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# Biological Monitoring of Nitrous Oxide Exposure in Surgical Areas

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Exposure to nitrous oxide in surgical theaters was evaluated for duration, numbers, and types of surgical procedures. The concentration of the gas in the air was 92–444 ppm. Before and after the surgical sessions, samples of urine and expired air were collected from surgical theater personnel for gas determination. Nitrous oxide concentrations in urine and in expired air showed a good correlation with gas concentration in the air ($r = 0.760$ and $r = 0.921$, respectively). Moreover, a good correlation ($r = 0.823$) between gas concentration in urine and that in expired air was also found. A biological threshold limit value (TLV) of 20.6 μg/liter for urine and of 29.6 ppm for expired air was calculated, based on the limit of 50 ppm in the air proposed by the American Conference of Governmental Industrial Hygienists (ACGIH). Other biological TLVs corresponding to higher proposed limits (200 and 500 ppm) were also calculated.

**Key words: nitrous oxide, biological monitoring, surgical room personnel**

## INTRODUCTION

In 1967, Vaisman first reported the existence of an occupational risk caused by the use of anesthetics in surgical theaters. In particular, he found a higher incidence of spontaneous abortion in exposed pregnant women. This observation was later confirmed by Askrog and Harvald [1970], Knill-Jones et al. [1972], Rosemberg and Kirves [1973], Garstka et al. [1974], and Gothe et al. [1976]. The results of some epidemiological studies on the toxicity of anesthetics are discussed later. A critical review pointed out several experimental errors [Robinson et al., 1976; Colton, 1982]; that is, these studies considered the environmental exposure without discriminating among different anesthetics. The present work focuses on exposure to nitrous oxide ($N_2O$), since inhalation anesthesia is frequently induced by this gas alone.

A clear correlation between environmental pollution by $N_2O$ and signs of toxicity has not been reported in the literature. Agranulocytosis [Lassen et al., 1956] and leukopenia [Green and Eastwood, 1963] have been reported in patients treated with high therapeutic (not anesthetic) doses of $N_2O$.

The aim of the present work is to describe the results of both environmental and biological monitoring of the exposure to $N_2O$ in personnel of surgical theaters (sur-

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geons, anesthetists, nurses), where $N_2O$ was the only inhalation agent used for general anesthesia.

## MATERIALS AND METHODS

The environmental concentration of $N_2O$ of five operating theaters (two of general surgery, one of orthopedics, one of gynecology, and one of otorhinolaryngology) was monitored twice at different times of the year. In none of the operating theaters was a specific scavenging system available. Rooms were supplied with 15–20 air changes per hour. $N_2O$ gas was administered using a Ruben valve during otorhinolaryngology operations, and a servo-ventilator during the others. The discharge of the gas was directed towards the surgeon during otorhinolaryngology procedures, and towards the anesthetist and the nurses during the others.

Exposure to the gas was monitored using TEDLAR bags, attached to the back of the personnel (anesthetists and nurses). Air samples were taken using DUPONT 4000 personal samplers (Delaware) calibrated at a flow of 250 ml/min. The samplers were changed hourly. The surgeons (five subjects) were provided with passive monitors [Ghittori et al., 1983], having a molecular sieve of 5 Å attached to the surgical mask. The sampling was carried out throughout the entire surgical session; therefore, several changes of the samplers were needed. $N_2O$ was determined with a Perkin-Elmer Sigma 3 B gas chromatograph connected to a Sigma 15 Data Station and equipped with an electron-capture detector (ECD). Commercial standards containing 0–4,000 ppm of $N_2O$ (SIO Blugas) were used. The coefficient of variation of the method was $\pm 0.3$ ppm. The values obtained with this method were compared with those of an infrared (IR) standard method (NIOSH, 1984) and the correlation coefficient was $r = 0.997$.

Twenty exposed operators, 12 men and 8 women (5 surgeons, 5 anesthetists, and 10 nurses), aged 25–50 years, underwent biological monitoring during the second assessment of the environmental concentration. $N_2O$ was determined in expired air and urine. Collection of the biological specimens was carried out before and immediately after (2–3 min) the surgical session (after about 6 hr of exposure), in a separate room not contaminated with $N_2O$. The expired air (end-tidal samples) was collected in 250-ml glass vials, and gas concentration was determined as above. Urine samples were immediately sealed in screw capped vials and equilibrated at 40°C for 2 hr; then 1 ml of the head space was injected into the gas chromatograph. $N_2O$ was determined according to the method of Sonander et al. (1983). A linear regression coefficient was calculated for the statistical evaluation of the results. The concentration of $N_2O$ in expired air was correlated with the environmental time-weighted average (TWA) of the gas concentration during the last hour of exposure. TWA was determined from the values found in sampler bags that were changed hourly throughout the surgical session.

