U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CINCINNATI, OHIO 45226

HEALTH HAZARD EVALUATION DETERMINATION
REPORT HE 78-62-526

LITTLETON VETERINARY CLINIC
LITTLETON, COLORADO

SEPTEMBER 1978

I. TOXICITY DETERMINATION

A Health Hazard Evaluation was conducted by the National Institute for Occupational Safety and Health (NIOSH) in the Littleton Veterinary Clinic, Littleton, Colorado. On May 25, 1978, environmental samples were collected to determine airborne concentrations of waste anesthetic gases.

Samples taken during a surgical procedure lasting approximately 1½ hours indicated exposures to halothane for that time period ranging from 4.3 to 20.5 ppm. While only one exposure would have been above 2 ppm if calculated on an 8 hour time weighted average basis, it is recommended that the concentration of halothane be reduced to a level below 2 ppm over the period of use.

The basis for this recommendation is that sufficient information is not available to state a safe level of exposure, but this level is attainable and should prevent the effects caused by acute exposure and significantly reduce the risk associated with long-term, low-level exposure.

II. DISTRIBUTION AND AVAILABILITY OF DETERMINATION REPORT

Copies of this Determination Report are currently available upon request from NIOSH, Division of Technical Services, Information Resources and Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days the report will be available through the National Technical Information Service (NTIS), Springfield, Virginia. Information regarding its availability through NTIS can be obtained from NIOSH, Publications Office at the Cincinnati address.

Copies of this report have been sent to:

a. Littleton Veterinary Clinic
b. U.S. Department of Labor, Region VIII
c. NIOSH, Region VIII

For the purpose of informing the approximately five "affected employees", the employer shall promptly "post" for a period of 30 calendar days the Determination Report in a prominent place near where exposed employees work.

III. INTRODUCTION

Section 20 (a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669 (a)(6) authorizes the Secretary of Health, Education, and Welfare following a written request by an employer or authorized representative of employees to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The National Institute for Occupational Safety and Health received such a request from the management of Littleton Veterinary Clinic.

There were no specific alleged health problems at the time the request was generated. The recognition of the potential health hazard associated with chronic exposure to anesthetic gases was primarily responsible for the health hazard evaluation request.

IV. HEALTH HAZARD EVALUATION

A. Process Description

The areas of Littleton Veterinary Clinic of interest to this study are those areas involved in surgical procedures on animals, primarily horses. These areas include the operating room and adjacent areas such as preparation and recovery rooms. The inhalation anesthetic used is halothane (2-bromo-2-chloro-1,1,1-trifluoroethane).

The animal is prepared for surgery by injection of an intravenous anesthetic. An endotracheal tube is inserted (during this study a Cole tube was used), the animal is moved into the operating room, and anesthesia by inhalation is began. Following the operation the animal is moved to a recovery room where the effects of the anesthesia are allowed to wear off.

The inhalation anesthesia machine vaporizes the halothane and combines it with oxygen, which is piped from cylinders outside the operating room. In addition to the vaporizer, the anesthesia machine also includes a soda lime canister (to absorb exhaled carbon dioxide), a breathing bag,

valves for assuring unidirectional gas flow, flexible hoses, and a "Y" piece terminating in an endotracheal tube. The breathing bag can be replaced by a ventilator to aid respiration.

The anesthetic gas mixture is delivered at a rate higher than the animal's metabolic needs. When a breathing bag is used, excess gases are vented out of the breathing system through the pop-off valve. The volume of gases and vapors escaping through the pop-off valve are highly variable since it depends on the animal's breathing pattern and metabolic rate. When a ventilator is in use the pop-off valve on the anesthetic machine is closed and the ventilator assumes the function of the pop-off valve. As the system is now designed, the pop-off valve and the ventilator are the major sources of waste anesthetic gas. Local exhaust ventilation was available and in use to remove waste anesthetic gas from around the pop-off valve, but not from the ventilator.

Five people are generally involved in surgery: one anesthetist, two technicians, and two veterinary surgeons. Since the surgical area is remote from any other areas of the building such as offices or reception area where other employees are located, no other exposures were expected.

