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Using a Refrigerant Leak Detector to Monitor Waste Gases from Halogenated Anesthetics

Henrik Rasmussen,[1,*] and Syvert Thorud[2]

Although halogenated gas anesthetics are indispensable in laboratory animal medicine, they are hazardous when present in the working environment. A simple technique of real-time leak detection and environmental spot monitoring can provide valuable adjunct information to current techniques of time-weighted monitoring. We investigated the minimal limit of detection of halothane, isoflurane, sevoflurane, and desflurane of a leak detector for halogenated gas refrigerants which provides a qualitative response only. We connected a container to an infrared gas analyzer to create a 135-l closed-circuit system and injected liquid halothane, isoflurane, sevoflurane, and desflurane to create calculated gas concentrations of 0.7 to 3.4 parts per million (ppm). The infrared absorbance and response of the leak detector were recorded, and a total of 5 measurements were made per concentration. The actual gas concentrations were calculated by comparison with the agent-specific absorbance standard curve. The leak detector clearly and consistently responded to halothane, isoflurane, sevoflurane, and desflurane from minimal concentrations of 2.1 ± 0.2, 1.4 ± 0.04, 0.8 ± 0.04, and 1.2 ± 0.4 ppm, respectively, as determined by infrared analysis. Although the detector does not provide numerical and time-weighted results, leak testing of equipment and repeated monitoring of the environment (spot monitoring) can provide valuable real-time information. In addition, with appropriate consideration of the methodological limitations, spot monitoring can be used to predict the likelihood of compliance with time-weighted exposure recommendations. A leak detector therefore represents a simple, effective, and inexpensive instrument for monitoring the leakage of halogenated anesthetic gases from equipment and into the working environment.

Abbreviations: IR, infrared; OEL, occupational exposure limits; ppm, parts per million; WAG, Waste anesthetic gases

Although gaseous anesthetics are generally safe and widely used in daily clinical practice, since the early 1970s waste anesthetic gases (WAG) have been considered to be hazardous agents if present in the working environment, in light of epidemiologic evidence of embryo toxicity and liver and kidney disease.[2,4,5,7,9-11] Other investigators[1,3] have questioned the validity of these conclusions,[4] which were not confirmed in prospective studies. Further, the conclusions regarding halogenated agents were based on agents that are either unavailable or not widely used today (for example, halothane and methoxyflurane). However, irrespective of the medical validity of the current WAG guidelines, the recommendations are in effect and largely reflect what could be achieved in clinical practice, provided that the current best practice of scavenging of waste gasses is used routinely.[1] Although closed gas-delivery systems and effective scavenging measures are common in current human anesthesia, open delivery systems and variably effective scavenging methods often occur in veterinary medicine. This situation is particularly frequent in laboratory animal and rodent anesthesia, in which the small size of the animal precludes the use of closed and low-flow circle systems and makes effective scavenging of WAG a technical challenge.[9,10]

The recommended time-weighted average occupational exposure limit (OEL) of halogenated gases is 2 parts per million (ppm) in the United States and 0.02 to 20 ppm in Norway.[4,6] The OELs of halogenated gases[4] were established before the advent of isoflurane, desflurane and sevoflurane. Therefore no recommended OELs exist for these compounds, which are currently the anesthetics used most frequently in the United States. Although recommendations and guidelines to reduce workplace exposure to anesthetic gases in general through prevention programs have been issued, "these guidelines are not new standard or regulation, and they create no new legal obligations."[11] Various OELs in effect in several European countries do reflect, to some degree, the toxicity profiles of both older and newer agents. In Norway, OELs were reviewed in 2000, and those for enflurane and halothane were reduced from 2 and 5 ppm, respectively, to 0.3 and 0.02 ppm, respectively, whereas the OELs of the newer agents desflurane and sevoflurane were established at 20 ppm. The OEL for isoflurane remained at 2 ppm.[6]

The anesthetic gas concentrations generally used (2% to 5%) are approximately 1000 to 10000 times higher than the OELs. Flow rates of fresh gas are usually in liters per minute, and leakage from anesthetic equipment, including the endotracheal tube–laryngeal mask interface, therefore will contribute markedly and rapidly to environmental WAG concentrations exceeding the OEL. In most countries, maximal recommended or allowable concentrations are based on time-weighted average measurements (1 to 8 h), which in practice make the limits difficult to use for real-time guidance.

