X. APPENDIX II

SAMPLING PROCEDURES FOR COLLECTION OF ANESTHETIC GASES

An evaluation of several available sampling and analysis methods was made by Whitcher et al [159] under NIOSH contracts HSM 99-73-73 and CDC 210-25-0007. All the methods tested were shown to be feasible. Table XII-6 presents some of the sampling and analytical equipment available for air monitoring programs.

General Requirements

(a) Air samples representative of the breathing zones of the most heavily exposed workers (anesthetist, oral surgeon) must be collected to characterize the exposure from each job or specific operation in each work area.

(b) Samples collected must be representative of exposure of individual workers.

(c) Suggested records:

(1) The date and time of sample collection.

(2) Sampling duration.

(3) Total sample volume.

(4) Location of sampling.

(5) Temperature, pressure, and relative humidity at time of sampling.

(6) Other pertinent information.

Sampling

(a) Samples should be collected as near as practicable to the breathing zone of workers without interfering with freedom of movement.

(b) Samples should be collected to permit determination of TWA workday exposures for every job involving exposure to anesthetic gases in sufficient numbers to express the variability of the exposures in the work situation.

Charcoal Tube Sampling

Charcoal tube sampling is possible for many of the volatile agents (halothane, trichloroethylene, methoxyflurane, etc). A general procedure is presented.

(a) Apparatus

(1) Pump, battery-operated, complete with clip for attachment to the worker. Airflow through the pump shall be within 5% of the desired rate.

(2) Charcoal tubes: Glass tube with both ends flame-sealed, 7-cm long, 6-mm O.D. and 4-mm I.D., containing two sections of 20/40 mesh activated coconut shell charcoal separated by a 2-mm portion of urethane foam. The first is the adsorbing section and contains 100 mg of charcoal from coconut shells. The second, or reserve section, contains 50 mg. A 3-mm portion of urethane foam is placed between the outlet of the tube and the reserve section. A plug of glass wool is placed in front of the adsorbing section. The pressure drop across the tube when in use must be less than 1 inch of mercury at a flowrate of 1 liter/minute.

(b) Calibration of Sampling Instruments

(1) Air sampling instruments should be calibrated with a representative charcoal tube in line, over a normal range of flowrates (25-1,000 ml/minute). Calibration curves must be established for each sampling pump and should be used in adjusting the pump prior to and during each field use. New calibration curves should be established for each sampling pump after making any repairs or modifications to the sampling system.

(2) The flowrate through the sampling system should be spot checked and the proper adjustments made before and during each study to ensure obtaining accurate airflow data.

(c) Collection and Handling of Samples

(1) Immediately before sampling, break both ends of the tube to provide openings at least one-half the I.D. of the tube (2 mm).

(2) The smaller section of charcoal is used as a reserve and should be positioned nearest the sampling pump.

(3) The charcoal tube should be placed in a vertical position during sampling.

(4) Tubing may be used to connect the back of the tube to the pump, but air being sampled should not be passed through any hose or tubing before entering the charcoal tube.

(5) The sample can be taken at flowrates of 25-1,000 ml/minute, depending on the pump. Total sample volumes of 1-12 liters are recommended, eg, a sample could be collected at 200 ml/minute for 15 minutes to give a total sample of 3 liters, or at 25 ml/minute for 8 hours to give a total sample volume of 12 liters. However, it is also recommended that each sample be collected in 4 hours or less.

(6) Samples should be collected over 15-minute periods at times when the highest exposure is expected. The TWA determination can be made from collecting a series of 15-minute samples.

(7) The charcoal tubes should be capped with inert plastic caps immediately after sampling. Under no circumstances should rubber caps be used.

(8) One charcoal tube, serving as an analytical blank, should be handled in the same manner as the sample tube (break, seal, and transport) except that no air is sampled through this tube.

Bag Sampling

Using sample bags or evacuated containers is a second method for collecting air samples to be analyzed for anesthetic gas content. Infrared or gas chromatographic methods of analysis may be used for samples collected in this manner.

(a) Apparatus

(1) A peristaltic sampling pump, diaphragm pump, or vacuum pump with filtered outlet to remove oil should be used.

