# Preparation of Anesthesia Machines for Patients Susceptible to Malignant Hyperthermia

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Malignant hyperthermia is a potentially lethal syndrome that can be triggered by inhaled anesthetics. Thus, it may be appropriate to utilize equipment that minimizes exposure of susceptible patients to inhaled anesthetics. The rate of release of anesthetic stored in anesthesia delivery systems is unknown. To determine residual anesthetic concentrations, the washout rates of halothane and isoflurane were compared, and the effects of a 1-l/min and a 10-l/min fresh gas flow were evaluated. Halothane concentrations were also measured in samples taken from the fresh gas outlet and the Y-piece of the circle system during four separate studies in which various components of the anesthesia system were replaced. In each study an Ohio® Modulus anesthesia machine equipped with an Air-Shields® ventilator was exposed to 2% halothane for 18 h. Anesthetic concentrations were determined by a gas chromatograph having a sensitivity of 0.1 ppm. Isoflurane washed out 3–4 times faster than halothane. Residual halothane concentration was ≈tenfold greater when the fresh gas flow was 1 l/min rather than 10 l/min: 194 *versus* 19 ppm after 1 h of washout. Using a 10-l/min fresh gas flow, halothane concentrations in samples obtained from the Y-piece were similar with original or fresh soda lime but were more than tenfold lower after the fresh gas outlet hose and circle system were replaced (≈50 ppm *vs.* ≈5 ppm after 5 min of washout). Halothane concentrations did not decrease more rapidly when the ventilator bellows was replaced. Halothane concentrations in samples taken from the end of the original fresh gas outlet hose decreased rapidly and were ≈10 ppm after 5 min of washout. After the outlet hose was replaced, halothane concentrations were <1 ppm after 5 min of washout. "Contaminated" machines should be prepared for use in susceptible patients by removing vaporizers, flushing with oxygen at a rate of 10 l/min for 5 min, replacing the fresh gas outlet hose, and using a new disposable circle. (Key words: Anesthetics, volatile: halothane, isoflurane. Complications: malignant hyperthermia. Equipment: anesthesia machine; circle system; ventilator.)

MALIGNANT HYPERTHERMIA is a potentially lethal syndrome that can be triggered by inhaled anesthetics. The minimum anesthetic concentration triggering this syndrome has not been determined. Consequently, it may be appropriate to choose equipment that minimizes exposure of susceptible patients to inhaled anesthetics.

The rate of release of anesthetic stored in the components of anesthesia delivery systems is unknown. It is also unknown how machine configuration affects release of residual anesthetics. Because unexpected release of inhaled anesthetics could trigger a malignant hyperthermia crisis in susceptible patients, some investigators recommend that a special anesthesia machine (never exposed to inhaled anesthetics) be reserved for these patients.[1] Others suggest that a "contaminated" machine can be used safely if flushed with oxygen or air for 18 h prior to use.[2]

To determine current methods of preparing contaminated machines for use with susceptible patients, we contacted the directors of ten North American malignant hyperthermia testing centers. Most directors recommend washout periods of 8–12 hours. However, using mass spectrometry with a sensitivity for volatile anesthetics of ≈0.01% (100 ppm), we were unable to detect residual inhaled anesthetic after only a few minutes of anesthesia machine washout. This finding suggested that low residual anesthetic concentrations might exist after a brief period of machine washout.

The present study determines the rate at which residual anesthetic concentrations decrease in an anesthesia machine with a circle system and anesthesia ventilator being flushed with oxygen. We first evaluated the relative washout rates of halothane and isoflurane. We then determined the effect of differing fresh gas flows on washout rate. Finally, we performed four separate experiments in which different components of the anesthesia system were replaced to determine their effects on anesthetic washout.

## Materials and Methods

We used an Ohio® Modulus 1 anesthesia machine (ABLH00200), an Air-Shields® ventilator equipped with disposable bellows (2002880), a portable Ohio Airco® halothane vaporizer (BAKH00898), and a rack-mounted Ohio Airco® isoflurane vaporizer (AKDJ00856). Prior to each study, fresh soda lime (Sodasorb®) was placed in the carbon dioxide ($CO_2$) absorber cannister and a new, 1.9-m long disposable polyethylene circle system (Marquest®) was attached to the anesthesia machine.