Currently WAG monitoring is based on agent-specific infrared (IR) absorbance by use of precalibrated IR gas analyzers and personal sampling using charcoal adsorption of WAG in tubes or badges (dosimetry). Newer models of IR analyzers are more suited for generating real-time results,[10] whereas charcoal tubes and badges require gas chromatographic analysis and data processing to generate the actual WAG and time-weighted average exposure level. Time-weighted analysis of WAG levels therefore typically is performed by equipment and personnel external to an anesthesia department (for example, an environmental health and safety department) and often at relatively infrequent inter-

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[1]GE Healthcare, Oslo, Norway; [2]National Institute of Occupational Health, Oslo, Norway.
[*]Corresponding author. Email: henrikrasmussen@ge.com

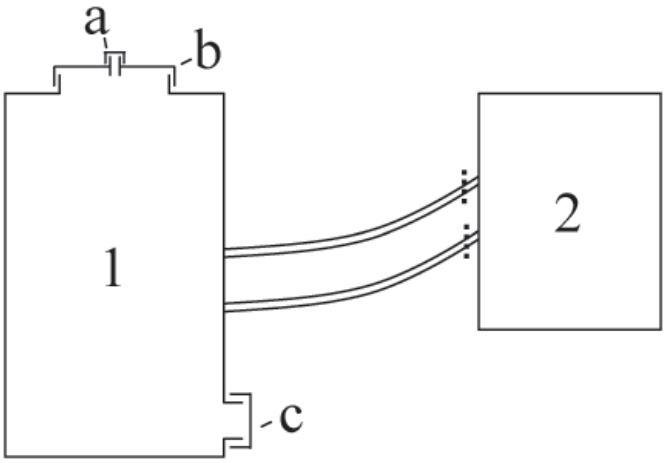

Figure 1. Setup of closed-circuit system with polyethene plastic container (1) and IR analyzer (2) connected by Teflon tubing. Liquid halogenated anesthetic agents were injected through a luer port (a). The leak detector was introduced through the container lid (b). The circuit system was evacuated through (c), while the container lid (b) was open. To create a closed loop during calibration, the IR analyzer was disconnected from the circuit system at the broken lines.

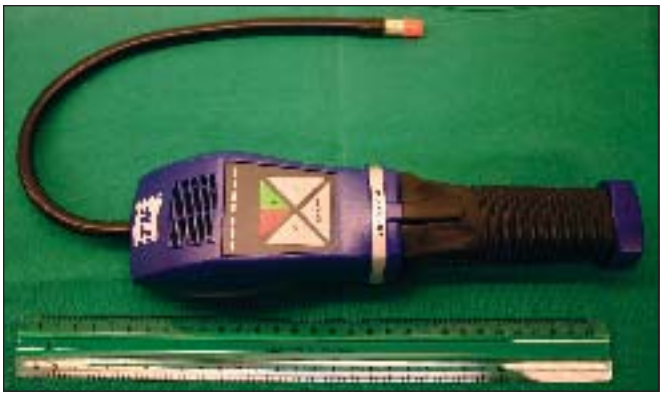

Figure 2. The leak detector for halogenated gas refrigerants.