## RESULTS

Table I shows the environmental concentrations of $N_2O$ in the different surgical theaters. Values are two- to ninefold higher than the threshold limit value (TLV) proposed by the American Conference of Governmental Industrial Hygienists

**TABLE I. Environmental Values of $N_2O$ in Different Surgical Areas at Level of Personnel***

| Surgical area | Anesthetist | Surgeon | Nurse |
|---|---|---|---|
| Gynecology | 444 ± 144 | 267 ± 68 | 387 ± 124 |
| Otorhinolaryngology | 330 ± 113 | 422 ± 87 | 171 ± 77 |
| Surgery 1 | 345 ± 43 | 100 ± 38 | 278 ± 102 |
| Surgery 2 | 108 ± 11 | 109 ± 59 | 92 ± 21 |
| Orthopedics | 254 ± 64 | 136 ± 13 | 218 ± 43 |

*Data are supplied in ppm as TWA.

(ACGIH, 50 ppm). Generally, the anesthetist shows the highest exposure. During otorhinolaryngologic surgery, the highest exposure is that of the surgeon.

Figure 1 shows the correlation between environmental $N_2O$ concentrations and those in expired air (Fig. 1a) or in urine (Fig. 1b) $N_2O$. A good correlation between environmental and expired air concentrations was observed ($r = 0.911$), slighty less so for urine ($r = 0.760$). The data reported in Figure 2 show a good correlation between $N_2O$ in expired air and urine ($r = 0.823$).

## DISCUSSION

Can the exposure to anesthetic gas and vapors be a health hazard? The concern generated by the results of epidemiological studies changed some anesthetic techniques: the waste gas in excess is now scavenged and monitoring programs for the periodic examination of exposed personnel were initiated.

Until now, it has been difficult to define tolerance limits for human exposure to anesthetic gases in surgical areas. $N_2O$ inactivates vitamin $B_{12}$ [Brodsky, 1983]; the inactivation is mediated by a dose-dependent inhibition [Sharer et al., 1983] of methionine-synthetase activity [Chanarin, 1980; Koblin et al., 1982]. However, no changes in serum methionine, folate, or vitamin $B_{12}$ were observed in surgical personnel exposed to $N_2O$ concentrations between 150 and 860 ppm [Nunn et al., 1982; Salo et al., 1984]. These studies concluded that no inactivation of vitamin $B_{12}$ develops for $N_2O$ exposure lower than 500 ppm. For this reason, the National Institute for Occupational Safety and Health (NIOSH, 25 ppm) and ACGIH (50 ppm) recommendations are contested by numerous authors. Particularly, Nunn et al. [1981] and Sharer et al. [1983] recommended a TLV of 200 ppm for $N_2O$ in the air, considering the NIOSH recommendation to be overprotective. Fiserova-Bergerova [1988] suggests, moreover, a TLV of as much as 500 ppm.

The environmental values reported in this study are two–nine times higher than the ACGIH proposed limits; they are, however, acceptable according to the limits proposed by Fiserova-Bergerova [1988]. The present study focuses on the environmental and biological monitoring of personnel exposed to $N_2O$ in surgical areas. No investigation on $N_2O$ toxicity has been attempted in this study. Environmental pollution is usually related to: (1) ventilation and scavenging systems; (2) status of the anesthetic apparatus; and (3) duration, number, and type of procedures. The induction phase of anesthesia procedures causes the maximum exposure; therefore, the greater the number of anesthetic inductions, the greater the environmental pollution. This effect is important in areas in which short operations are performed such as those of otorhinolaryngologic surgery. Moreover, in these areas, the surgeon is more exposed

