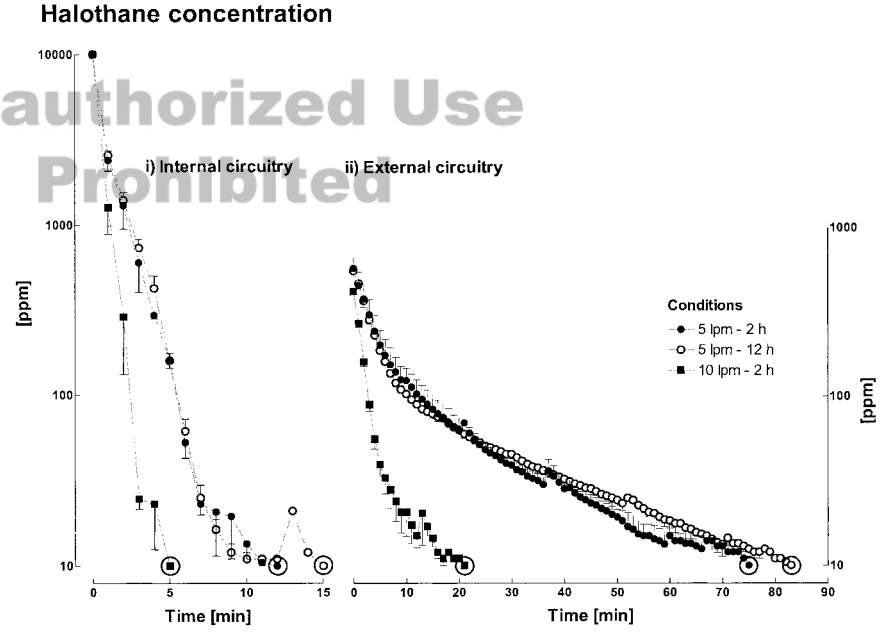

Fig 2. Halothane concentration, (time profiles for the three conditions in part 1.) During washout of the internal circuit, the halothane concentration decreased exponentially, reaching 10 ppm in 5 to 16 min. After reaching 10 ppm halothane, fresh gas was directed through the ventilator and patient cassette. The washout of the circuit was slower, reaching 10 ppm in 22 to 84 min. depending on the conditions. The large circles designate a halothane concentration of 10 ppm. Date are mean ± standard deviation..

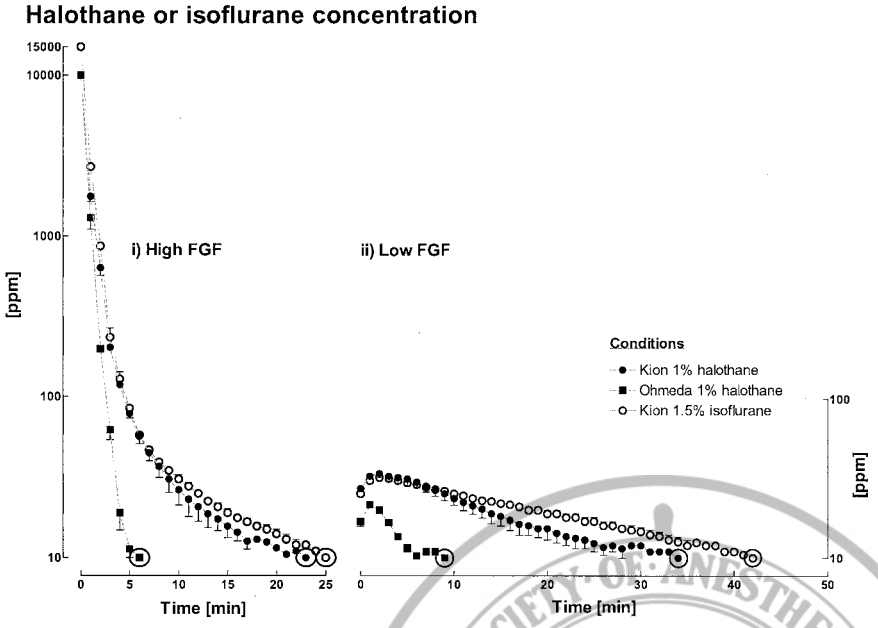

Fig 3. Concentration, (time profiles for halothane and isoflurane for the three conditions in part 2). With a high (10 l/min) FGF, the concentration of both halothane and isoflurane decreased exponentially to 10 ppm. When the FGF was decreased to 5 l/min, the concentration of inhalational anesthetic increased to approximately 40 ppm and decreased in 9 min to 10 ppm in the Ohmeda Excel and in 34 to 41 min in the KION. The large circles designate a concentration of 10 ppm of the inhalational anesthetic. Data are mean ± standard deviation.

concentration during the washout periods were evaluated using two-way analysis of variance (ANOVA). Curve fitting and statistical analysis were performed using Stata version 7 (Stata Corporation, College Station, TX, USA). $P < 0.05$ was accepted as statistically significant.