All equipment was exposed to 2% halothane delivered in a 1-l/min inflow for 18 h. The components listed above were connected to a 1-l breathing bag (artificial lung) at the end of the circle system. The halothane vaporizer was connected in series between the

fresh gas outflow and the circle system. The ventilator was set to deliver a tidal volume of 600 ml at a rate of 10 breaths/min. We chose a 1-l/min flow to conserve oxygen, to assure that the liquid anesthesia supply in the vaporizer would not become exhausted and to maximize saturation of the soda lime. The ventilator bellows and the fresh gas outlet hose were not changed prior to exposure.

During the washout period, vaporizers were removed from the machine because prior reports have indicated that some vaporizers leak while in the "off" position.[3,4] In addition, the artificial lung was replaced with a fresh breathing bag, the ventilator was retained, and the fresh gas flow was increased to 10 l/min. Gases were sampled from the Y-piece of the circle system, and the concentration of halothane was determined during 16 h of washout.

Gas samples were collected in 60-ml glass syringes that were capped and stored in the vertical position until analyzed. Samples were analyzed within 4.5 h for halothane and/or isoflurane by a Gow-mac® model 750 FID gas chromatograph having a sensitivity of ≈0.1 ppm. Samples were analyzed twice and the results of each determination averaged. A 1.0-ml sample loop was used during the initial portion of each washout (when anesthetic concentrations were high) to prevent saturating the detector. During the middle and terminal portions of each washout, a 0.05-ml loop was used to increase detector sensitivity. The gas chromatograph was calibrated in triplicate prior to each use with standards ranging from 1.1% to 0.01% halothane and/or isoflurane. The concentration range and time spanned by the study required that the chromatograph be calibrated three times during each washout.

Our first experiment evaluated the relative washout rates of halothane and isoflurane. The anesthesia system was exposed to 2% halothane and 2% isoflurane in a 1-l/min inflow for 18 h. Because halothane and isoflurane elute from the chromatographic column at different rates, the concentrations of each were determined simultaneously. Gases were sampled from the Y-piece of the circle system during 16 h of washout.

In a second study, the effect of fresh gas flow rate on the washout of halothane was determined by saturating the anesthesia circuit with 2% halothane for 18 h as in the first study. Again, none of the anesthesia equipment (except the artificial lung) was changed during washout. Fresh gas flow was initially 10 l/min. After 1 h of washout, a gas sample was collected from the Y-piece of the circle system, the fresh gas flow was decreased to 1 l/min for 5 min, a second gas sample was taken, and the fresh gas flow was returned to 10 l/min. This process was repeated at 2, 4, 8, and 16 h of washout. Samples were not tested prior to 1 h of washout because decreasing fresh gas flow to 1 l/min for more than 10% of the washout period may have distorted the overall washout rate. This protocol tested the exposure a patient might experience during anesthesia using low fresh gas flows.

