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 NO. 78-80-521

DENVER GENERAL HOSPITAL
DENVER, COLORADO

AUGUST 1978

## I. TOXICITY DETERMINATION

A health hazard evaluation was conducted by the National Institute for Occupational Safety and Health (NIOSH) at Denver General Hospital, Denver, Colorado, on June 27 and 28, 1978. Environmental breathing zone samples were collected to determine concentrations of halothane, ethrane, and nitrous oxide in the operating rooms.

Atmospheric concentrations of halothane, ethrane, and nitrous oxide indicate that a potential health hazard existed during this evaluation when compared to NIOSH recommended levels. Since information on adverse health effects due to exposure to halothane, ethrane, and nitrous oxide are not completely defined, and many unknown factors still exist, recommended permissible levels of exposure are not defined as safe levels but rather as levels which are attainable under current technology. NIOSH recommends an 8-hour exposure limit of 25 parts per million (ppm) for nitrous oxide and 2 ppm for the halogenated anesthetics (halothane and ethrane). Throughout this evaluation, nitrous oxide was used in conjunction with either ethrane or halothane. When used in this manner, the recommended standard of 0.5 ppm for halogenated anesthetic agents should be followed. These levels should prevent both chronic and acute effects. Two out of 20 halothane breathing zone samples exceeded the NIOSH recommended level of 0.5 ppm; one out of 20 ethrane breathing zone samples exceeded the NIOSH recommended level of 0.5 ppm. The nitrous oxide NIOSH recommended level of 25 ppm was exceeded in 6 out of 65 breathing zone samples. The scavenging system which has been installed on all anesthetic carts at this hospital is capable of exhausting the waste anesthetic gases. The slightly excessive levels of waste anesthetic gases found during this survey were presumably caused by difficulty in administering the gas to small patients, improperly fitted face masks, and the technique of administration by the anesthesiologist. Levels were very low in comparison to other hospital operating rooms surveyed by the author.

## II. DISTRIBUTION AND AVAILABILITY

Copies of this determination report are currently available upon request from NIOSH, Division of Technical Services, Information 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. Denver General Hospital
2. U. S. Department of Labor/OSHA - Region VIII
3. NIOSH - Region VIII

For the purpose of informing the approximately 70 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.

## 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 any 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.

NIOSH received such a request from the Chief of Anesthesiology at Denver General Hospital. There were no specific health problems at the time of this request. The recognition by operating room personnel of the potential health hazards associated with chronic exposures to anesthetic gases was responsible for the health hazard evaluation request.

## IV. HEALTH HAZARD EVALUATION

### A. Process Description

Denver General Hospital has 6 operating rooms. These operating rooms operate basically from 7 a.m. until 5 or 6 p.m. However, they are open 24 hours a day, and emergency surgery is performed in these rooms. During this evaluation all operating rooms were monitored for waste anesthetic gas exposures. There are 70 workers covering three shifts in the operating rooms, with approximately 40 of these on the day shift. Surgery performed in these operating rooms includes almost any conceivable procedure from a simple bunionectomy to multiple coronary artery bypass grafts. The workload during the two days of this evaluation was typical of their normal workload. The operating rooms have a totally isolated ventilation system, with no recirculating air. The scavenging system on each anesthetic cart is plugged into the vacuum system, which feeds into the operating room ventilation system.

B. Evaluation Design

Nitrous oxide samples were collected in 20 liter mylar bags using a vacuum pump operated at 300 cubic centimeters (cc) per minute. These samples were analyzed immediately on the surgical floor by infrared spectrometry using a Wilks Miran 1A with a sensitivity of 5 ppm. Instrument settings were wave length 4.47 microns, path length 5.25 meters, and slit width 0.5 milliters (mm). Halothane and ethrane samples were collected on charcoal tubes using vacuum pumps operated at 200 cc per minute. Analysis of these samples was performed using gas chromatography and P&CAM Method No. 127. Breathing zone air samples of operating room personnel were collected during each surgical procedure for the above anesthetic gases.