B. Evaluation Design

A preliminary observational study was conducted on May 24, 1978, and preparations were made to measure environmental levels of waste anesthetic gas. On May 25, breathing zone and general area air samples for halothane were collected on charcoal tubes, and direct analysis of air at various points was made by infrared spectrometry in an attempt to locate sources of contamination.

The breathing zone samples were obtained by attaching battery powered personal sampling pumps to belts worn by the operating room personnel. These pumps were attached by plastic tubing to small glass tubes containing activated charcoal which were placed in the breathing zone of the wearer. Air was drawn through the charcoal at a rate of 200 cc/minute for the duration of the approximately 1½ hour procedure. The charcoal adsorbed the halothane from the air as it passed through the tube. These samples were subsequently analyzed in the laboratory by gas chromatography.

General area samples were obtained using the charcoal tube method. These samples were located on a stand approximately at breathing zone level between the anesthetist and a surgeon.

Direct analysis of air during the procedure was accomplished by drawing air through flexible inert plastic tubing into a portable infrared spectrometer. The air pump, analyzer and stripchart recorder were placed on a wheeled cart and could be moved around the operating room.

The flexible tubing could then be held at any desired point. By placing the tubing near a seal or fitting, and measuring the halothane concentrations at that location, it was possible to locate leaks in the system. The measurements were made at an analytical wavelength of 8.7 microns (1150 cm^{-1}) and a pathlength of 14.75 meters. The instrument response time was approximately 15 to 30 seconds. The lower limit of detection in this mode of operation was 0.5 parts per million (ppm). The instrument was calibrated immediately prior to use and the calibration was checked immediately after use.

C. Evaluation Criteria

In the Criteria for a Recommended Standard for Occupational Exposure to Waste Anesthetic Gases and Vapors (1), NIOSH states: "Current scientific evidence obtained from human and animal studies suggests that chronic exposure to anesthetic gases increases the risk of both spontaneous abortion among female workers and congenital abnormalities in the offspring of female workers and the wives of male workers. Risks of hepatic and renal diseases are also increased among exposed personnel. In addition, physiological function may be impaired. A few studies have suggested increased risk of cancer. Effects on the central nervous system due to acute exposures of anesthetic gases have been associated with headaches, nausea, fatigue, irritability, etc." Control procedures and work practices presented in that document, however, should prevent the effects caused by acute exposure and significantly reduce the risk associated with long term, low level exposure.

That same NIOSH publication recommends a maximum exposure of 2 ppm halogenated anesthetic. This recommendation is based primarily on available technology in reducing waste anesthetic gas levels.

Reports by Vaisman (2), and Askrog and Harvald (3) were among the first to identify an increased incidence of spontaneous abortion in women exposed to anesthetic gases and in wives of men exposed to anesthetic gases. Results of a more recent and comprehensive nationwide survey of occupational disease among operating personnel were published in 1974 by American Society of Anesthesiologists (ASA) (4). The results of this study indicate "that female members of the operating room-exposed group were subject to increased risks of spontaneous abortion, congenital abnormalities in their children, cancer and hepatic and renal disease. This increased risk of congenital abnormalities was also present among the unexposed wives of male operating room personnel. No increase in cancer was found among the exposed males, but an increased incidence of hepatic disease similar to that in the female was found.

While several investigators have reported increased rates of resorption of fetuses in animals, particularly rats, most of these studies involved concentrations of anesthetic gases well above the levels found in occupational exposure. One investigator (5), however, showed increased

fetal death rates in two groups of rats following exposure of 1,000 and 100 ppm of nitrous oxide. Doenicke et al (6) concluded from their study of anesthetized pregnant rats that halothane demonstrates an abortive effect directly proportional to the concentration inhaled, again referring to anesthetic concentrations, but nitrous oxide does not produce an abortive effect. Bruce (7) reports no significant difference, including implantations and resorptions per pregnancy, in his exposure of rats to 16 ppm halothane.

Several epidemiological studies that indicate increased spontaneous abortions also indicate an increased rate of congenital abnormalities. The ASA study (4) as well as surveys by Knill-Jones et al (8) and Corbett et al (9) indicated an increased rate of congenital abnormalities in children of women with occupational exposures to anesthetic gases, and to wives of men with similar exposures. These studies also indicated an increase in liver and kidney abnormalities. This increase, however, was less pronounced in both rate and severity.