To investigate the effect of specific circle components on anesthetic absorption and washout, we conducted a third study. Halothane concentrations were sampled from the Y-piece of the circle system and evaluated during 16 h of washout under four machine conditions: 1) without changing any components of the system; 2) after changing only the soda lime; 3) after changing the soda lime, circle system, fresh gas outlet hose, but not the ventilator bellows; and 4) after replacing the soda lime, circle system, fresh gas outlet hose, and the ventilator bellows.
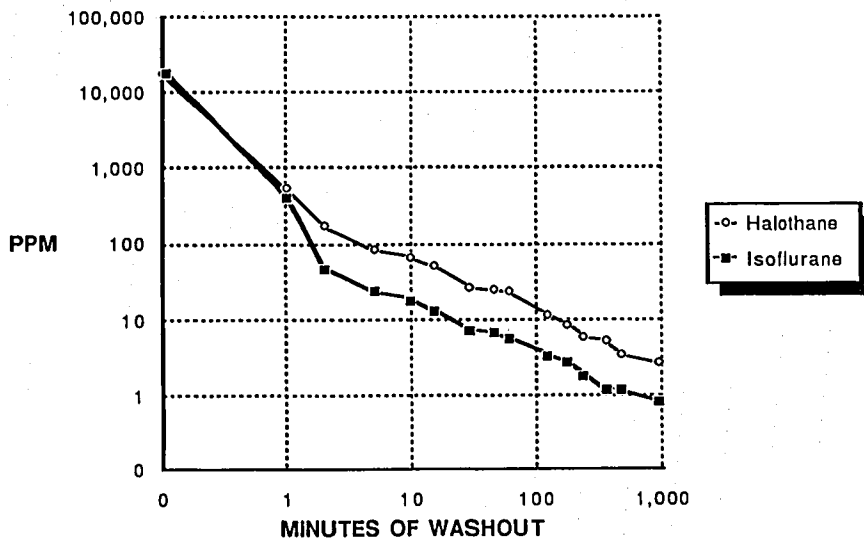
FIG. 2. Washout from an Ohio Modulus® 1 anesthesia machine saturated with 2% halothane. Gas samples were taken from the Y-piece of the circle system without changing any anesthesia equipment. Measurements were made with a fresh gas flow of 10 l/min. To test the halothane concentration a patient might experience during low-flow anesthesia, a second sample was obtained at each sampling interval after fresh gas flow was reduced to 1 l/min for 5 min. Halothane concentrations were inversely proportional to the fresh gas flow.
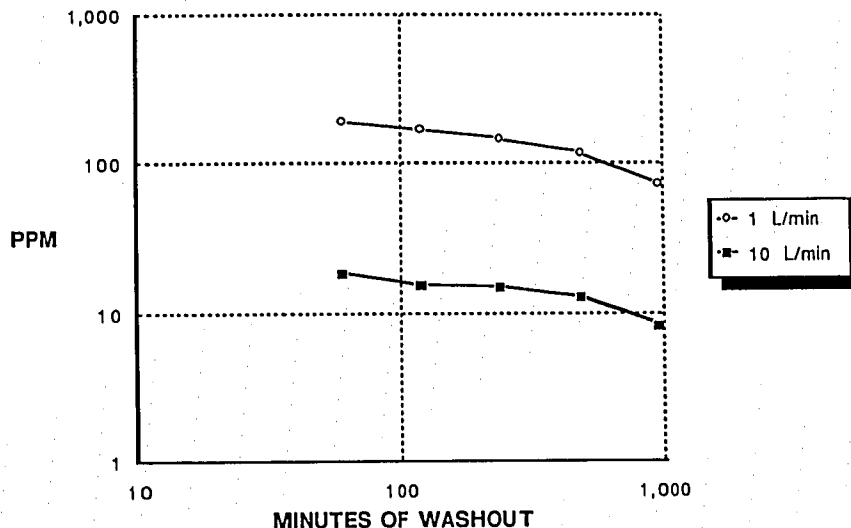


To estimate the anesthetic exposure from a disposable nonrebreathing system (*e.g.*, a Bain circuit), halothane concentrations were also determined in washout samples taken from the end of the fresh gas hose. Halothane was measured for 16 h with the original, exposed fresh gas hose and for 4 h after replacing the original hose with a new one.

Each anesthetic circuit configuration was tested once. Consequently, we attempted no statistical analysis. Results were plotted using log-log axes to emphasize concentration changes occurring during the first minutes of washout.

## Results

Halothane concentrations remained 3–4 times greater than the isoflurane concentrations throughout

the 16 h of washout (fig. 1). The concentration of halothane remaining in the system was almost tenfold greater when the fresh gas flow was 1 l/min rather than 10 l/min: 194 *versus* 19 ppm after 1 h of washout and 148 *versus* 15 ppm after 4 h of washout (fig. 2).

Halothane concentrations in samples obtained from the Y-piece were similar with original or fresh soda lime but were more than tenfold lower after the fresh gas outlet hose and circle system were replaced (fig. 3). Halothane concentrations did not decrease more rapidly when the ventilator bellows was replaced.