C. Evaluation Criteria

In the NIOSH criteria document for a recommended standard for occupational exposure to anesthetic gases, NIOSH states:[1] "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 congential 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. A dose response relationship for halogenated anesthetic toxicity has not been defined.

That same NIOSH publication recommends maximum exposures of 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[2] and Askrog and Harvald[3] 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).[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 in animals, particularly rats, most of these studies involved concentrations of anesthetic gases well above the levels found in occupational exposure. One investigator[5] 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. While most animal exposure studies have been conducted at anesthetic levels, one study[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 that indicated an increase in spontaneous abortion and congenital abnormalities 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,[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 on 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, 14] and damage to cerebral cortical neurons has been seen in rats after sub-anesthetic exposure to halothane.[15] Quimby, et al.,[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 [17, 18, 19, 20] indicate the most widely accepted mechanism of bio-transformation is the production of trifluoroacetic acid with resulting urinary excretion of trifluoroacetic acid and bromide. The literature regarding enflurane[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.

D. Evaluation Results

Table I shows the results of 20 samples taken for halothane and ethrane. Only one of the ethrane samples exceeded the standard of 2 ppm if used alone. However, since the ethrane and halothane were always used with nitrous oxide during this evaluation, the standard of 0.5 ppm was still only exceeded in one out of the 20 samples for ethrane and in 2 out of 20 samples for halothane. These results may be reviewed in Table I. Nitrous oxide concentrations exceeded the NIOSH recommended level of 25 ppm in 6 out of 65 samples. Nitrous oxide levels found during this evaluation may be reviewed in Table II.

E. Results and Discussion

Findings during this evaluation indicate that this hospital has done a lot of work in eliminating exposures to employees from waste anesthetic gases, even though the NIOSH recommended levels for nitrous oxide and the halogenated anesthetics were exceeded. The recommended standards were never grossly exceeded; and when they were exceeded, it was not due to the scavenging system or the hospital ventilation system. Reasons for the elevated levels of these gases were due to difficulty in administering the gas to small patients, improperly fitted face masks, and the technique of administration by the anesthesiologist. It is doubtful that there was a leak in any of the anesthetic gas-administering machinery, since levels during this survey were relatively low when compared with other NIOSH studies.[23] If there had been a leak in any of the anesthetic gas-administering machinery, concentrations would have been much higher than those found during this evaluation. Most of the employees, including surgeons, anesthesiologists, nurses, and operating room technicians, seemed to think that they were working in a safe place and that their work had no ill effects on their health. The NIOSH health hazard evaluation team agree with this opinion.

Conclusions

The operating rooms at Denver General Hospital were immaculate. There were scavenging systems on all anesthetic carts. All operating room personnel were aware of the hazards associated with chronic exposures to anesthetic gases. Concentrations found during this survey were extremely low and do not pose an immediate danger to the health of the operating room personnel. Every effort should be made to lower these concentrations to levels that are less than those recommended by NIOSH.

## V. RECOMMENDATIONS

1. Anesthetic equipment should be checked and maintained on a regular basis.

2. Face masks, tubing, and breathing bags should all be checked for cracks and other leaks.

3. All high pressure connections and valves should be checked periodically. Care should be taken when pouring the halogenated agents into the anesthetic gas-administering machinery so that they are not spilled on the floor.

4. Operating rooms should be monitored at least once a year to make sure that workers are not being overexposed to waste anesthetic gases.

## VI. REFERENCES

1. Criteria For a Recommended Standard...Occupational Exposure to Waste Anesthetic Gases and Vapors. NIOSH, 1977.

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

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

4. Cohen, E.N., Brown, B.W., Bruce, D.K., Cascorbi, H.F., Corbett, T.H., Jones, T.H., and Whitcher, C.E. Occupational Disease Among Operating Room Personnel--A National Study. Anesthesiology 41:321-40, 1974.

