### Anesthetic Gases: Guidelines for Workplace Exposures

**Most Commonly Used Anesthetic Gases:**

<table>
<thead>
<tr>
<th>Generic or chemical name</th>
<th>Commercial name</th>
<th>Year of introduction</th>
<th>Currently in use?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrous oxide</td>
<td>Nitrous oxide</td>
<td>1844</td>
<td>Yes</td>
</tr>
<tr>
<td>Halothane</td>
<td>Fluothane®</td>
<td>1956</td>
<td>Yes</td>
</tr>
<tr>
<td>Enflurane</td>
<td>Ethrane®</td>
<td>1974</td>
<td>Yes</td>
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<tr>
<td>Isoflurane</td>
<td>Forane®</td>
<td>1980</td>
<td>Yes</td>
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<tr>
<td>Desflurane</td>
<td>Suprane®</td>
<td>1992</td>
<td>Yes</td>
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<tr>
<td>Sevoflurane</td>
<td>Ultane®</td>
<td>1995</td>
<td>Yes</td>
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</tbody>
</table>

It is estimated that more than 200,000 health care professionals --including anesthesiologists, nurse anesthetists, surgical and obstetric nurses, operating room (OR) technicians, nurses aides, surgeons, anesthesia technicians, postanesthesia care nurses, dentists, dental assistants, dental hygienists, veterinarians and their assistants, emergency room staff, and radiology department personnel --are potentially exposed to waste anesthetic gases and are at risk of occupational illness. Over the years there have been significant improvements in the control of anesthetic gas pollution in health-care facilities. These have been accomplished through the use and improved design of scavenging systems, installation of more effective general ventilation systems, and increased attention to equipment maintenance and leak detection as well as to careful anesthetic practice. However, occupational exposure to waste gases still occurs.

Exposure measurements taken in ORs during the clinical administration of inhaled anesthetics indicate that waste gases can escape into the room air from various components of the anesthesia delivery system. Potential leak sources include tank valves, high- and low-pressure machine connections; connections in the breathing circuit, defects in rubber and plastic tubing, hoses, reservoir bags, and ventilator bellows, and the Y-connector. In addition, selected anesthesia techniques and improper practices such as leaving gas flow control valves open and vaporizers on after use, spillage of liquid inhaled anesthetics, and poorly fitting face masks or improperly inflated tracheal tube and laryngeal mask airway cuffs also can contribute to the escape of waste anesthetic gases into the OR atmosphere.

Studies of the effects of these agents in the health-care setting have been made more difficult due to high job turnover of affected employees. Publications report a wide range of exposure levels in hospital, medical, dental, and veterinary facilities (Askgro and Petersen 1970; American Society of Anesthesiologists 1974; Sweeney et al. 1985; Jastak 1989; Burkhart and Stobbe 1990; Henry and Jerrell 1990; Rowland et al. 1992; NIOSH 1977, 1994).

Unlike the situation in the OR, health-care workers in the recovery room (also known as the postanesthesia care unit or PACU) encounter occupational exposure to waste anesthetic gases from the patients instead of the anesthesia delivery system. While in the OR, patients anesthetized with inhaled anesthetic agents take-up varying quantities of these agents depending on the specific agent and its solubility, the duration of
anesthesia, and the physiological make-up of the patient. In the PACU, these gases are eliminated by the patient’s respiratory system into the ambient environment. In contrast to the OR, the ambient air in the PACU may contain multiple anesthetic gases, which include but are not limited to nitrous oxide, halothane, enflurane, isoflurane, desflurane, and sevoflurane.

Because PACU nurses must monitor vital functions in close physical proximity to the patient, they can be exposed to measurable concentrations of waste anesthetic gases. While random room samples may indicate relatively low levels of waste gases, the breathing zone of the nurses may contain higher levels. Consequently, air samples obtained within the breathing zone of a nurse providing bedside care are most likely to represent the gas concentrations actually inhaled.

In general, the detection of halogenated anesthetic agents by their odor would indicate the existence of very high levels, as these agents do not have a strong odor at low concentrations. For example, detection of high levels of halothane may be difficult for PACU nurses because one study (Hallen et al. 1970) found that fewer than 50% of the population can detect the presence of halothane until concentrations are 125 times the NIOSH REL.

