HETA 86-328-1773
FEBRUARY 1987
MEMORIAL HOSPITAL OF SOUTHERN OKLAHOMA
ARDMORE, OKLAHOMA

NIOSH INVESTIGATOR:
Bobby J. Gunter, Ph.D., CIH

I. SUMMARY

In June l986 the National Institute for Occupational Safety and Health (NIOSH) received a request to evaluate exposures to nitrous oxide, ethrane, halothane, and isoflurane in the Department of Surgery at Memorial Hospital of Southern Oklahoma, Ardmore, Oklahoma. In October, 1986 breathing zone and general room air samples were collected on nurses in all operating rooms and in the recovery room for nitrous oxide, ethrane, halothane and isoflurane. Direct reading measurements were taken during surgical procedures in order to locate leaks in the anesthesiologists' equipment, leaks in the pop-off valve scavenging equipment and other sources of anesthetic waste gas contamination.

Two of 22 (or 9 percent) of the ethrane air samples exceeded the NIOSH evaluation criteria of 0.5 parts per million (ppm) for halogenated anesthetic agents used in combination with nitrous oxide. The NIOSH evaluation criteria for the halogenated agents is 2 ppm when used alone. One of 22 (or 5 percent) of the halothane air samples exceeded the NIOSH evaluation criteria of 0.5 ppm; halothane concentrations ranged from below the detection limits of 0.00l ppm to l.4 ppm. Of the 22 air samples analyzed for isoflurane none exceeded the NIOSH evaluation criteria of 0.5 ppm. Twenty-two breathing zone air samples were collected and analyzed for nitrous oxide. Twelve of the 22 nitrous oxide samples were below the detection limits of l ppm. Only l of the 22 nitrous oxide samples or 5 percent exceeded the NIOSH evaluation criteria of 25 ppm. There were no leaks in the equipment and in the pop-off valve. This was a new surgical department and each operating room had approximately 26 air changes per hour. Employees were informally interviewed at random and no medical problems that could be attributed to work were reported.

On the basis of the environmental data, it was concluded that a health hazard did not normally exist in the operating rooms at Memorial Hospital from exposures to ethrane, halothane, isoflurane, and nitrous oxide. Recommendations on work practices that will assist in maintaining low exposure levels are included in this report.

KEYWORDS: SIC: 8070 (Hospitals) surgery, ethrane, halothane, isoflurane, nitrous oxide

II. INTRODUCTION

NIOSH received a request from management in June l986 to evaluate the operating rooms for waste anesthetic gases at the Memorial Hospital of Southern Oklahoma, Ardmore, Oklahoma. An environmental evaluation was conducted on October 20, 2l, and 22, l986. The delay in conducting this evaluation was due to the surgery department moving into new quarters during July, August and September, l986. Results of the environmental investigation were discussed with management during the survey and by telephone when the air sampling results were received from the laboratory in December, l986.

III. BACKGROUND

Memorial Hospital of Southern Oklahoma located in Ardmore, Oklahoma has six surgery rooms and a recovery room. Four of the operating rooms were in use during this evaluation and were evaluated. The recovery room was also evaluated. Scrub and circulating room nurses as well as recovery room nurses were monitored for ethrane, halothane, isoflurane, and nitrous oxide. The scrub and circulating room nurses are in close proximity to the patients and the anesthetic administering equipment. Therefore, exposure data collected from these individuals should present accurate exposure levels for all those working in the surgical operating rooms. During this evaluation the anesthesiologists were using ethrane, halothane, and isoflurane with and without nitrous oxide.

IV. EVALUATION DESIGN AND METHODS

Environmental

Nitrous oxide breathing zone air samples were collected by using vacuum pumps and 20 to 40 liter metallic bags attached to the worker. The samples were analyzed immediately on the surgical floor using infrared spectrometry. Ethrane, halothane and isoflurane samples were collected on workers using organic vapor charcoal sampling tubes and vacuum pumps. These samples were analyzed according to NIOSH method l003. Most operating room personnel were interviewed.