Halothane concentrations in samples taken from the end of the original fresh gas outlet hose decreased rapidly and were ≈10 ppm after 5 min of washout. After the outlet hose was replaced halothane concentrations were <1 ppm after 5 min of washout (fig. 4).

FIG. 3. Washout from an Ohio Modulus® 1 anesthesia machine saturated with 2% halothane. Gas samples were taken from the Y-piece of the circle system during four conditions: 1) without changing the anesthesia equipment; 2) after changing the soda lime; 3) after changing the soda lime, circle system, and fresh gas outlet hose; and 4) after replacing the soda lime, circle system, fresh gas outlet hose, and the ventilator bellows. Halothane concentrations in samples obtained from the Y-piece were similar with original or fresh soda lime, but were more than tenfold lower after the fresh gas outlet hose and circle system were replaced. Halothane concentrations did not decrease more rapidly when the ventilator bellows were replaced.
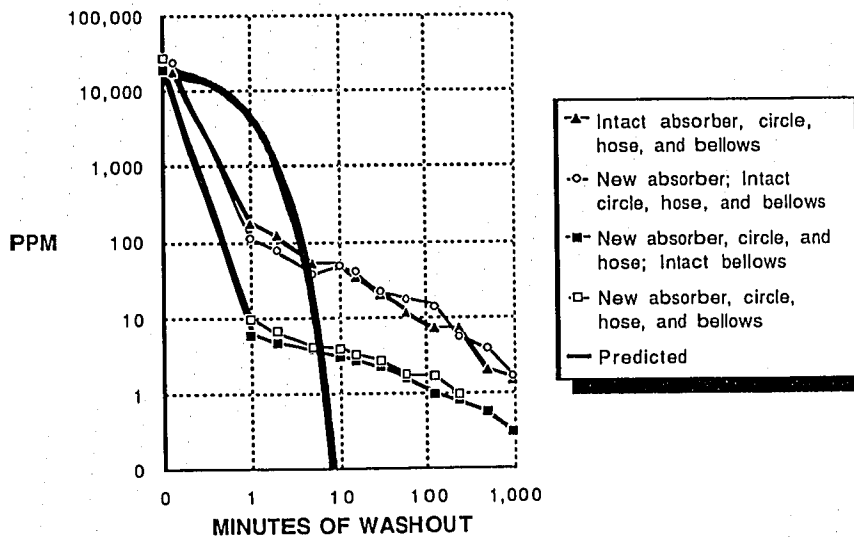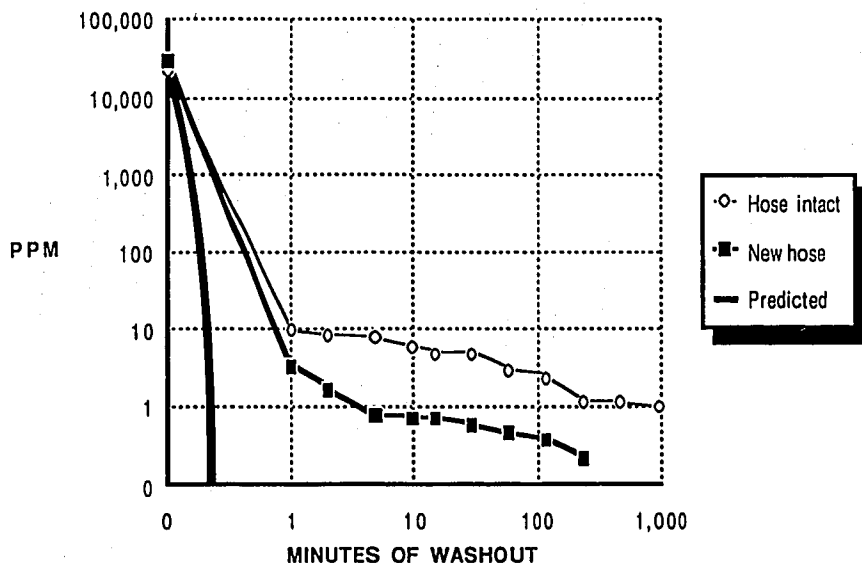
FIG. 4. Washout from an Ohio Modulus® anesthesia machine saturated with 2% halothane. Gas samples were taken from the end of thé fresh gas outlet hose (FGF). When a new fresh gas outlet hose was placed on the machine just prior to washout, the halothane concentration in the fresh gas supply decreased to <1 ppm after 5 min of washout.