(2) Sampling bags of Tedlar, Mylar, or Saran, or evacuated containers may be used.

(b) Collection of Samples

The sampling containers should be flushed or evacuated before use. Obtain samples by filling the sampling containers with air either by using a sampling pump to fill a bag or by opening the valve on an evacuated container and allowing it to reach atmospheric pressure. After the sample has been taken, all parts should be sealed to minimize leakage in or out of

the containers. Care must be taken not to alter or damage the existing sample while transporting it to the laboratory.

Syringe Sampling

A clean, gastight, grease-free syringe should be filled in a representative exposure area. The syringe must be capped and the sample analyzed by a satisfactory method. Disadvantages of this sampling technique include failure to give a representative exposure level from a single sample and vulnerability to hot spots usually occurring during normal anesthetic procedures. Multiple samples over a period of time will be necessary to obtain a representative exposure level.

XI. APPENDIX III

ANALYTICAL PROCEDURE FOR DETERMINATION OF HALOTHANE BY GAS CHROMATOGRAPHY

The analytical procedure presented in this appendix is adaptable to a number of anesthetic agents including trichloroethylene, fluroxene, methoxyflurane, enflurane, and nitrous oxide. Only modification of the chromatographic operating conditions should be necessary. Halothane, because of its predominant use, is used here as an example compound.

Principle of the Method

(a) A known volume of air is drawn through a charcoal tube to trap the halothane vapor.

(b) The halothane is desorbed from the charcoal with carbon disulfide.

(c) An aliquot of the desorbed sample is injected into a gas chromatograph.

(d) The area of the resulting peak is determined and compared with areas obtained from the injection of standards.

Range and Sensitivity

(a) The lower limit for detection of halothane on a gas chromatograph with a flame ionization detector is 1μg/sample.

(b) The upper limit value for halothane is 4.0 mg/sample. This is the estimated amount of halothane which the front section will hold before this compound breaks through to the reserve section of charcoal. If a

particular atmosphere is suspected of containing a high concentration of halothane, it is recommended that a smaller volume of air be sampled.

Interferences

(a) Halothane cannot be trapped when the amount of water in the air is so great that condensation occurs in the charcoal sampling tube.

(b) Any compound which has the same retention time as halothane with the chromatographic conditions described in this method could interfere. These can be eliminated by altering operating conditions of the gas chromatograph using a different column packing or using a selective detector, ie, electron capture.

Advantages of the Method

(a) This method provides one basic method for determining many different organic compounds.

(b) The sampling device is small, portable, and involves no liquids.

(c) The analysis of the tubes can be accomplished rapidly.

Disadvantages of the Method

(a) The amount of sample which can be taken is limited by the weight of halothane which the tube will hold before overloading.

(b) When the sample value obtained for the reserve section of charcoal exceeds 25% of that found on the front section, the possibility of appreciable sample loss exists.

(c) Other organic compounds in high concentrations may displace halothane from the charcoal.

Apparatus

(a) Gas chromatograph equipped with a flame ionization detector.

(b) Stainless steel column (6 m x 3 mm) with 10% free fatty acid polymer (FFAP) stationary phase on 80/100 mesh Chromosorb W (or equivalent), acid-washed and treated with dimethyldichlorosilane.

(c) A recorder and some method for determining peak area.

(d) Glass-stoppered microtubes of 2.5-ml capacity or 2-ml vials that can be sealed with inert caps.

(e) Microsyringe of 10-μl capacity, and convenient sizes for making standards.

(f) Pipets 0.5-ml delivery pipets or 1.0-ml pipets graduated in 0.1-ml increments.

(g) Volumetric flasks of 10-ml capacity or convenient sizes for making standard solutions.

Reagents

(a) Spectroquality carbon disulfide.

(b) Halothane, preferably chromatoquality grade.

(c) Bureau of Mines Grade A helium.

(d) Prepurified hydrogen.

(e) Filtered compressed air.

Analysis of Samples

(a) All equipment used in the analysis should be washed in detergent followed by appropriate tap and distilled water rinses.

