I. SUMMARY

On January 30, 1987, the National Institute for Occupational Health and Safety (NIOSH) received a request to evaluate exposures to halothane and isoflurane in the Department of Surgery at Primary Children's Medical Center, Salt Lake City, Utah. In June of 1986, NIOSH had performed a health hazard evaluation in this facility (HETA-86-375-1735). This evaluation included breathing zone and general room air concentrations of nitrous oxide, halothane, isoflurane, and ethrane. The reason for this second evaluation was due to ethrane being found in the samples taken on HETA 86-375-1735 although ethrane had not been used in these operating rooms in over three years. During this follow-up evaluation, breathing zone samples were collected on nurses in all operating rooms and in the recovery room for halothane, isoflurane, and ethrane. Nitrous oxide was not measured since concentrations were well documented on HETA 86-375.

Thirteen breathing zone and 2 general room air samples were collected for halothane, isoflurane, and ethrane. Nine of 15 (60 percent) of these samples exceeded the evaluation criteria of 0.5 parts per million (ppm) for halothane; none of the isoflurane samples were over the evaluation criteria of 0.5 ppm. Ethrane was not found in any of the samples. The average concentration for halothane was 0.85 ppm. Trace quantities of isoflurane were found in 6 of the 15 samples; the average concentration was 0.04 ppm.

Employees were informally interviewed at random and interest in the toxicology of anesthetic waste gas was expressed. Medical problems directly attributed to operating room waste anesthetic gas exposure were not identified.

On the basis of environmental data, it was concluded that a health hazard existed in the operating rooms at Primary Children's Medical Center from overexposures to halothane. Recommendations on work practices and ventilation that will assist in controlling these exposures are included in this report.

KEYWORDS: SIC: 8070 (Hospitals) surgery, halothane, and isoflurane
II. INTRODUCTION

NIOSH received a request from management on January 30, 1987 to evaluate the operating rooms for halothane and isoflurane at Primary Childrens Medical Center, Salt Lake City, Utah. An environmental evaluation was conducted on February 11 and 12, 1987. Results of the survey were discussed with management on March 2, 1987.

III. BACKGROUND

Primary Childrens Medical Center in Salt Lake City, Utah has five surgery rooms and a large recovery room. All the operating rooms and the recovery room were evaluated during the two day evaluation. Scrub and circulating nurses as well as recovery room nurses were monitored for halothane and isoflurane. Anesthesiologists and surgeons declined to wear the air sampling equipment. 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 most of the anesthesiologists were using halothane and nitrous oxide. The requestor asked for only halothane, isoflurane, and ethrane, since nitrous levels had been documented in the previous health hazard evaluation HETA 86-375.

IV. EVALUATION DESIGN AND METHODS

A. Environmental

Fifteen halothane, isoflurane, and ethrane samples were collected on scrub, circulating, and recovery room nurses using charcoal tubes and vacuum pumps. These samples were analyzed according to NIOSH Method 1003.

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 (TLVs), and 3) the U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH recommendations and ACGIH TLVs are lower than the corresponding OSHA standards. Both NIOSH recommendations and ACGIH TLVs 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.

### Environmental Exposure Limits

#### 8-Hour Time-Weighted Average (TWA)

<table>
<thead>
<tr>
<th>Substance</th>
<th>TWA</th>
<th>Ceiling Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halothane</td>
<td>2.0a</td>
<td>0.5 (NIOSH)</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>2.0a</td>
<td>0.5 (NIOSH)</td>
</tr>
<tr>
<td>Ethrane</td>
<td>2.0a</td>
<td>0.5 (NIOSH)</td>
</tr>
</tbody>
</table>

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 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 (Reference 5) showed increased fetal death rates in two groups of rats following exposures of 1,000 and 100 ppm of nitrous oxide. Dornicke, 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 abortion 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 question 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 enfurane (References 21, 22) does not indicate any one accepted mechanism, but increased serum and urinary fluoride levels were found in patients receiving enfurane 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.
VI. RESULTS

Nine of the 15 air samples (60 percent) taken for halothane exceeded the evaluation criteria of 0.5 ppm. The highest concentration of halothane was 1.9 ppm and the lowest was 0.23 ppm. The average concentration of halothane was 0.84 ppm. All isoflurane air samples were below the evaluation criteria of 0.5 ppm. Isoflurane was found in only 6 of the 15 samples and the average concentration was 0.04 ppm. Ethrane was not found in any of the samples. All results may be reviewed in Table I.