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., Wittmann, R., Heinrich, H., and Pausch, H. (Abortive effect of halothane). Anesth Analg (Paris) 32:47-51, 1975 (Fre).

7. Bruce, D.L. Murine Fetility 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 Anaesth Soc J. 22:330-37, 1975.

11. Chang, L.W., Dudley, A.W., Jr., Lee, Y.K., 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., Katz, J., and 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.J. Trace Effects of Anesthetic Gases on Behavioral Performance of Operating Room Personnel. HEW Publication No. NIOSH 76-169, 1976, 33 pp.

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., Dudley, A.W., Jr., Lee, Y.K., 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.J., Bowman, R.E., Katz, J., and Chang, L.W. Enduring Learning Deficits and Cerebral Synaptic Malformation From Exposure to Ten Parts of Halothane Per Million. Science 185:625-27, 1974.

17. Rehder, 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. Hazard Evaluation Report 77-85. Mesa Veterinary Hospital, Golden, Colorado, 1977 (NIOSH).
Technical Assistance Report 77-31. Boulder Memorial Hospital, Boulder, Colorado, 1977 (NIOSH).

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TABLE I

BREATHING ZONE AND GENERAL ROOM AIR CONCENTRATIONS OF HALOTHANE AND ETHRANE

Denver General Hospital
Denver, Colorado

June 27-28, 1978

| Sample Number | Job Classification | Operating Room No. | Time of Sample | Halothane PPM | Ethrane PPM |
|---|---|---|---|---|---|
| 1 | Circulating Nurse | 1 | 8:05 AM - 10:50 AM | * | * |
| 2 | Scrub Nurse | 1 | 8:05 AM - 10:45 AM | * | * |
| 3 | Scrub Nurse | 6 | 8:02 AM - 10:50 AM | 0.53 | * |
| 4 | Scrub Nurse | 2 | 7:58 AM - 10:40 AM | 0.46 | * |
| 5 | Scrub Nurse | 2 | 7:58 AM - 10:35 AM | 0.41 | * |
| 6 | Circulating Nurse | 6 | 8:02 AM - 11:14 AM | * | * |
| 7 | Anesthesiologist | 2 | 7:58 AM - 10:52 AM | 1.73 | * |
| 8 | Anesthesiologist | 6 | 8:03 AM - 11:17 AM | 0.30 | * |
| 9 | Area Sample | Recovery | 8:35 AM - 10:35 AM | * | * |
| 10 | Area Sample | Recovery | 11:50 AM - 1:30 PM | * | 16 |
| 11 | Scrub Nurse | 2 | 12:35 PM - 1:40 PM | * | 0.37 |
| 12 | Circulating Nurse | 5 | 8:00 AM - 11:00 AM | * | * |
| 13 | Anesthesiologist | 5 | 7:50 AM - 11:30 AM | * | 0.12 |
| 14 | Circulating Nurse | 4 | 7:55 AM - 8:50 AM | * | * |
| 15 | Circulating Nurse | 3 | 8:00 AM - 12:07 PM | * | * |
| 16 | Scrub Nurse | 3 | 8:00 AM - 12:05 PM | * | * |
| 17 | Scrub Nurse | 5 | 7:58 AM - 8:55 AM | * | * |
| 20 | Scrub Nurse | 4 | 7:50 AM - 12:30 PM | * | * |
| 21 | Anesthesiologist | 3 | 8:00 AM - 9:05 AM | * | 0.12 |
| 22 | Anesthesiologist | 4 | 7:55 AM - 12:05 PM | * | 0.20 |
| | | | EVALUATION CRITERIA | 0.5 | 0.5 |
| | | | LABORATORY LIMIT OF DETECTION IN mg/sample | 0.01 | 0.01 |

* = below limit of detection

TABLE II

BREATHING ZONE AND GENERAL ROOM AIR CONCENTRATIONS OF NITROUS OXIDE ($N_2O$)