(b) Preparation: Each charcoal tube is scored with a file in front of the first section of charcoal and broken open. The glass wool is removed and discarded. The charcoal in the first (larger) section is transferred to a small stoppered test tube. The separating foam is removed and discarded; the second section is transferred to another similar tube or vial. These two sections are analyzed separately. Prior to analysis, 0.5 ml of carbon disulfide is pipetted into each test tube to desorb halothane from the charcoal. Do not pipette by mouth.

EXTREME CAUTION MUST BE EXERCISED AT ALL TIMES WHEN USING CARBON DISULFIDE BECAUSE OF ITS HIGH TOXICITY AND FIRE AND EXPLOSION HAZARDS. IT CAN BE IGNITED BY HOT STEAM PIPES. ALL WORK WITH CARBON DISULFIDE MUST BE PERFORMED UNDER AN EXHAUST HOOD.

(c) Typical chromatographic operating conditions:

(1) 40 ml/minute (70 psig) helium carrier gas flow.

(2) 65 ml/minute (24 psig) hydrogen gas flow to detector.

(3) 500 ml/minute (50 psig) airflow to detector.

(4) 200 C injector temperature.

(5) 200 C manifold temperature (detector).

(6) 60 C isothermal oven or column temperature.

(d) Injection: The first step in the analysis is the injection of the sample into the gas chromatograph. To eliminate difficulties arising from blowback or distillation within the syringe needle, the solvent flush injection technique is employed. The 10-μl syringe is first flushed with carbon disulfide several times to wet the barrel and plunger. Three microliters of carbon disulfide are drawn into the syringe to increase the accuracy and reproducibility of the injected sample volume. The needle is removed from the carbon disulfide solvent, and the plunger is pulled back about 0.2 μl to separate the solvent flush from the sample, with a pocket of air to be used as a marker. The needle is then immersed in the sample, and a 5-μl aliquot is withdrawn, taking into consideration the volume of the needle, since the sample in the needle will be completely injected. After the needle is removed from the sample and prior to injection, the plunger is pulled back a short distance to minimize evaporation of the sample from the tip of the needle. Duplicate injections of each sample and standard should be made. No more than a 3% difference in area is to be expected.

(e) Measurement of area: The area of the sample peak is determined and preliminary sample results are read from a standard curve prepared as discussed below.

Determination of Desorption Efficiency

It is necessary to determine the percentage of halothane on the charcoal that is removed in the desorption process. This desorption efficiency is determined once for a given compound provided the same batch of charcoal is always used.

Activated charcoal, equivalent to the amount in the first section of the sampling tube (100 mg), is measured into a 2-inch long tube, with an inside diameter of 4 mm, flame-sealed at one end. This charcoal must be from the same batch used in obtaining the samples and can be obtained from unused charcoal tubes. The open end is capped with inert plastic. A known amount of the compound is injected directly into the activated charcoal with a microliter syringe, and the tube is capped with inert plastic.

A minimum of six tubes are prepared in this manner and allowed to stand at least overnight to ensure complete adsorption of halothane onto the charcoal. These six tubes will be referred to as the "desorption samples." A parallel blank tube should be treated in the same manner except that no halothane is added to it. The desorption samples and blanks are desorbed and analyzed in exactly the same manner as previously described.

Two or three desorption standards are prepared for analysis by injecting the same volume of halothane into 0.5 ml of carbon disulfide with the same syringe used in the preparation of the desorption samples. These are analyzed with the desorption samples.

The desorption efficiency equals the difference between the average peak area of the desorption samples and the peak area of the blank divided by the average peak area of the desorption standards, or

$$\text{desorption efficiency} = \frac{\text{area of sample} - \text{area of blank}}{\text{area of standard}}$$

Calibration and Standards

It is convenient to prepare standards in terms of mg halothane/0.5 ml of carbon disulfide because samples are desorbed in this amount of carbon disulfide. To minimize error due to the volatility of carbon disulfide, 20 times the weight can be injected into 10 ml of carbon disulfide. For example, to prepare a 0.3 mg/0.5 ml standard, 6.0 mg of halothane is injected into exactly 10 ml of carbon disulfide in a glass-stoppered flask. The density of halothane (1.86 g/ml) is used to convert 6.0 mg into microliters for easy measurement with a microliter syringe. A series of standards is prepared, varying in concentration over the range of interest and analyzed under the same gas chromatographic conditions and during the same time period as the unknown samples. Curves are established by plotting concentration versus average peak area.