V. EVALUATION CRITERIA

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV's), and 3) the U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH recommendations and ACGIH TLV's are lower than the corresponding

OSHA standards. Both NIOSH recommendations and ACGIH TLV's usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH-recommended exposure limits, by contrast, are based primarily on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet those levels specified by an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short-term exposures. Exposure limits used in this evaluation are:

			Recommended Exposure Limits Time-Weighted Average Exposure Basis (PPM)	
Nitrous Oxide			25.0 (NIOSH)	
Ethrane		A/2.0	0.5 (NIOSH)	75* ACGIH
Halothane		A/2.0	0.5 (NIOSH)	50* ACGIH
Isoflurane	A/2.0		0.5 (NIOSH)	

ppm - parts of vapor or air per million parts of contaminated air.
* - 1985 ACGIH TLV
A - when used without nitrous oxide

OSHA does not have standards for these compounds.

Toxicological

In the NIOSH criteria document for a recommended standard for occupational exposure to anesthetic gases, 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 to 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. A dose response relationship for halogenated anesthetic toxicity has not been defined. (Reference 2)

That same NIOSH publication recommends maximum exposures to 25 ppm nitrous oxide (eight-hour time-weighted average) and 2 ppm halogenated anesthetic when used alone, or 0.5 ppm when used with nitrous oxide. These recommendations are based upon available technology in reducing waste anesthetic gas levels.

Reports by Vaisman (Reference 3) and Askrong and Harvald (Reference 4) were among the first to identify 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 the American Society of Anesthesiologists (ASA). (Reference 1) The results of this study indicate "that female members of the operating room-exposed group were subject to

increase 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 in animals, particularly rats, most of these studies involved concentrations of anesthetic gases well above the levels found in occupational exposure. One investigator (Reference 5) showed increased fetal death rates in two groups of rats following exposures of 1,000 and 100 ppm of nitrous oxide. Doenicke, et. al., (Reference 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 (Reference 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 (Reference 1) (as well as surveys by Knilljones, et al., (Reference 8) and Corbett, et al. (Reference 9) indicated an increased rate of congenital abnormalities in children of women with occupational exposures to anesthetic levels. One study (Reference 10, 11, 12) indicated liver, kidney, and brain tissue changes in pups born to rats exposed to sub-anesthetic concentrations of halothane during pregnancy.

The same epidemiological and toxicological studies, (Reference 10, 11, 12) have indicated an increase in spontaneous abortions and congenital abnormalities. This increase, however, was less pronounced in both rate and severity.

In a study published by NIOSH (Reference 13), "nitrous oxide and halothane in respective concentrations as low as 50 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 (References 2, 14); and damage to cerebral cortical neurons has been seen in rats after sub-anesthetic exposure to halothane. (Reference 15) Quimby, et al., (Reference 16) 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, halothane, or ethrane as suspected carcinogens.

Literature reviews regarding halothane (References 17, 18, 10, 20) indicate the most widely accepted mechanism of bio-transformation is the production of trifluoroacetic acid and bromide. The literature regarding enflurane (References 21, 22) does not indicate any one accepted mechanism, but increased serum and urinary fluoride levels were found in patients receiving enflurane anesthesia. While epidemiological and toxicological studies have indicated several symptoms apparently related to sub-anesthetic exposure to anesthetic gases, no cause and effect relationship has yet been shown.

A mail survey of 30,650 dentists and 30,547 chairside assistants grouped according to occupational exposure to inhalation anesthetic/sedatives in the dental operatory indicated increased general health problems and reproductive difficulties among anesthetic-exposed respondents. For heavily anesthetic-exposed male dentists, the increase in liver disease was 1.9-fold, kidney disease 1.2-fold, and neurological disease