In a study published by NIOSH, (10) "nitrous oxide and halothane in respective concentrations as low as 50 parts per million (ppm) and 1.0 ppm, caused measurable decrements in performance on some psychological tests taken by healthy male graduate students. Nitrous oxide alone caused similar effects. The functions apparently most sensitive to these low concentrations of anesthetics were visual perception, immediate memory, and a combination of perception, cognition and motor responses required in a task of divided attention to simultaneous visual and auditory stimuli". Headache, fatigue, irritability, and disturbance of sleep have also been reported (2,11); and damage to cerebral cortical neurons has been seen in rats after subanesthetic exposure to halothane (12). Quimby et al (13) reported permanent learning deficits in rats exposed to anesthetic concentrations of halothane during early development (from conception).

Mortality and epidemiological studies have raised the questions of possible carcinogenicity of anesthetic gases, but sufficient data are lacking to list nitrous oxide or halothane as suspected carcinogens.

Literature reviews regarding halothane (14,15,16,17) indicate the most widely accepted mechanism of bio-transformation is the production of trifluoroacetic acid with resulting urinary excretion of trifluoroacetic acid and bromide.

A recently completed two year study (18) exposing rats to either (A) 50 ppm N_2O and 1 ppm halothane or (B) 500 ppm N_2O and 10 ppm halothane, reported chromatid and chromosomal changes in bone marrow cells, toxic effects on reproduction, and spermatogonial cell aberrations in one or both groups.

Very little work has been done on the effects of the halogenated agents alone, since in most cases they are used in combination with nitrous oxide. However, the halogenated agent is thought to be the primary cause of health effects, especially renal and hepatic diseases, since a large number of halogenated hydrocarbons have been shown to produce such effects. Also, the biodegradation products of these potent anesthetics would similarly associate them with such toxic effects.

Technology is currently available to reduce halogenated anesthetic levels to 2 ppm during the time of use and by doing so there is little likelihood of any toxic effect being seen in this situation.

D. Evaluation Results

Table I shows the results of six environmental samples collected with solid sorbent (charcoal) tubes. All samples were taken for the duration of the approximately 1½ hour operation.

Table II lists measurements made by infrared spectrometry at various locations during the operation. Unlike the solid sorbent measurements listed in Table I, these samples were of short duration (on the order of a minute) and serve to indicate sources of atmospheric contamination and trends during the procedure. The samples are listed sequentially, with the first ten being taken before the ventilator was put into operation, and the last six taken during or after the addition of the ventilator. It would appear from these results that the greatest exposure is caused by the ventilator.

E. Summary and Conclusions

Findings of this evaluation indicate that all persons sampled were exposed to concentrations of halothane slightly in excess of the recommended standard during the surgical procedure, although only the anesthetist had an exposure high enough to exceed that limit on an 8 hour time weighted average basis. However, it is recommended that measures be taken to reduce exposures of all personnel to below 2 ppm during surgical procedures. This recommendation is more stringent than just reducing exposures to below 2 ppm for an 8 hour average, but it will provide greater assurance that no toxic effects are experienced.

V. RECOMMENDATIONS

Since the sampling data indicates that the greatest source of waste anesthetic gas is the ventilator, it is recommended that a scavenging system be installed for this device. This could be either a separate exhaust similar to that already servicing the anesthesia machine, or possibly an alteration to that existing exhaust system to enable it to service both devices.

There were also indications (see Table II) of waste anesthetic gas leaking from various fittings in the system, especially at the connection of the ventilator to the anesthesia machine. Exposures can be reduced by making sure such fittings seal properly. Tightening the fitting at the bottom of the CO_2 absorber during the procedure resulted in a reduction in leakage at that point of greater than 90 percent.

Anesthesia equipment should be checked and maintained on a regular basis. Tubing, breathing bags and endotrachial tubes should be visually checked for cracks and other leak sources. The assembled system can be tested using the procedure presented in Appendix I of the NIOSH Criteria Document on Waste Anesthetic Gases (1):

(a) Assemble the anesthesia machine as in the usual manner for clinical anesthesia with breathing tubes, Y-piece, breathing bag, and high-pressure hoses or cylinders connected.

(b) Occlude the Y-piece securely with the thumb or palm of hand.