Calculations

(a) The weight in mg corresponding to the peak area is read from the standard curve. No volume corrections are needed, because the standard curve is based on mg halothane/0.5 ml carbon disulfide, and the volume of sample injected is identical to the volume of the standards injected.

(b) Separately determine the weights of halothane on the front and reserve sections of the charcoal tube.

(c) Corrections must be made to the halothane weights determined on both the front and reserve sections for the weights of the respective sections of the blank charcoal tube.

(1) Subtract the weight of halothane found on the front section of the blank charcoal tube from the weight of halothane found on

the front section of the sample charcoal tube to give a corrected front section weight.

(2) Subtract the weight of halothane found on the reserve section of the blank charcoal tube from the weight of halothane found on the reserve section of the sample charcoal tube to give a corrected reserve section weight.

(3) Add the corrected amounts of halothane present on the front and reserve sections of the sample tube to determine the total measured halothane in the sample.

(4) Divide this total weight by the determined desorption efficiency to obtain M, the total mg/sample.

(d) Convert the liters of air sampled (V) to volume (V') at standard conditions of 25 C and 760 mmHg, as follows:

$$V' = \frac{298VP}{760(T+273)} = \frac{0.392VP}{(T+273)}$$

where:

V' = volume of sampled air in liters at 25 C and 760 mmHg

V = measured volume of sampled air in liters

P = barometric pressure in mmHg, measured at time of sampling

T = temperature of air in degrees celsius, measured at time of sampling

(e) The concentration of halothane in the sampled air can be expressed in various ways using M, the weight of halothane obtained in (c)(4), and V', the standardized sample volume, obtained in (d), as follows:

(1) mg/liter = M/V'

(2) mg/cu m = g/liter = 1,000 M/V'

(3) ppm = 124.1 M/V'

XII. APPENDIX IV

ANALYTICAL PROCEDURE FOR DETERMINATION OF ANESTHETIC GASES BY INFRARED SPECTROPHOTOMETRY

Principle of the Method

Air is passed directly through portable infrared (IR) instruments, through tubing to remote IR instruments, or air samples are collected in plastic bags, evacuated containers, or syringes and analyzed by IR. Analysis by IR is dependent on the total number of anesthetic agent molecules introduced into the sample cell.

Range and Sensitivity

(a) The lower limit for detection of gases by IR depends on the path length and volume of the gas cell.

(b) Portable IR units should have a minimum working range of 1 to at least 100 ppm for nitrous oxide and 0.05-2 ppm for halothane. Instruments with this capability are available.

Interferences

Many compounds present in operating rooms and dental suites may interfere with IR analysis of anesthetic agents if present in significant concentrations. Some interfering compounds are formal in, isopropyl alcohol, ethyl alcohol, carbon dioxide, and water vapor.

Advantages of the Method

For continuous IR monitoring, the sampling and analysis is nearly a simultaneous operation. Exposed workers and those responsible for air monitoring are given an immediate indication of control system efficiency. When operating on battery power, a great advantage of a portable IR unit is the number of areas that can be sampled. One portable unit may be used to monitor operating areas, recovery rooms, storage and pipeline areas, and other exposure areas.

Disadvantages of the Method

A continuous sampling IR system currently costs approximately $2,500. Portable IR units are also expensive but may be more feasible because of their versatility.

Apparatus

(a) Various types of infrared spectrophotometers are available. A representative sample of suppliers is listed below. Completeness of the list cannot be guaranteed and inclusion in the list does not constitute official NIOSH endorsement.