Figures 3 and 4 also illustrate the predicted anesthetic washout rate using the equation:

$$C(t) = C_i e^{-F(t/V)}$$

where C(t) is the halothane concentration in parts per million at time t, $C_i$ is the initial halothane concentration in partś per million, F is the fresh gas flow rate in liters per minute, V is the volume of the system in liters, and t is the washout time in minutes. This equation assumes thát complete mixing occurs within the specified volumé and that no anesthetic is released by components in the delivery system. In both figures, the initial concèntration was specified as 20,000 ppm (2%) and the fresh gas flow rate as 10 l/min. A system volume of 7 l wás used to estimate washout from the entire anesthesia sÿstèm, including the corrugated hoses and ventilätor (fig. 3).[5,6] Washout from the anesthesia machine and fresh gas hose was predicted using a volume of 200 ml estimated by a representative of Ohio® Inc. (fig. 4).

## Discussion

Absorption of anesthetics by components of the delivery system is normally unimportant because the amounts absorbed are small compared with those administered during anesthesia. However, absorbed volatile anesthetics may bé released over a long time period. Prolonğed release is a potential hazard to patients susceptible to malignant hyperthermia because it can result in unintentional exposúre to anesthetic gases.

Modern anesthesia delivery systems incorporate many plastic and rubber components. The inhaled anesthetics are soluble in rubber and plastic. The rubber/gas partition coefficients for halothane range from 120:1 to 160:1, depending on the age and type of rub-

ber, whereaŝ these coefficients for isoflurane range from 62:1 to 33:1.[7,8]‡ Polyvinylchloride:gas partition coefficients are 90:1 for halothane and 35:1 for isoflurane and those for polyethelene:gas are 110:1 and 45:1, respectively.‡

More highly soluble anesthetics, such as halothane, wash out more slowly than less soluble ones (fig. 1). Consequently, more highly soluble anesthetics pose a greäter risk to malignant hyperthermia-susceptible patients. We used halothane for the remainder of our studies because it is more highly soluble than the other clinically used inhaled anesthetics.

The amount of anesthetic ultimately released from contaminated rubber or plastic is determined by the amount dissolved. Although the amount dissolved may be substantial, the rate at which it is released is limited by the slow diffusion of anesthetic molecules to the surface of the plastic or rubber. During washout, anesthetic concentration in the gas phase decreases slowly and is inversely proportional to the rate of gas inflow (fig. 2).

The volume of the entire anesthetic delivery system (machine, ventilator, corrugated tubing, *etc.*) is ≈7 l.[5,6] Assuming complete and rapid gas mixing, anesthetic concentration in this volume decreases with a simple, single exponential decay rate. The predicted concentration following 1 h of washout with 1 l/min fresh gas flow is 4 ppm, whereas only $10^{-33}$ ppm will remain when the flow is 10 l/min. Both predicted concentrations are much lower than those observed experimentally (194 and 19 ppm), indicating substantial release of anesthetic from system components. Furthermore, the predicted concentrations are higher than those ob-

‡ Targ A: Personal communication.

served during the first 5 min of washout, suggesting that gas mixing was incomplete during this period.

Another potential anesthetic reservoir is the carbon dioxide absorbant. Self-indicating soda lime absorbs ethylene, but such absorption has not been reported with modern anesthetics.[9] The soda lime/halothane partition coefficient is $\approx$1:1, but this value increases logarithmically as the water content of the soda lime decreases.[8] Commercially supplied absorbant is hydrated ("wet") and becomes still wetter during clinical use because exhaled gases are moist and water is released by the absorption of $CO_2$. (Fresh gas flow continued between cases will not dry soda lime because the gas will exit from the Y-piece without passing through the $CO_2$ absorber.) Thus, soda lime is unlikely to absorb large amounts of halothane during routine clinical use. The present study confirmed this prediction by demonstrating that washout rates were similar with anesthetic-saturated or fresh soda lime.