Operating room and recovery room personnel were informally interviewed. All the workers were interested in the toxicology of waste anesthetic gases. None of the workers that were interviewed had medical problems that they thought were work related.

VII. CONCLUSIONS

Exposure to halothane greater than the evaluation criteria were found in four of the five operating rooms. Room 4 did not have an overexposure; this room also has from 20 to 25 air changes per hour. If adequate ventilation was installed in the other four rooms, it would lower the exposure levels. Since this is a childrens' hospital; the method of anesthetic gas administration is different from that used in adult procedures; for example, small babies and infants are unique in that they are not intubated for all surgical procedures and generally are not intubated with a cuffed indotracheal tube. As a result, gas leaks around the non-cuffed indotracheal tube contaminating the room. It would be difficult under the present conditions to lower the anesthetic gases below our evaluation criteria except by increasing ventilation as exists in operating room 4.

VIII. RECOMMENDATIONS

1. Air monitoring should be continued in order to eliminate exposures and ensure proper maintenance of the ventilation system and scavenging systems.

2. More ventilation is needed in operating rooms 1, 2, 3, and 5, in order to help lower the levels of the anesthetic gas exposure. Twenty air changes per hour would lower levels of anesthetic gases.

IX. REFERENCES


X. AUTHORSHIP AND ACKNOWLEDGEMENTS

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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. Primary Childrens Hospital Annex
2. U.S. Department of Labor/OSHA - Region VIII.
3. NIOSH - Denver Region.
4. Utah 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 Halothane and Isoflurane at Primary Children's Hospital Annex Salt Lake City, Utah February 11, 1987

<table>
<thead>
<tr>
<th>Sample #</th>
<th>OR</th>
<th>Nurse</th>
<th>Sampling Time</th>
<th>HALO</th>
<th>ISOF</th>
<th>ETHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>General room</td>
<td>8:45a - 11:05a</td>
<td>0.45</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>Scrub</td>
<td>9:03a - 12:45p</td>
<td>1.18</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>General room</td>
<td>8:54a - 12:32p</td>
<td>1.30</td>
<td>0.05</td>
<td>*</td>
</tr>
<tr>
<td>4</td>
<td>Rec</td>
<td>Reco.</td>
<td>7:45a - 12:25p</td>
<td>0.31</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>General room</td>
<td>8:53a - 12:40p</td>
<td>1.90</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>Scrub</td>
<td>7:34a - 10:50a</td>
<td>0.23</td>
<td>0.11</td>
<td>*</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>Scrub</td>
<td>7:32a - 11:10a</td>
<td>0.55</td>
<td>0.11</td>
<td>*</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>Scrub</td>
<td>7:32a - 11:00a</td>
<td>0.49</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>Circ.</td>
<td>7:32a - 12:36p</td>
<td>0.31</td>
<td>0.06</td>
<td>*</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>Circ.</td>
<td>7:39a - 11:00a</td>
<td>0.55</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>Scrub</td>
<td>7:30a - 12:34p</td>
<td>0.98</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>Circ.</td>
<td>7:29a - 11:10a</td>
<td>1.10</td>
<td>0.1</td>
<td>*</td>
</tr>
<tr>
<td>13</td>
<td>4</td>
<td>Scrub</td>
<td>7:27a - 11:18a</td>
<td>0.25</td>
<td>0.1</td>
<td>*</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>Circ.</td>
<td>9:08a - 12:23p</td>
<td>1.17</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>15</td>
<td>2</td>
<td>Circ.</td>
<td>7:25a - 12:45a</td>
<td>1.85</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

**Evaluation Criteria**

0.5 0.5 0.5

**Limits of Detection (mg/sample)**

0.01 0.01 0.01

* - Below detection limits

HALO = Halothane
ISOF = Isoflurane
ETHR = Ethrane