Air Products and Chemicals, Inc., P.O. Box 538, Allentown, Pennsylvania 18105

Cavitron/DKC Corporation, 1528 West Embassy Street, Anaheim, California 92802

Ohio Medical Products, P.O. Box 1319, Madison, Wisconsin 53701

Wilks, P.O. Box 449, South Norwalk, Connecticut 06856

(b) For remote monitoring, a high volume vacuum pump with a capacity of 25-30 liters/minute and sample probe lines, such as polyethylene tubing. Sampling distances up to 200 feet may use 0.5-inch I.D. tubing; greater lengths should use 3/4-inch I.D. tubing to prevent pressure drop. Tubing should be unreactive to groups of chemicals usually found where anesthetic agents are used, eg, alcohols, cleaning agents, etc.

(c) Manometer and vacuum pump (capable of reducing pressure to 1 mmHg).

(d) Gastight syringes (100μl, 500μl, 1,000μl).

(e) Gas tank regulators, connections, and needle valves for introducing dilution gas, anesthetic gas, and samples.

Reagents

(a) Spectroquality nitrous oxide, halothane, or any other frequently used inhalation anesthetic.

(b) Pure air, nitrogen, argon, oxygen, etc, to zero the instrument and prepare calibration samples.

Analysis of Samples

(a) The gas cell is connected to a manometer via a "T" connection and evacuated to approximately 1 mmHg.

(b) The sample is introduced into the cell. If a rigid sample container is used, the equilibrium pressure (Pe) must be noted and the cell filled to atmospheric pressure with the zero gas. A 15-minute waiting

period before analysis is necessary to establish equilibrium.

(c) The spectrum is scanned from 4-10 μ and the absorbance at 4.48 μ is used to determine nitrous oxide content. The absorbance at 8.8 μ is used to determine halothane or other halogenated anesthetic agent content of the samples. Absorbance is measured by the baseline technique.

Calibration and Standards

(a) The volume of the gas cell is determined by standard techniques. The simplest procedure is to evacuate the cell and then bring it to atmospheric pressure by permitting air to enter via a wet-test meter. The volume of the cell is the volume of air shown on the meter. After the volume has been determined, the cell is evacuated and known volumes of gaseous agents (eg, nitrous oxide) or samples of a known volatile agent in a zero-gas mixture (eg, halothane-nitrogen) are added using gastight syringes. Standard samples may be introduced through a rubber serum cap attached to the inlet of the cell, or through the rubber tubing which connects the gas cell with the tank of dilution gas. An alternative is to use a set of serial dilutions that span the concentrations of interest. The pressure in the cell is brought to atmospheric pressure with zero gas and the appropriate absorbance is measured.

(b) The anesthetic agent concentration is calculated from the quantity of agent added and the volume of the cell. For example, 1.0 ml nitrous oxide in a 2.5-liter cell gives a concentration of 400 ppm. With a volatile agent, such as halothane, 1.0 ml of a gas mixture known to contain 500 ppm or 0.5 μl halothane vapor, when introduced into a 2.5-liter cell, results in a cell concentration of 0.2 ppm halothane. A calibration curve

relating absorbance to concentration is prepared from a series of known volumes of an anesthetic agent introduced into the IR cell.

Calculations

(a) The concentration of the unknown is read from the calibration curve. To calculate the standard curve concentrations in parts per million (ppm), the following equation may be used:

$$\text{Sample concentration (ppm)} = \frac{V'}{V}$$

where:

V' = Volume of anesthetic gas added (μl)

V = Volume of IR cell (liter)

(b) The observed concentration from the calibration curve is corrected for the volume of the sample actually introduced into the cell. For samples introduced into the cell with syringes, the volume is readily known and the correction applied using the following equation:

$$\text{(ppm)} = C \times \frac{V}{V'}$$

where:

C = Observed concentration from the calibration curve

V = Volume of IR cell (liters)

V' = Volume of sample cell (liters)

For samples introduced from nonrigid bags with volumes greater that the IR cell, V' = V and the sample concentration = C.

(c) For samples introduced by pressure measurements, the sample concentration is calculated as follows:

$$\text{Sample concentration (ppm)} = C \times \frac{Pa}{Pa-Pe}$$

where:

C = Observed concentration from the calibration curve (ppm)

Pe = Equilibrium pressure after connecting the sample container to the IR cell

Pa = Atmospheric pressure