(c) Pressurize the breathing system to 30 cm water, observed on the absorber pressure gauge. This may be accomplished by using the oxygen flush valve.

(d) Add a sufficient flow of oxygen through the low-range flowmeter to maintain a constant pressure of 30 cm water in the breathing system. The oxygen flow required to maintain the pressure is a measure of the leak rate. This test may be abbreviated by using an oxygen flowrate of 100 ml/minute. If pressure in the system increases, the breathing system is below the maximum allowed leak rate.

(e) Determine the presence of check valves downstream from the flowmeters by consulting the manufacturer or a serviceman. These valves must be tested differently. With oxygen flowing as indicated in (d), briefly turn off in turn each flowmeter which is equipped with a check valve until there is a rise in pressure on the absorber gauge. An increase in pressure indicates absence of leakage in the circuit tested. The low pressure leak rate should be below 100 ml per minute.

Small components such as breathing bags and hoses can be leak tested separately by pressurization, immersion in water and observation of any bubbles. In situations where this is not practical, it is recommended that fittings and seals be checked periodically to make sure gaskets and o-rings are in place properly, that connections are tight and not worn, and that moisture or chemical action has not caused corrosion or degradation of materials. Typical places to check, and where leaks have been found in other studies, include the seals at the domed unidirectional valves, seals at the top, bottom and center of the CO_2 absorber, and fittings where the breathing tubes connect to the machine and to the "Y" piece.

VI. REFERENCES

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VII. AUTHORSHIP AND ACKNOWLEDGEMENTS

Report Prepared By:

G.E. Burroughs
Industrial Hygienist
Industrial Hygiene Section
Hazard Evaluations & Technical
Assistance Branch
Cincinnati, Ohio

Originating Office:

Jerome P. Flesch
Acting Chief
Hazard Evaluations & Technical
Assistance Branch
Cincinnati, Ohio

Study Participants:

Darrel L. Ruby
Industrial Hygienist
Institute of Rural and Environmental
Health
Colorado State University
Fort Collins, Colorado

Report Typed By:

Carol Goetz
Clerk-Typist
Industrial Hygiene Section
Hazard Evaluations & Technical
Assistance Branch
Cincinnati, Ohio

Table I

Halothane Concentrations
Measured by Solid Sorbent Tubes

Littleton Veterinary Clinic

May 25, 1978

HE 78-62

Description*	PPM Halothane (Corrected to Standard Pressure)
Personal breathing zone sample on Vet. Surgeon "A"	6.3
Personal breathing zone sample on Vet. Surgeon "B"	4.3
Area sample approx. 5 ft. to left of anesthetist	9.4
Personal breathing zone sample on Vet. Assistant "A"	4.6
Personal breathing zone sample on Vet. Assistant "B"	Equipment failure
Personal breathing zone sample on Anesthetist	20.5
Recommended Standard	2.0

*All samples ran for the duration of the approximately 1 1/2 hour operation.

Table II

Halothane Concentrations
Measured by Infrared Spectrometry*

Littleton Veterinary Clinic

May 25, 1978

HE 78-62

Location	Concentration
Near animal's mouth	2 - 7 ppm
Hose connection to machine outlet	4 - 5 ppm
" " " inlet	7 - 9 ppm
Dome valve on machine outlet	6 - 8 ppm
" " " inlet	up to 42 ppm
Bottom of CO_2 absorber	>>50 ppm**
Same - after tightening bolts	5 - 7 ppm
top of CO_2 absorber	9 - 11 ppm
Near pop-off valve	1 - 5 ppm
Near breathing bag connection	1 - 3 ppm
Breathing zone of anesthetist during change from bag to ventilator	up to 50 ppm
Near connection of ventilator to anesthesia machine	>>50 ppm
At ventilator pressure relief valve	>>50 ppm
Near breathing zone of surgeon	7 - 8 ppm
Near animal's mouth (animal on ventilator)	13 - 21 ppm
In Recovery Room (two to five feet from animal's mouth)	1 - 4 ppm

*These samples are not time weighted average breathing zone concentrations and should not be compared with the recommended standard of 2 ppm.

**Maximum measurable concentration was 50 ppm. Locations showing ">> 50 ppm" possibly have concentrations of several hundred ppm.