vals. In addition, all current equipment for WAG monitoring is relatively expensive in terms of instruments (IR analyzer and gas chromatographs) or operation. Because a multitude of anesthesia equipment combinations and settings are used in different animal species, the IR absorbance results may actually be little relevant for anything but the specific equipment combination and setting used on the day of testing. Dependent upon the frequency of testing, infrequent testing by IR absorbance may therefore may be more of a formal rather than a real contribution to compliance with existing guidelines. In comparison, testing for WAG exposure by badges or tubes can be done more frequently, but the lack of real-time information precludes real-time identification of the sources of leakage or WAG levels in excess of maximal peak concentrations. Real-time leak testing according to need by the users of gas anesthesia (for example, after reassembly of anesthetic equipment or when starting new procedures) and real-time monitoring of the working environment therefore represent a valuable adjunct technique, even if the results do not constitute a time-weighted average of WAG. To be of guidance on a frequent basis (for example, between regular IR measurements of time-weighted average WAG), equipment used for leak detection or on-site ('spot') monitoring of WAG must be simple and easy to operate and provide consistently reliable real-time data.

Halogenated refrigerant leak detectors (halogen leak detectors) originally were intended for leak detection of refrigeration systems, but they also can detect halogenated anesthetic gases. The halogen leak detectors are handheld devices which are simple to operate, run on battery power, and autocalibrate in the ambient environment. By the nature of their intended use, halogen leak detectors of various types are widely available at relatively low cost. A leak detector is qualitative only, giving an audible signal on detection, and does not provide any numerical output or time-weighted average results. We have previous experience with using a halogen leak detector (TIF 5500, SPX Corporation, Owatonna, MN) for leak detection of halogenated anesthetic gases. Preliminary sensitivity testing of that model of detector indicated a calculated isoflurane sensitivity limit of 18 ppm.[8] This previous test was performed in principle as described herein but with less optimal equipment and technique (for example, a 55-l container, delivery of isoflurane by disposable micropipette tips, cling film closure of container, less effective method of gas mixing, and no parallel IR analysis). We recently acquired a new halogen leak detector (TIF RX-1A, SPX Corporation) and wanted to determine its detection limit. If sufficiently sensitive, a halogen leak detector may fulfill the described requirements for both leak detection and spot monitoring of environmental WAG concentrations and may be used at the discretion of the users of gas anesthesia. To validate the new halogen leak detector in the most optimal way, the actual concentrations tested were simultaneously analyzed by IR analysis (Miran-80, Foxboro Analytical, Foxboro, MA), which is the current 'gold standard' in WAG analysis. The 4 halogenated anesthetic gases included in the study are all in current use internationally; halothane has been withdrawn in most countries.

The purpose of this study was to 1) determine the minimal detection limits of isoflurane, sevoflurane, desflurane, and halothane by using a standard refrigerant gas leak detector and 2) perform concurrent quantitative IR analysis of the gas concentrations tested. Our hypothesis was that the detection limit of this refrigerant gas leak detector would enable 1) sensitive detection of leaked halogenated anesthetic gases and 2) spot monitoring of environmental WAG at concentrations relevant to the time-weighted exposure recommendations.

Materials and Methods

A 129.2-l polyethene plastic container (Gerdmans, Oslo, Norway) with a large gas-tight lid was used. A female luer port mounted in the container lid was used for injection of liquid gas anesthetics. A 12-volt direct-current axial fan unit of 27 m^3/h capacity (Jamicon, City of Industry, CA) was located inside the polyethene container to ensure uniform gas distribution after injection of liquid anesthetics. The polyethene container was connected to the infrared analyzer (Miran-80, Foxboro Analytical) by Teflon tubing (inner diameter, 2 mm; SVAFAS, Stavanger, Norway) to create a closed-circuit system of 134.9-l in total (Figure 1). Volumes of 0.5 to 2.0 µl isoflurane (Baxter, Oslo, Norway), sevoflurane (Abbott, Oslo, Norway), desflurane (Baxter), and halothane (Hoechst, Frankfurt [Main], Germany) corresponding to calculated concentrations of 0.7 to 3.4 ppm were injected into the closed-circuit system by use of a 2-µl Hamilton syringe (model 7002, Hamilton Company, Reno, NV). Because of its high vapor pressure, desflurane was maintained in ice-water before and during aspiration. The volumes of each agent were chosen so as to create 2 anesthetic agent concentrations that were clearly detectable and 1 concentration clearly not detectable by the halogen leak detector (Figure 2). Through pilot studies, we