C. HEALTH EFFECTS

In anesthetizing locations and PACUs where exposure to waste gases is known to occur, it is important for health-care workers and their employers to understand the potential risks of excess exposure to waste anesthetic gases and to implement the appropriate controls to minimize these risks. During the past 25 years multiple studies have attempted to elucidate the risk of exposure to anesthetic agents. Animal and human studies have assessed hematopoietic, central nervous system, and behavioral effects and the effects of anesthetic agents on fertility, carcinogenicity, teratogenicity, and reproduction. Epidemiological studies have generally focused on OR and dental workers, the two occupational groups most frequently exposed to anesthetics. The following discussion highlights these findings.

1. Nitrous Oxide

While mutagenicity testing of nitrous oxide (N₂O) has demonstrated negative results (Baden 1980), reproductive and teratogenic studies in several animal species have raised concern about the possible effects of nitrous oxide exposure in humans. In general, studies demonstrate reproductive and developmental abnormalities in animals exposed to high concentrations of N₂O. In one study by Viera et al. (1980), spontaneous abortion was observed in rats at 1000 ppm or more. According to NIOSH (1994), similar concentrations of 1000 ppm have been found in operating rooms and in dental operatories not equipped with scavenging systems.

Smith, Gaub, and Moya (1965) reported fetal resorption in rats exposed to nitrous oxide at high doses. Fink, Shepard, and Blandau (1967) administered 45% to 50% nitrous oxide and 21% to 25% oxygen to pregnant rats for 2, 4, and 6 days starting at day 8 of gestation. Surviving fetuses from these rats demonstrated rib and vertebral defects. Corbett and colleagues (1973) also reported an increase in fetal deaths and a smaller number of offspring in rats exposed to levels ranging from 1,000 to 15,000 ppm of nitrous oxide.

There are also studies involving human subjects. A recent retrospective study (Rowland et al. 1992) reported that female dental assistants exposed to unscavenged N₂O for 5 or more hours per week had a significantly increased risk of reduced fertility compared with non-exposed female dental assistants. The exposed assistants had a 59% decrease in probability of conception for any given menstrual cycle
compared with the non-exposed assistants. For dental assistants who used scavenging systems during N\textsubscript{2}O administration, the probability of conception was not significantly different from that of the non-exposed assistants. The Rowland study authors suggest that "exposure to high levels of unscavenged N\textsubscript{2}O can impair fertility and scavenging equipment is important in protecting the reproductive health of women who work with the gas." The study revealed that the mean time to conception among the women who worked with scavenged N\textsubscript{2}O was similar to that among the non-exposed women, but it was much longer among the women who worked with unscavenged N\textsubscript{2}O for 5 or more hours a week.

Rowland and colleagues (1995) examined the relationship between occupational exposure to N\textsubscript{2}O and spontaneous abortion in female dental assistants. Duration of exposure was a surrogate for exposure data. Nitrous oxide exposure was divided into two separate variables: scavenged hours (hours of exposure per week in the presence of scavenging equipment) and unscavenged hours of exposure per week. Women who worked with N\textsubscript{2}O at least 3 hours per week in offices not using scavenging equipment had an increased risk of spontaneous abortion (relative risk = 2.6, 95% confidence interval [CI] = 1.3-5.0) adjusted for age, smoking, and number of amalgams prepared per week. This finding was not observed among workers in offices where scavenging equipment was in use. The authors concluded, "Scavenging equipment can make large differences in exposure levels at moderate cost and appears to be important in protecting the reproductive health of women who work with nitrous oxide."

Several summaries of the epidemiologic studies of exposure to N\textsubscript{2}O and reviews of the topic generally including animal and retrospective studies (Purdham 1986; Kestenberg 1988; and NIOSH 1994) have been published. They report a consistent excess of spontaneous abortion in exposed women. Other summaries of the epidemiologic studies do not establish a cause-effect relationship (Buring et al. 1985; Tannenbaum and Goldberg 1985). Evidence for congenital abnormalities is less strongly associated with exposure.