1.9-fold. For wives of heavily anesthetic-exposed male dentists the increase in spontaneous abortion rate was 1.5-fold. Among heavily anesthetic-exposed female chairside assistants, the increase in liver disease was 1.6-fold, kidney disease 1.7-fold and neurological disease 2.8-fold. The increase in spontaneous abortion rate among heavily exposed assistants was 2.3-fold. Cancer rates in women heavily exposed to inhalation anesthetics were increased 1.5-fold but this finding was only borderline significant (P = 0.06). Separate analysis of the data for disease rates and birth difficulties by type of inhalation anesthetic indicates that in both dentists and chairside assistants chronic exposure to nitrous oxide alone is associated with an increase rate of adverse response. (Reference 23) It would not be correct to directly extrapolate nitrous oxide epidemiological data taken on dentists and dental assistants to surgical operations. Dentists and their assistants are much closer to their work and are breathing higher concentrations than surgeons, scrub nurses, and anesthesiologists.

In November, 1986 NIOSH performed a computer search of the scientific literature on the anesthetic waste gases. Information received from this search did not add additional light on the toxicology of these agents.

VI. RESULTS

Two of 22 air samples (9 percent) taken for ethrane exceeded the NIOSH criteria of 0.5 ppm. One of 22 air samples (5 percent) taken for halothane exceeded the NIOSH criteria of 0.5 ppm. None of the 22 air samples collected for isoflurane exceeded the NIOSH criteria of 0.5 ppm. Only one of 22 air samples collected for nitrous oxide exceeded the evaluation criteria of 25 ppm. Leaks were not found in the anesthesia administering machine, the pop-off valve scavenging system, or any other area of the operating room. The operating rooms had approximately 26 air changes per hour. Operating room personnel were informally interviewed. Complaints were very few and none of the workers had medical problems they thought were associated with their work. All workers were interested in what they were exposed to and the chronic and acute effects of these exposures. An hour of inservice training was provided by NIOSH personnel discussing the toxicological aspects of waste anesthetic gas exposure. This presentation consisted of 35 mm slides of operating room ventilation.

VII. CONCLUSIONS

One overexposure to nitrous oxide, two overexposures to ethrane, and one overexposure to halothane were observed during this evaluation. There were a total of 66 analyses performed. It would be difficult to lower levels below those found during this evaluation. There were no leaks in either the anesthetic administering equipment or in any other segment of the operating room ventilation. The four elevated exposures can be attributed to items such as a improper fit on an intubation tube and face masks. These sources of leaks are going to occur and there is little that can be done about them under normal operating procedures except to use care in choosing these devices for proper fit to patients.

VIII. RECOMMENDATIONS

1. Continue the checks on all parts of the anesthetic gas administering system for wear and possible leakage.

2. Excerise care in choosing proper fitting face masks and intubation tubes for patients.

3. Air monitoring with the passive dosimetry should be continued.

IX. REFERENCES

1. Cohen, E.N., et al, ad Hoc Committee on the Effect of Trace Anesthetics on the Health of Operating Room Personnel: Occupational Disease Among Operating Room Personnel: A National Study. Anesthesiology 41:321-340, 1974.

2. Criteria for a Recommended Standard...Occupational Exposure to Waste Anesthetic Gases and Vapors. DHEW (NIOSH) Publication No. 77-140, 1977, 194 pp.

3. Vaisman, A.I. (Working conditions in surgery and their effect on the health of anesthesiologists). Eksp Khir Anest 3:44-49, 1967 (Rus.).

4. Adkrog, V., and Harvald, B. (Terateogenic effect of inhalation anesthetics). Nord Med 83:498-504, 1970.

5. Corbett, T.H., Cornell, R.G., Endres, J.L., and Millard, R.I. Effects of Low Concentrations of Nitrous Oxide on Rat Pregnancy. Anesthesiology 39:299-301, 1973.

6. Doenicke, A., Wittman, R., Heinrich, H., and Pausch, H. (Abortive Effect of Halothane). Anesth Analg (Paris) 32:47-51, 1975 (Fre).

7. Bruce, D.L. Murine Fertility Unaffected by Traces of Halothane. Anesthesiology 38:473-77, 1973.

8. Knill-Jones, R.P., Moir, D.D., Rodrigues, L.V, and Spence, A.A. Anesthetic Practice and Pregnancy–Controlled Survey.

9. Corbett, T.H., Cornell, R.G., Lieding, K., and Endres, J.L. Incidence of Cancer AMong Michigan Nurse-Anesthetists. Anesthesiology 41:34-44, 1974.