Table 1. Calibration parameters for refrigerant leak detector

Parameter	Isoflurane	Sevoflurane	Desflurane	Halothane
Wavelength (μm)	8.80	8.31	8.59	8.97
Concentration range (ppm)	0.35–7.05	0.33–6.59	0.38–7.58	0.41–8.22

The following settings were used for all agents during calibration: path length, 20.25 m; slit setting, 1.0; delay time, 1; read time, 1; and scan speed, 2.

determined that the maximal time to homogenous atmosphere (indicated by stable IR absorbance values) after administration of anesthetic agents and activating the fan unit in the container and the pump of the analyzer was 6 min. We therefore operated the fan unit in the container and the pump of the analyzer for 6 to 7 min after injection of anesthetic agent before recording the IR absorbance and response of the leak detector (TIF RX-1A, SPX Corporation). The response of the detector was assessed by introducing the tip sensor into the center of the container immediately after opening the lid. The gas inside the circuit system then was evacuated (out of the building) immediately by use of a dedicated gas anesthesia vacuum system (Medicvent AB, Umeå, Sweden) operating at 15 m^3/h for 10 to 12 min after each recording. The efficacy of the chosen evacuation time was confirmed by IR absorbance in pilot studies to be consistently effective in removing all traces of the anesthetic agents in the circuit system in less than 10 min (IR absorption, 0). A total of 5 measurements were made per concentration.

Experiments were performed in a 27-m^2 (80-m^3) laboratory in an animal facility, in which there were 20 air changes hourly and a dedicated gas anesthesia vacuum system is used throughout the facility during all procedures involving gas anesthesia. The halogenated agents were stored and aspirated into a Hamilton syringe inside a ventilated safety cabinet (KR-200 Biowizard, Kojair, Vilppula, Finland) immediately adjacent to the experimental setup. The halogen leak detector autocalibrates in the ambient environment every time it is turned on. To ensure calibration in an environment without halogenated gases, autocalibration always was performed in the empty room adjacent to the room containing the experimental setup. According to the agent concentrations generated, laboratory versus testing circuit volumes, a general room ventilation of 20 air changes hourly, repeated 10- to 12-min evacuation of the circuit system at 15 m^3/h, and because anesthetics were handled as liquids inside a ventilated safety cabinet, exposure to waste anesthetic gases was considered to be minimal and probably well below the time-weighted recommendations for maximum exposure. For similar reasons and because IR absorbance during pilot studies confirmed complete absence of anesthetic gases after no more than 10 min of system evacuation, background levels of WAG were not measured during the experiment and are presumed not to influence on the results.

The IR analyzer was calibrated using the closed-loop calibration system, resulting in a total loop volume of 5.64 l. All 4 anesthetic agents were calibrated at 6 concentration levels, ranging from 0.3 to 8.5 ppm. The lower concentrations of isoflurane, sevoflurane, and halothane were diluted (1:100) in carbon disulphide (Rathburn Chemicals, Walkerburn, Scotland) before calibration, whereas the higher concentrations were injected as undiluted agent during calibration of the analyzer. At the lowest concentrations of the gas anesthetics tested in this study, dilution in carbon disulphide was required to enable reproducible injections into the closed-loop calibration system during calibration of the analyzer. Carbon disulphide was chosen as the dilution solvent because it has no interfering absorbance in the wavelength ranges used in this study. Because of its low boiling point, all concentrations of desflurane were diluted in carbon disulphide before injection into and calibration of the analyzer.