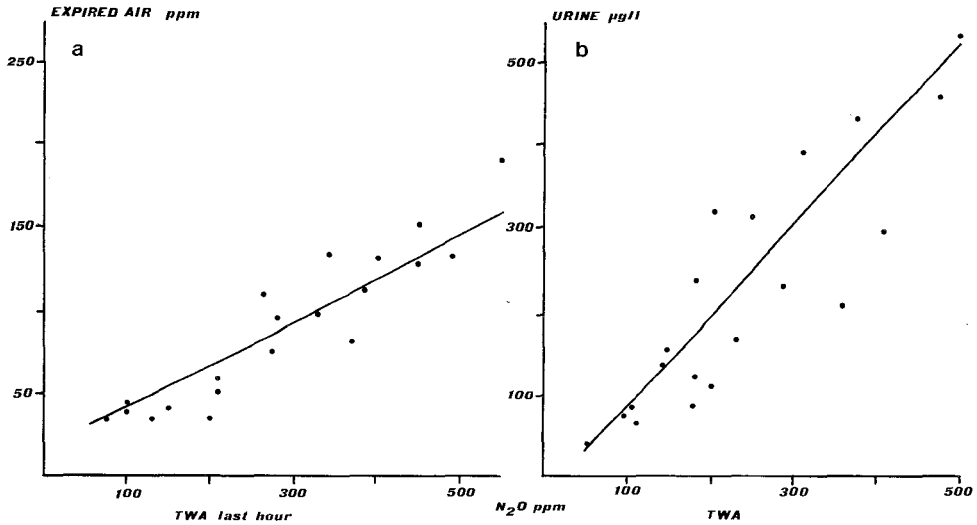


Fig. 1. Biological monitoring of nitrous oxide in surgical personnel. **a:** Correlation between $N_2O$ concentrations in air and in expired air ($y = 0.25x + 17.14$, $r = 0.911$). **b:** Correlation with $N_2O$ in urine ($y = 1.14x - 36.4$, $r = 0.760$).

**TABLE II. Biological TLVs Proposed at Different Environmental TLVs of $N_2O$**

| TLV ppm | 50 | 200 | 500 |
|---|---|---|---|
| Urine (µg/liter) | 20.6 | 191.6 | 533.6 |
| Expired air ppm | 29.6 | 67.1 | 142.1 |

than the anesthetist because the wastes of the Ruben valve are discharged towards the surgeon.

Determination of $N_2O$ in urine and expired air is a good index of exposure. Using a regression line, it was possible to define biological TLVs based on ACGIH recommendations and other proposed limits (200 and 500 ppm). These biological TLVs are reported in Table II. In the literature, a biological TLV in venous blood (at the end of a workshift) of 1.9 mmoles/liter has been proposed [Krapez et al., 1980]. The biological TLV in urine suggested by the results of this study (20.6 µg/liter) is in agreement with that (18 µg/liter) proposed in the same biological fluid by Pezzagno et al. [1985].

Generally, determination of environmental pollutants is meaningless if it is not correlated with body absorption. The problem is to determine if the index of exposure is correlated with a critical effect in the critical organ. Moreover, it is important to define the correlations among environmental concentrations, internal dose, and critical effect.

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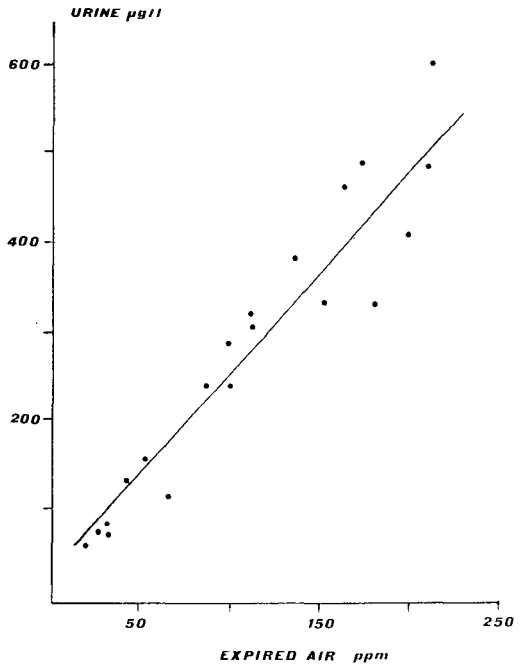


Fig. 2. Biological monitoring of nitrous oxide in surgical personnel. Correlation between $N_2O$ in expired air and urine ($y = 0.32x + 25.9$, $r = 0.867$).

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