10. Chang, L.W., Lee, Y.K., Dudley, A.W., Jr., and Katz, J. Ultrastructural Evidence of the Hepatotoxic Effect of Halothane in Rats Following In-Utero Exposure. Can Anesth Soc J. 22:330-37, 1975.

11. Chang, L.W., Lee, Y.K., Dudley, A.W., Jr., and Katz, J. Ultrastructural Studies on the Pathological Changes in the Neonatal Kidney Following In-Utero Exposure to Halothane. Environ. Res 10:174-89, 1975.

12. Chang, L.W., Dudley, A.W., Jr., and Katz, J., Martin, A.H. Nervous System Development Following In-Utero Exposure to Trace Amounts of Halothane. Teratology 9:A-15, 1974.

13. Bruce, D.L., and Bach, M.H. Trace Effects of Anesthetic Gases on Behaviorial Performance of Operating Room Personnel. HEW Publication No. NIOSH 76-169, 1976, 33pp.

14. Uhlirova, A., and Pokorny, J. (Results of questionnaire survey of health damage to anesthesiologists). Rozhl Chir 53:761-70, 1976 (Cze).

15. Chang, L.W., Lee, Y.K., Dudley, A.W., Jr., and Katz, J. Ultrastructural Changes in the Nervous System After Chronic Exposure to Halothane. Exp Neurol 45:209-19, 1974.

16. Quimby, K.L., Aschkenase, L.H., Bowman, R.E., Katz, J., and Chang, L.W. Enduring Learing Deficits and Cerebral Synaptic Malformation From Exposure to Ten PArts of Halothane Per Million. Science 185:625-27, 1974.

17. Redhar, K., and Sessler, A.D. Biotransformation of Halothane. Int Anesthesiol Clin 12:41-53, 1974.

18. Sawyer, D., and Eger, E., II. Hepatic Metabolism of Halothane. Int Anesthesiol Clin 12:55-62, 1974.

19. Cascorbi, H.F. Factors Causing Differences in Halothane Biotransformation. Int Anesthesiol Clin 12:63-71, 1974.

20. Van Dyke, R.A. Biotransformation of Volatile Anesthetics with Special Emphasis on the Role of Metabolism in the Toxicity of ANesthetics. Can Anesth Soc J 20:21-33, 1973.

21. Mazze, R.I., and Cousins, M.J. Biotransformation of Methoxyflurane. Int Anesthesiol Clin 12:93-105, 1974.

22. Cousins, M.D., and Mazze, R.I. Biotransformation of Enflurane (Ethrane) and Isoflurane (Forane). Int Anesthesiol Clin 12:111-119, 1974.

23. Cohen, E.N., et al, Occupational Disease in Dentistry and Exposure to Anesthetic Gases 1980. This research supported by the National Institutes of Health OH-00775, and a grant in aid from the American Dental Association.

X. AUTHORSHIP AND ACKNOWLEDGEMENTS

Report Prepared By:

Bobby J. Gunter, Ph.D.
Regional Industrial Hygienist
NIOSH - Region VIII
Denver, Colorado

Mike King, CIHT
NIOSH/HETAB/DSHEFS
Cincinnati, Ohio

Originating Office:

Hazard Evaluation and Technical Assistance Branch (HETAB)
Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS)
NIOSH, Cincinnati, Ohio

Report Typed By:

Marile F. DiGiacomo
NIOSH - Denver Region
Denver, Colorado

XI. DISTRIBUTION AND AVAILABILITY

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, 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:

1. Memorial Hospital of Southern Oklahoma
2. U.S. Department of Labor/OSHA - Region VIII
3. NIOSH - Denver Region
4. Oklahoma State Health Department
5. State Designated Agency

For the purpose of informing affected employees, a copy of this report shall be posted in a prominent place accessible to the employees for a period of 30 calendar days.