A limitation of our study is that washout from each anesthetic circuit configuration was tested only once. Although random error will influence the value of individual points, it is unlikely to change significantly the shape of an entire washout curve. Systematic measurement errors also are unlikely because analysis of each washout curve required that the gas chromatograph be calibrated three times using different loops and concentration standards. We tested only one anesthesia machine and one ventilator. However, washout from other types of anesthesia machines is reported to be similar.[10] Markedly slower washout would be required to produce residual anesthetic concentrations likely to be unsafe for malignant hyperthermia patients. Two percent halothane was chosen because it is a concentration greater than that routinely used to maintain anesthesia. Consequently, residual concentrations observed in this study are likely to be greater than those occurring clinically.

The lowest concentration of potent inhaled anesthetic that can trigger malignant hyperthermia crises is unknown. This quantity will probably remain unknown because it would be unethical to expose susceptible patients deliberately to inhaled anesthetics. It is known that triggering of susceptible swine occurs more slowly as halothane concentration is decreased from 3 to 0.5%.[11] Furthermore, a malignant hyperthermia crisis that occurs following exposure to low anesthetic concentrations cannot be assumed to result from the exposure because stress alone can precipitate a malignant hyperthermia crisis[12] and crisis have been reported in unanesthetized humans[13-15] and in humans anesthetized with "nontriggering" drugs.[16]

One part per million (a concentration similar to that in samples from a new fresh gas hose after 5 min of washout) is below the National Institute of Occupational Safety and Health standard for waste gas exposure.§ Typical ambient operating room concentrations were frequently 10 times that concentration before waste gas scavenging became the standard.§ Nonetheless, there is no report of malignant hyperthermia triggered in operating room personnel (some of whom are presumably susceptible) by waste anesthetic gases. Therefore, it is unlikely that concentrations $\approx$1 ppm will trigger malignant hyperthermia.

Malignant hyperthermia is triggered by anesthetic drugs; thus, crises typically occur during anesthesia. When such a crisis is suspected, a common practice is to change the soda lime and circle hoses and ventilate the lungs using high fresh gas flows.[17] Some clinicians recommend changing to an uncontaminated anesthesia machine.[18] The data from our study suggest that changing the anesthesia delivery system should be a low priority. Even starting with a system exposed to 2% halothane, residual concentrations in the fresh gas flow are $\approx$100 ppm within 1 min of discontinuing anesthetic administration. This concentration is likely to be 50–100 times lower than that in the patient's exhaled gas. Thus, exposure to "new" anesthetic will be small, compared with the relatively large quantity remaining within the patient. Measures to minimize additional anesthetic exposure in susceptible patients are prudent, but such measures should not distract from more urgent priorities including dantrolene administration, hyperventilation, and cooling measures.

In summary, we have demonstrated that anesthetic washout from an anesthesia machine is rapid but dependent on machine configuration. Anesthetics such as halothane, with high solubility in system components, wash out more slowly than less soluble anesthetics such as isoflurane, and anesthetic concentration in the system is inversely proportional to fresh gas flow rate. Soda lime is not a significant reservoir. Rubber and plastic portions of the anesthesia system are the most important anesthetic reservoirs; removing these components greatly speeds anesthetic washout. The (Air-Shields®) ventilator contains a rubber diaphragm in addition to the bellows. Consequently, even when all easily accessible rubber and plastic components of the anesthesia system are replaced, small but measurable anesthetic concentrations remain. Anesthetic concentrations in samples from the end of a new fresh gas flow hose of $\approx$1 ppm within 5 minutes of beginning washout will be obtained from a "contaminated" machine by

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§ National Institute of Occupation Safety and Health: A Recommended Standard for Occupation Exposure to Waste Anesthetic Gases and Vapors. Washington DC, US Government Printing Office, 1977, pp 1–3.

removing vaporizers, flushing with oxygen at a rate of 10 1/min for 5 min, replacing the fresh gas outlet hose, and using a new disposable circle. Contaminated ventilators should be avoided.

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