Results

Part 1

During the washout of the internal circuitry, the concentration of halothane decreased exponentially, reaching 10 ppm within a maximum of 16 min at 5 l/min FGF and 5 min at 10 l/min FGF (fig. 2i) (table 2, part 1, Internal Circuitry). The time to reach 10 ppm halothane depended on the FGF ($P = 0.026$), but not on the duration of priming the circuit with halothane.

During the washout of the external circuitry, the concentration of halothane increased immediately to a mean maximum of 515 ppm (range 410–740) and then decreased exponentially to 10 ppm within 84 min at 5 l/min FGF and 22 min at 10 l/min FGF (fig. 2ii) (table 2, part 1, External Circuitry). The peak concentration of halothane was independent of the duration of priming and the FGF during the washout. The time to reach 10 ppm depended on the duration of the priming with halothane ($P = 0.046$) and the FGF ($P < 0.001$).

Part 2

During the washout of halothane and isoflurane from the KION at high FGF, the concentrations reached 10 ppm within a maximum of 23 and 25 min respectively whereas the washout of halothane at the same FGF from the Ohmeda Excel 210 reached 10 ppm within a maximum of 6 min, or one-fourth that of the KION (Fig. 3i; table 2, part 2, high FGF). The difference in the washout at high FGF in part 2 depended on the type of anesthetic machine ($P < 0.001$) but not on the anesthetic agent.

When the FGF was decreased to 5 l/min, the concentrations of halothane and isoflurane in the effluent from the KION increased from 10 to 34 (range 31–38) and 32 (32–33) ppm respectively, and the concentration of halothane from the Ohmeda Excel 210 increased from 10 to 23 ppm (20–23) (fig. 3ii). The magnitude of the increase in anesthetic concentration depended on the type of anesthetic machine ($P < 0.0006$), but not on the inhalational anesthetic. The time for the concentration of halothane or isoflurane to reach 10 ppm followed the order: Ohmeda Excel 210 with 1% halothane (maximum 9 min) < KION with 1% halothane (maximum 34 min) < KION 1.5% isoflurane (maximum 41 min) (table 2, part 2, low FGF and fig. 3ii). The washout at low FGF depended on the anesthetic machine ($P < 0.001$) and the inhalational anesthetic ($P = 0.01$).

Discussion

To prepare anesthetic machines for use with MHS patients, all residual inhalational anesthetic should be removed. This is usually achieved by flushing the anesthetic machine with clean fresh gas and replacing contaminated components with clean new components. Although published studies have described the washout of halothane from Ohmeda anesthetic machines,[1–4] the presence of silicone and other rubber components in the internal gas circuitry of KION machines precludes the application of those results to the KION. To compare the washout of inhalational anesthetics under the conditions of this study, we controlled the circuit configuration and components, ventilation parameters, period of exposure to

anesthetic, and FGF. Our results demonstrate that the difference in the time to washout of inhalational anesthetics between KION and Ohmeda anesthetic machines varies by approximately four-fold, with the KION requiring more time. In light of these findings, it is imperative that guidelines for the preparation of anesthetic machines for MHS patients be customized for each type of anesthetic machine.

Our data for the washout of halothane from Ohmeda Excel 210 machines are consistent with published data.[1–3] The absence of rubber or rubberlike components in the internal circuitry of the Excel 210 anesthetic machine facilitates a rapid and complete washout of even soluble inhalational anesthetics such as halothane from the internal circuitry. Although we did not investigate the washout of inhalational anesthetics from the external circuit of the Excel 210 (*i.e.*, the bellows of the ventilator), we suspect that any potential or real reservoir of inhalational anesthetic should be flushed or replaced to avoid contamination of an otherwise vapor-free machine.

That the concentration of inhalational anesthetic increased suddenly when the FGF was decreased in part 2 was surprising. In spite of flushing the machine with 10 l/min FGF until the concentration of anesthetic reached 10 ppm, we detected a small but substantial peak in the concentration of inhalational anesthetic in the effluent when the FGF was decreased from 10 to 5 l/min. These data suggest that decreasing the FGF may place MHS patients at risk for an MH reaction. We posit that this second peak of halothane and isoflurane results from the slow release of these inhalational anesthetics from silicone or other rubber components (within the machine) that becomes apparent only when the FGF is reduced. Our observations suggest that all possible reservoirs of inhalational anesthetic within anesthetic machines must be flushed or replaced when preparing anesthetic machines for MHS patients and that a high FGF should be maintained during anesthesia when anesthetizing MHS patients.