Table 1

Breathing Zone and General Room Air Concentrations of
Ethrane, Halothane, and Isoflurane at
Memorial Hospital of Southern Oklahoma
Ardmore, Oklahoma
October 21 - 22, 1986

Sample #	OR	Nurse	Sampling Time	PPM ETHR	PPM HALO	PPM ISOF
1	5	Circ.	7:30a - 1:39p	0.22	*	0.07
2	1	Scrub	7:35a - 10:30a	*	*	*
3	4-6	Scrub	7:38a - 9:03a	*	*	*
4	4-6	Circ.	7:42a - 9:10a	*	*	*
5	1	Circ.	7:45a - 12:58p	0.16	*	0.21
6	4-6	Circ.	7:50a - 12:10p	*	*	*
7	5	OR Tech.	7:56a - 12:05p	0.15	*	0.07
8	Recov.	Rec. Nurse	9:17a - 12:10p	0.61	*	0.30
9	Recov.	Gen. Area	9:25a - 1:00p	0.20	*	0.25
10	6	Circ.	9:32a - 12:05p	0.18	*	*
11	6	Circ.	9:40a - 12:05p	0.36	*	0.12
12	6	Scrub	9:45a - 11:57a	*	*	*
20	5	Circ.	8:30a - 12:00p	0.40	1.4	0.40
21	4	Circ.	8:07a - 12:05p	*	*	*
22	4	Scrub	8:05a - 9:20a	*	*	0.22
23	5	Circ.	8:05a - 9:40a	*	.34	0.24
24	Cysto	Scrub	8:52a - 12:35p	0.11	*	0.11
25	Cysto	Circ.	8:52a - 12:35p	0.13	*	0.13
26	5	Dent. Asst.	8:11a - 9:10a	*	*	*
27	5	Dent. Surgeon	8:10a - 9:14a	*	*	*
30	1	Scrub	7:25a - 12:00p	1.32	*	0.07
31	1	Circ.	7:25a - 12:00p	0.19	*	0.06
Evaluation Criteria				0.5 A/2.0	0.5 A/2.0	0.5 A/2.0
Limits of Detection (mg/sample)				0.01	0.01	0.01

* - Below detection limits
A - The NIOSH recommended limit of 2.0 ppm when used without nitrous oxide

ETHR = Ethrane
HALO = Halothane
ISOF = Isoflurane

Table 2

Breathing Zone and General Room Air Concentrations of
Nitrous Oxide at
Memorial Hospital of Southern Oklahoma
Ardmore, Oklahoma
October 21 - 22, 1986

Sample #	OR	Nurse	Sampling Time	PPM Nitrous Oxide
100	5	Circ.	7:30a - 9:20a	0
101	1	Scrub	7:35a - 10:30a	0
102A	4-6	Scrub	7:38a - 9:10a	5
103A	4-6	Circ.	7:42a - 9:10a	4
105A	1	Circ.	7:45a - 10:06a	0
105B	1	Circ.	10:11a - 12:45p	0
108	4-6	Circ.	7:42a - 9:10a	4
104A	4-6q	Circ.	7:50a - 10:00a	4
106A	5	OR Tech.	7:56a - 9:17a	0
107	Rec.	Rec. Nurse	9:17a - 12:18p	4
108A	Rec.	Gen. Area	9:25a - 12:20p	0
104B	6	Circ.	9:32a - 12:05p	0
103B	6	Circ.	9:40a - 12:05p	0
102B	6	Scrub	9:45a - 11:57a	0
108B	Rec.	Gen. Area	11:04a - 1:30p	0
106B	5	Circ.	11:15a - 1:39p	5
108C	Rec.	Gen. Room	12:54p - 2:35p	0
102C	Rec.	Rec. Nurse	1:00p - 2:35p	0
202	5	Circ.	7:30a - 10:40a	5
203	4	Scrub	8:05a - 9:20a	5
200	5	Circ.	8:30a - 10:20a	50
201	4	Circ.	8:07a - 9:20a	5
Evaluation Criteria				25
Limit of Detection				1