Known amounts of the carbon disulphide solutions of the anesthetics were injected in the closed loop by using a 10-μl Hamilton syringe (Microliter 701, Hamilton Company). The undiluted agents were injected by using a 1-μl Hamilton syringe (Microliter 7001, Hamilton Company). After equilibration of the solution in the loop, IR absorbance was recorded 5 times for every injection at all levels (relative standard deviation for all readings was 0.07% to 5.8 %). Every calibration point was determined as the mean of 5 consecutive and independent injections (relative standard deviation for all calibration points was 0.77% to 12.7%). The IR calibration curves were created without using the origin. Calibration of the IR analyzer gave an R^2 of 0.995 to 0.999 for the 4 agents, which indicates good linearity over the actual concentration range. Detailed IR calibration parameters for all 4 agents are shown in Table 1.

Results

Measurements of the anesthetic agent concentrations with the IR analyzer corroborated the calculated anesthetic agent concentrations. Measured values were lower than calculated values at the lower concentrations for all agents, except desflurane, for which measured values were higher than calculated values (Figure 3). The leak detector clearly and consistently responded to isoflurane, sevoflurane, desflurane, and halothane at concentrations of at least 1.4 ± 0.04, 0.8 ± 0.04, 1.2 ± 0.4, and 2.1 ± 0.2 ppm, respectively, as measured by IR analysis.

Discussion

Although detection was somewhat variable at the lower concentrations of isoflurane and halothane, the response of the leak detector at and above the recommended exposure limits was consistent and clear for all agents tested. The lower measured versus calculated values, particularly at the lowest concentrations, most likely were due to evaporation of the fluid agent during transfer into the closed circuit and adsorption to the inner surfaces of the polyethene container and Teflon tubing. Both evaporation during transfer and adsorption in the closed circuit will have a relatively greater effect on low concentrations of anesthetic. The high variability in measured desflurane concentrations most likely was related to the high vapor pressure of this agent. During testing, desflurane was maintained in an ice-water bath before aspiration into the syringe, which was at room temperature. However, during calibration of the IR analyzer, reproducible desflurane concentrations were impossible, even when using this technique with a cold syringe. We therefore used carbon disulphide for all concentrations of desflurane during calibration, and the discrepant methods of transferring desflurane likely contributed to the poor correlation between the measured and calculated concentrations of this particular agent.

The calculated concentrations generally exceeded the measured values. The variability in measured values was relatively low for all gases except desflurane, and the technique used for creating the different concentrations of isoflurane, sevoflurane,