We attributed the slower washout of inhalational anesthetics from the KION when compared with the Ohmeda Excel 210 (fig. 3) to the slow release of anesthetic from silicone and other rubber components within the KION. The quantity of anesthetic that is released from these components depends on the solubility of the inhalational anesthetic in the components, the volume of these components, and the FGF. For example, the solubility of halothane in the major components of anesthetic circuits ranges from 19.1 for the polypropylene Y-piece to 199 for the black rubber bellows[6] of the ventilator. Thus, differences in the washout of inhalational anesthetics between anesthetic machines may be explained in part, by differences in the characteristics of components within the machines.[4,6–8]

We expected the washout profiles of halothane and isoflurane from the KION in part 2 to parallel their solubilities in rubber, but were surprised to find the opposite to be the case. This observation contradicts our understanding of the pharmacokinetics of inhalational anesthetics in anesthetic circuits. We posit two plausible explanations for this observation. First, we administered 50% more isoflurane than halothane during the period of exposure. Whether the increased dose of isoflurane resulted in the prolonged release of this anesthetic compared with halothane remains speculative. Second, the solubilities of halothane and isoflurane in the silicone components of the gas circuit in the KION are unknown. Neither the specific composition of the silicone components in the gas circuitry of the KION nor the solubilities of inhalational anesthetics in those components are published, leaving the authors to speculate on the contribution of the silicone components to the discrepancy in washout between the two inhalational anesthetics. The washout profiles of the less soluble anesthetics, sevoflurane and desflurane, which were not studied, remain undetermined.

The design of the experiment may be critiqued from several points of view. First, we elected not to flush the anesthetic machines to eliminate residual anesthetic before commencing this study. We did this to simulate the clinical situation, as if each study were the first case of the morning. Given the high concentrations of inhalational anesthetic during the exposure period, 10,000 ppm for halothane (or 1%) and 15,000 ppm for isoflurane (or 1.5%), it is unlikely that any residual trace anesthetic within the machine biased our measurements of the anesthetic concentration. Second, the FGFs used in this experiment were dictated by limitations in the equipment and standards in clinical care. The maximum FGF that a KION anesthetic machine can deliver is 18 l/min. We flushed the anesthetic machines with 10 l/min because both anesthetic machines could deliver this flow rate and because it is the current standard for preparing machines for MHS patients.§ We expect that the time to reach 10 ppm of the anesthetic would decrease if the FGF were increased beyond 10 l/min. Third, it is possible that the test lungs released inhalational anesthetic into the effluent, thereby augmenting the concentration during the washout. We tested for this possibility by circulating vapor-free fresh gas at a low flow rate after completing the washout and measuring the concentration of anesthetic in the effluent from the test lung with the Miran. At no time did we find measurable concentrations of inhalational anesthetic in the effluent.

We flushed the anesthetic machine with fresh gas until the concentration of inhalational anesthetic in the effluent gas reached 10 ppm. Previous studies have used

§ Malignant Hyperthermia Association of the United States. Preventing malignate hyperthermia: An anesthesia protocol [Web site]. Available at: http://www.mhaus.org/ananesprotocol2.html. Accessed December 3, 2001.

10 ppm or less as their end-point for anesthetic washout.[1–3,5] From a safety perspective, the Recommended Exposure Limit (REL)‖ recommended by the National Institute for Occupational Safety and Health (NIOSH) for chronic exposure is 2 ppm for Halothane, and the Threshold Limit Value (TLV) by both NIOSH and the World Health Organization#,** for acute exposure is 50 ppm. Since these two standards were introduced, no MH reactions have been reported in either healthcare workers or susceptible patients who were exposed to these concentrations of inhalational anesthetics. Whether 10 ppm is the minimum concentration of inhalational anesthetic that we should strive to achieve to prevent MH reaction in MHS individuals, remains to be established.

On the basis of our findings, the current recommendations of the Malignant Hyperthermia Association of the United States (MHAUS) for the preparation of anesthetic machines for use with MHS patients§ now appear to be inadequate for several reasons. First, all guidelines must be qualified for the machines from which the data were generated. Second, all guidelines should specify the FGF used during the washout and these flows should be the minimum flows used during anesthesia unless additional flushing occurs. Third, the washout should include all components of the machine and circuit that will be used during the anesthetic, including the ventilator bellows.

In conclusion, we recommend the following guidelines for preparing the KION anesthetic machine for use with MHS patients: (1) disconnect the contaminated carbon dioxide absorber from the circuit, (2) ventilate a new circuit and test lung with a FGF of 10 l/min for 25 min, and (3) maintain a 10 l/min FGF throughout the trigger-free anesthetic.

The authors acknowledge the assistance and technical expertise of Jim Tibbals (Product Specialist, Siemens Canada Limited, Markham, Ontario, Canada) in the conduct of this study.

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** World Health Organization, International Programme on Chemical Safety, and International Labour Organization. International Chemical Safety Cards: Halothane [Web site]. Available at: http://www.cdc.gov/niosh/ipcsneng/neng0277.html. Accessed December 3, 2001.