2. Halogenated Agents

Halogenated agents are used with and without N\textsubscript{2}O and have been linked to reproductive problems in women and developmental defects in their offspring. As early as 1967 there were reports from the Soviet Union, Denmark, and the United States (Vaisman 1967; Askrog and Petersen 1970; Cohen, Bellville, and Brown 1971) that exposure to anesthetic agents including halothane may cause adverse pregnancy outcomes in health-care personnel. Several animal studies in rats, mice and hamsters showed embryolethal and teratogenic effects and supported the findings in humans (Basford and Fink 1968; Wharton 1979), although often at quite high concentrations (3000-6000 ppm). One (Popova et al. 1979) reported fetal resorptions in rats at 9 ppm.

A number of human epidemiologic studies have been performed since the early 1970s to assess the potential harm to reproductive health that exposure to anesthetics might cause. Generally, these were mailed questionnaire surveys completed by persons (usually anesthesiologists and nurses) identified through registries. As such, the studies were retrospective and inquired about previous reproductive outcomes for which validation was not available. In addition, no exposure data were available and many of the early studies predated the use of scavenging systems. Studies documenting a statistically significant excess of spontaneous abortions in exposed female anesthesiologists include those of Cohen and colleagues 1971, Knill-Jones and colleagues 1972, ASA 1974, and Pharoah and colleagues 1977. Studies also documented increases in spontaneous abortion among nonphysician female OR personnel (Cohen et al. 1971; Rosenberg and Kirves 1973; ASA 1974; Knill-Jones et al. 1975; and Tomlin 1979). Also of interest, one study documented increased incidence rates of spontaneous abortion among wives of exposed males (ASA 1974). In some exposed populations, studies failed to show that exposure to anesthetic agents caused increased risk of spontaneous abortion (Rosenberg and Vanttinnen 1978; Axelsson and Rylander 1982; Tannenbaum and Goldberg 1985; Buring et al. 1985).
The evidence for an association between anesthetic exposure and congenital anomalies is less consistent. Only a few studies in some subpopulations of exposed workers found a positive association (Corbett et al. 1974; ASA 1974; Pharoah et al. 1977). Other studies reported no association with congenital anomalies (Axelsson and Rylander 1982; Lauverys et. al. 1981; Cohen et. al. 1980; Rosenberg and Vanttinnen 1978).

The retrospective study by Cohen and colleagues (1980) reported that female dental chairside assistants who had experienced heavy exposure (defined as more than eight hours per week) to waste anesthetic gases reported a significant increase in the rate of spontaneous abortions (19.1 per 100 pregnancies) compared with the rate in the non-exposed pregnant control (8.1 per 100). For the wives of dentists who had also experienced heavy exposure, a significant increase in the rate of spontaneous abortions (10.2 per 100) was also reported compared with the rate in the wives of dentists not exposed (6.7 per 100). The non-exposed group was restricted to those who did not report anesthetic exposure in any of the years before conception and including the year of conception.

Another study of reproductive outcomes associated with exposure to anesthetic gases (also a questionnaire survey, conducted between 1981 and 1985) documented both a statistically significantly increased odds ratio for spontaneous abortion in exposed females (odds ratio 1.98; CI = 1.53-2.56) and spouses of exposed male workers (odds ratio 2.30; CI = 1.68-3.13), and for congenital abnormality in offspring of exposed females \ (odds ratio 2.24; CI = 1.69-2.97) and offspring of spouses of exposed male workers (odds ratio 1.46; CI = 1.04-2.05) (Guirgis et al. 1990). Duration of exposure as estimated by a hygiene investigation was used as an exposure surrogate. These findings of a positive association were surprising because scavenging systems were thought to have been more likely in use during the study period compared to many of the previously cited papers, almost a decade older.

In the mid 1970's, human studies testing the cognitive and the motor skills of male subjects/volunteers, showed that exposure to concentrations of anesthetic gas mixtures commonly found in the unscavenged operating room, resulted in decreased ability to perform complex tasks (Bruce et al. 1974, 1975, later invalidated by the author, 1983, 1991). These volunteers exhibited decrements in performance following exposures at: 500 ppm N2O in air; 500 ppm N2O plus 15 ppm halothane in air; and 500 ppm N2O plus 15 ppm enflurane in air. However, studies that attempted to replicate the results of the human performance studies that showed decrements failed to confirm these findings (Smith and Shirley 1978).