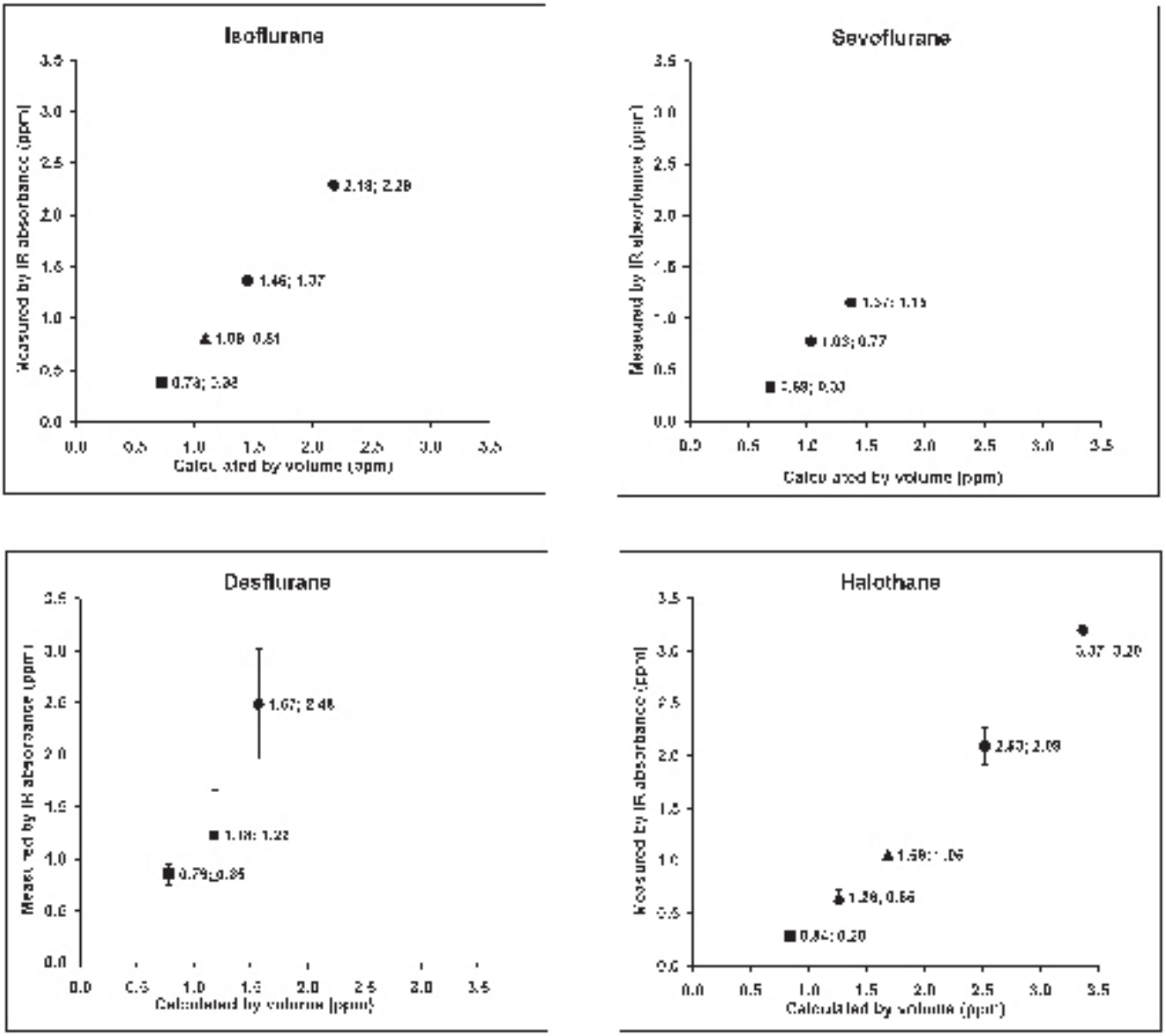

Figure 3. Measured (by IR analyzer) versus calculated concentrations of isoflurane, sevoflurane, desflurane, and halothane and their detectability with the halogen leak detector (■, consistently not detectable; ▲, variable detection; ●, consistently detectable). Measured concentrations are mean ± 1 standard deviation [error bars]; n = 5). Calculated and measured (mean) values, respectively, indicated at each figure symbol. When error bars are not shown, the standard deviation is smaller than the corresponding amount covered by the graphic symbols.

and halothane therefore was relatively robust and reproducible at the concentrations tested. If the validation had been based on the calculated values only, the detection limits for isoflurane, sevoflurane, and halothane would have been 1.5, 1.0, and 2.5 ppm, respectively, in this study. In comparison, the corresponding values measured with the IR analyzer were 1.4 ± 0.04, 0.8 ± 0.04, and 2.1 ± 0.2 ppm. The parallel IR measurement of actual gas anesthetic concentrations in the circuit system was very important for our confidence in the described detection limit validation of this particular halogen leak detector. We therefore recommend parallel IR measurement of the gas concentrations generated in the circuit system as an initial procedure before a leak detector is used for monitoring waste anesthetic gases. However, given our initial experience and the established relationship between measured and calculated gas concentrations in our circuit system, we are considering that our future revalidation of this particular halogen leak detector may be based on calculated ppm values only.