Denver General Hospital
Denver, Colorado

June 27, 1978

| Sample Number | Job Classification | Operating Room No. | $N_2O$ PPM |
|---|---|---|---|
| U | Scrub Nurse | 2 | 175 |
| 101 | Circulating Nurse | 6 | 5 |
| 103 | Anesthesiologist | 6 | 20 |
| 105 | Anesthesiologist | 6 | < 5 |
| 4 | Scrub Nurse | 6 | < 5 |
| F3 | Circulating Nurse | 1 | 20 |
| X | Scrub Nurse | 2 | 20 |
| 104 | General Room | Recovery | |
| B | Scrub Nurse | 2 | 50 |
| 106 | Circulating Nurse | 6 | < 5 |
| E1 | Scrub Nurse | 1 | 15 |
| 108 | Scrub Nurse | 6 | < 5 |
| 5 | Circulating Nurse | 6 | < 5 |
| 101 | Scrub Nurse | 1 | 15 |
| A3 | Anesthesiologist | 2 | 10 |
| G | Anesthesiologist | 2 | 20 |
| 103 | Anesthesiologist | 2 | 30 |
| B1 | Anesthesiologist | 6 | 10 |
| 106 | Scrub Nurse | 2 | 15 |
| 105 | Scrub Nurse | 2 | 10 |
| W | General Room | Recovery | 5 |
| U | Circulating Nurse | 1 | 45 |
| E1 | Scrub Nurse | 2 | 5 |
| X | Scrub Nurse | 6 | 10 |
| 4 | Scrub Nurse | 1 | 15 |
| A3 | Circulating Nurse | 1 | 25 |
| F3 | Circulating Nurse | 6 | 5 |
| C2 | Anesthesiologist | 6 | 15 |
| C2 | General Room | Recovery | < 5 |
| 103 | General Room | Recovery | 85 |
| 104 | Circulating Nurse | 2 | < 5 |
| A3 | General Room | Recovery | 10 |
| Y | Circulating Nurse | 2 | 10 |
| | June 28, 1978 | | |
| W | Scrub Nurse | 3 | < 5 |
| A3 | Anesthesiologist | 3 | < 5 |
| 4 | Circulating Nurse | 3 | < 5 |
| Y | Anesthesiologist | 4 | 5 |

TABLE II (continued)

| Sample Number | Job Classification | Operating Room No. | $N_2O$ PPM |
|---|---|---|---|
| E1 | Anesthesiologist | 5 | < 5 |
| U | Scrub Nurse | 4 | 10 |
| G | Circulating Nurse | 5 | < 5 |
| B1 | Circulating Nurse | 3 | N/D |
| 108 | Scrub Nurse | 4 | 10 |
| B | Anesthesiologist | 5 | N/D |
| C2 | Circulating Nurse | 5 | N/D |
| D2 | Anesthesiologist | 4 | 20 |
| W | Anesthesiologist | 5 | N/D |
| 101 | Scrub Nurse | 5 | N/D |
| 5 | Circulating Nurse | 4 | 5 |
| Y | Circulating Nurse | 4 | 10 |
| E1 | Scrub Nurse | 5 | N/D |
| A3 | Circulating Nurse | 3 | < 5 |
| 4 | Scrub Nurse | 3 | N/D |
| U | Scrub Nurse | 4 | 5 |
| B1 | Circulating Nurse | 3 | N/D |
| G | Anesthesiologist | 5 | < 5 |
| D2 | Anesthesiologist | 5 | 5 |
| B | Scrub Nurse | 5 | < 5 |
| Y | Circulating Nurse | 3 | N/D |
| E1 | Scrub Nurse | 3 | N/D |
| W | Anesthesiologist | 4 | 10 |
| 5 | Anesthesiologist | 3 | N/D |
| 4 | Scrub Nurse | 5 | N/D |
| C2 | Circulating Nurse | 4 | 5 |
| A3 | Scrub Nurse | 4 | 5 |
| B1 | Scrub Nurse | 3 | N/D |
| B | Circulating Nurse | 3 | N/D |
| | EVALUATION CRITERIA | | 25 |

N/D = none detected