Potential harmful effects due to desflurane exposure have been addressed in a few recent studies, including those of Holmes and colleagues (1990), an animal study; and Weiskopf and colleagues (1992), a study conducted with human volunteers. However, desflurane’s potential as a hazard to health-care personnel has not been thoroughly evaluated. Sevoflurane (Ultane®), the newest anesthetic agent in clinical practice, has also not been thoroughly evaluated. The levels of risk for isoflurane, desflurane, and sevoflurane have not been established. Since there are limited data, occupational exposure limits for these agents have not been determined. Therefore, until more information is available, it is prudent to attempt to minimize occupational exposure to these as with all anesthetic agents.

Unlike N2O, there is evidence that halothane is mutagenic in certain in vitro test systems (Garro and Phillips 1978) and that halothane is metabolized to reactive intermediates that covalently bind to cellular macromolecules, suggesting potential mechanisms of toxicity (Gandolfi et al. 1980).

3. Summary

Despite questions about design issues or selection bias in some studies, the weight of the evidence regarding potential health risks from exposure to anesthetic agents in unscavenged environments suggests that clinicians need to be concerned. Moreover, there is biological plausibility that adds to the concern that high levels of unscavenged waste anesthetic gases present a potential for adverse
neurological effects or reproductive risk to exposed workers or developmental anomalies in their offspring (Cohen et al. 1980; Rowland 1992).

While the use of prospective studies and carefully designed research protocols is encouraged to elucidate areas of controversy, a responsible approach to worker health and safety dictates that any exposure to waste and trace gases should be kept to the lowest practical level.

D. THE BASIC ANESTHESIA MACHINE

An anesthesia machine is an assembly of various components and devices that include medical gas cylinders in machine hanger yokes, pressure regulating and measuring devices, valves, flow controllers, flow meters, vaporizers, CO₂ absorber canisters, and breathing circuit assembly. The basic two-gas anesthesia machine has more than 700 individual components.

The anesthesia machine is a basic tool of the anesthesiologist/anesthetist and serves as the primary work station. It allows the anesthesia provider to select and mix measured flows of gases, to vaporize controlled amounts of liquid anesthetic agents, and thereby to administer safely controlled concentrations of oxygen and anesthetic gases and vapors to the patient via a breathing circuit. The anesthesia machine also provides a working surface for placement of drugs and devices for immediate access and drawers for storage of small equipment, drugs, supplies, and equipment instruction manuals. Finally, the machine serves as a frame and source of pneumatic and electric power for various accessories such as a ventilator, and monitors that observe or record vital patient functions or that are critical to the safe administration of anesthesia.

1. Gas Flow in the Anesthesia Machine and Breathing System

The internal piping of a basic two-gas anesthesia machine is shown in Figure 1. The machine has many connections and potential sites for leaks. Both oxygen and N₂O may be supplied from two sources (Figure 2): a pipeline supply source (central piping system from bulk storage) and a compressed gas cylinder supply source. In hospitals, the pipeline supply source is the primary gas source for the anesthesia machine. Pipeline supplied gases are delivered through wall outlets at a pressure of 50-55 psig through diameter indexed safety system (DISS) fittings or through quick-connect couplings that are gas-specific within each manufacturer's patented system.

Because pipeline systems can fail and because the machines may be used in locations where piped gases are not available, anesthesia machines are fitted with reserve cylinders of oxygen and N₂O. The oxygen cylinder source is regulated from approximately 2,200 psig in the tanks to approximately 45 psig in the machine high-pressure system, and the N₂O cylinder source is regulated from 745 psig in the tanks to approximately 45 psig in the machine high-pressure system.
The flow arrangement of a basic two-gas anesthesia machine. A, The fail-safe valve in Ohmeda machines is termed a pressure sensor shut-off valve; in Dräger machines it is the oxygen failure protection device (OFPD). B, Second-stage oxygen pressure regulator is used in Ohmeda (but not Dräger Narkomed) machines. C, Second-stage nitrous oxide pressure regulator is used in Ohmeda Modulus machines having the Link 25 Proportion Limiting System; not used in Dräger machines. D, Pressure relief valve used in certain Ohmeda machines; not used in Dräger machines. E, Outlet check valve used in Ohmeda machines except Modulus II Plus and Modulus CD models; not used in Dräger machines. The oxygen take-off for the anesthesia ventilator driving gas circuit is downstream of the main on/off switch in Dräger machines, as shown here. In Ohmeda machines, the take-off is upstream of the main on/off switch.