The guidelines from the National Institute of Occupational Safety and Health regarding OELs[4] were issued in 1977, when halothane was the newest gas anesthetic available and when gas anesthesia was thought to be linked to a much higher rate of infertility, miscarriage, and fetal birth defects in personnel exposed to WAG.[11] These apparent adverse clinical effects were observed despite the absence of such effects in preclinical studies with halothane. In addition, the guidelines have never been updated with the release of new agents, and no recommended OELs exist for the isoflurane, desflurane, and sevoflurane. The current halogenated gas anesthetics are considered to be safer than halothane and methoxyflurane,[6] and an OEL of 2 ppm for these newer agents can therefore be argued to be too low and unsupported by experimental data or reports in the literature. Other new and revised OEL guidelines are in effect in other countries, often with differentiation between the more toxic (older) and less toxic (newer) halogenated agents. However, recommended WAG concentration limits below 2 ppm may

reflect what is technically achievable in a human healthcare situation, with routine use of best practice and best equipment, rather than what is indicated or warranted by experimental data.[1] Open delivery systems with relatively high flow rates and variable methodologies and routines of gas scavenging represent a technical challenge that may result in considerably higher emission of WAG during gas anesthesia of laboratory animals.[9,10] This increased emission will particularly be the case when batch-type repeated procedures are performed at high throughput rates and when gas anesthesia is used for induction (for example, induction chamber without adequate scavenging ability). Although WAG concentrations considerably exceeding 2 ppm therefore are more likely and common during laboratory animal anesthesia, many current routines and equipment can be improved[10] with respect to reduced WAG emission.

The minimal detection limit of the tested refrigerant leak detector for halothane, isoflurane, sevoflurane, and desflurane ranged from 0.8 to 2.1 ppm. Although the detection limit for spot monitoring of halothane by using the detector exceeds the time-weighted average exposure recommendations, we consider this drawback of little practical importance, given that halothane has been replaced by other agents with more favorable efficacy and is currently little or no longer used. The detection limits for each gas determined in this study were based on spot monitoring only and will not provide information about compliance with the time-weighted average exposure recommendations for halogenated anesthetic gases. However, because the detection limit for spot monitoring with the tested detector is below recommended OELs,[4] spot monitoring can provide valuable information for an educated and real-time prediction about compliance with time-weighted recommendations. If repeated spot monitoring indicates WAG levels below the detection limit, the procedures and equipment for delivery and scavenging of gas anesthesia are likely to result in time-weighted WAG levels that are in compliance with the recommendations regarding time-weighted exposure limits. This assumption will be strengthened if a thorough leak detection survey of the anesthesia equipment and delivery system fails to identify a source of leakage. If repeated testing results in positive responses during spot monitoring of the laboratory environment, a thorough leak detection survey of the procedures and equipment is warranted. If the leak is not found, or is found and not corrected, and spot monitoring of the environment remains positive, WAG monitoring by regular time-weighted analytical methods is indicated to define whether the time-weighted WAG levels exceed current guidelines.

Current techniques (for example, IR analysis) of time-weighted workplace exposure testing remain the methods of choice for regular testing of compliance with current regulations and recommendations. However, between such time-weighted testing sessions, real-time identification of sources of leakage from anesthetic equipment and procedures, as well as spot monitoring of environmental WAG levels, can be provided effectively by using a relatively inexpensive halogen leak detector. Although the leak detector provides only an audible signal and no numerical output, its minimal detection limits of just below 2 ppm for currently used halogen gas anesthetics make the leak detector very sensitive for monitoring sources of WAG. We suggest that, in addition to standard checkout procedures for anesthetic machines,[11] initial use of the halogen leak detector for leak testing of the entire anesthesia setup will provide additional projections about the anticipated WAG load.

In addition, the minimal detection limit of less than 2 ppm is relevant to the time-weighted exposure recommendations. Provided that the implications of real-time versus time-weighted results are considered appropriately, repeated spot monitoring of the laboratory environment can carry considerable predictive value on compliance with the time-weighted exposure recommendations. With the leak detector, users of halogenated gas anesthetics can test anesthetic equipment and its interface with the animal or patient as often as desired and whenever the equipment has been reassembled or is used in a new setting. In addition, existing and new equipment or procedures can be evaluated to provide evidence of and impetus for improvement in reducing WAG emissions. When leak detection is combined with spot monitoring of environmental WAG levels, a halogen leak detector provides a valuable and simple adjunct method of ensuring compliance with current regulations and recommendations regarding exposure to halogenated anesthetic agents.

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