# Nitrous Oxide Concentrations in the Posterior Nasopharynx During Administration by Nasal Mask

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## Abstract

**Purpose:** Nitrous oxide ($N_2O$) administration with nasal mask produces variable outcomes in dental patients. This study describes a novel sampling method to measure actual inspired/expired $N_2O$ concentrations ([$N_2O$]).

**Methods:** Fifteen adult volunteers (32.5±8.5 years) underwent placement of a nasopharyngeal probe. With a nasal mask, 100% oxygen ($O_2$) was administered for 2 minutes. $N_2O$ was introduced incrementally every 2 minutes for a final flowmeter [$N_2O$] of 50% and subsequently decreased in the same manner. Anesthesia gas monitors analyzed inspired/expired [$N_2O$], [$O_2$], and $P_{ET}CO_2$ from the nasopharynx and end-inspired/expired [$N_2O$] in the mask. Data were measured every 20 seconds and analyzed. Inspired/expired nasopharyngeal and nasal mask [$N_2O$] and [$O_2$] were expressed as the median value at each time point for all subjects and plotted against flowmeter settings.

**Results:** Average inspired nasal mask [$N_2O$] was 31% lower than flowmeter settings and decreased by another 19% on the way to the nasopharyngeal sampling site. During the phase of increasing $N_2O$, average expired nasopharyngeal [$N_2O$] was 22% lower than inspired [$N_2O$]. When $N_2O$ was decreased, the effect was reversed and average expired [$N_2O$] was 18% higher than inspired. Expired [$N_2O$] was on average 51% lower than flowmeter settings. Mean $P_{ET}CO_2$ was 39.7±1.4 mm Hg.

**Conclusions:** Nasopharyngeal end-expired [$N_2O$] varied markedly from flowmeter settings. Correlation of $P_{ET}CO_2$ with expected physiologic values validates sampling methodology. This method allows accurate, continuous, and actual measurements of inhaled/exhaled gases in awake patients as well as decision-making/analysis of effectiveness of mask type to determine average [$N_2O$] during administration by nasal mask. (*Pediatr Dent.* 2004;26:410-416)

KEYWORDS: NITROUS OXIDE, NASOPHARYNGEAL SAMPLING, AIR ENTRAINMENT, NASAL MASK, DENTISTRY

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In dentistry and emergency medicine, nitrous oxide ($N_2O$) is frequently administered via nasal mask in concentrations of up to 70% (with oxygen) to reduce anxiety and provide analgesia. During dental procedures, $N_2O$ is used as an adjunctive sedative and analgesic, because primary pain control is produced by local anesthesia. The safety and efficacy of properly administered $N_2O$ are well documented.[1-7] Undesirable side effects (eg, nausea, vomiting, and sexual phenomena), are rare and primarily observed when inspired concentrations exceed 50%.[2, 6]

During conscious sedation procedures in children, a failure rate of approximately 25% is reported.[8,9] It is not clear if these failures should be attributed to inadequate doses of orally administered drugs, subtherapeutic nitrous oxide concentrations ([$N_2O$]), or patient factors. In dental practice, $N_2O$ is administered via standardized nasal masks while the mouth remains open for treatment. Although the National Institute for Occupational Safety and Health (NIOSH) regulations mandate that mask delivery systems must be equipped with a scavenging system to reduce ambient air contamination, compliance with these regulations is inconsistent.[10-12] Variations in the scavenging flow rate caused by poorly adjusted and/or calibrated scavenging systems affect $N_2O$ concentrations in the nasal

mask to an unknown degree. Leakage around the nasal mask due to improper fit, patient movement, and/or oral entrainment of room air may further dilute the $N_2O$/oxygen ($O_2$) gas mixture with room air. As a result, alveolar $N_2O$ concentrations may be markedly lower than flowmeter dial settings suggest.

Many randomized, double-blind, and placebo-based studies report that $N_2O$ is an effective anxiolytic for painful procedures.[1,3-5,13] Most base their conclusions and/or recommendations for effective therapeutic $N_2O$ concentrations, however, on subjective criteria (eg, improvement of patient behavior/cooperation) or flowmeter $N_2O$ concentration settings only. Unlike endotracheal general anesthesia, where the composition of all inhaled and exhaled gases is constantly analyzed, these reported results are not reproducible nor directly comparable, because the studies do not account for variables that may cause dilution of the $N_2O/O_2$ mixture leaving the gas delivery unit. A literature search did not yield any publication that describes continuous end-expired alveolar $N_2O$ concentrations during traditional nasal mask gas delivery.

The purpose of this study was to develop a simple yet reliable method to continuously measure the actual true inspired and expired concentrations of $N_2O/O_2$ compared to flowmeter $N_2O$ dial settings. This comparison allowed the authors to assess the amount of $N_2O$ leakage/dilution from the delivery unit to the pulmonary alveoli. The authors' hypothesis was that end-expired $N_2O$ concentrations would be significantly lower than the concentrations indicated by flowmeter settings.

## Methods

For the Institutional Review Board-approved study, 15 healthy (American Society of Anesthesiologists class I) adult male (N=6) and female (N=9) volunteer subjects (age=22-51 years, mean age=32.5 years) were recruited. During the study period, a subject was seated in a dental chair and reclined into the customary supine position for dental treatment. A flexible plastic tubing (replacement sample line no. 625I, CSI Criticare Systems Inc, Waukesha, Wis) of 1.5 mm in diameter, with a modified 2.5-mm wide and 7-mm long solid and blunt polyvinyl chloride tip serving as a probe and sample line, was inserted approximately 5 to 8 cm into a subject's nasopharynx and taped to the upper lip. In cases of slight discomfort with probe insertion, 1 to 2 puffs of lidocaine 4% and oxymetazoline 0.05% were sprayed into each nostril. The gas delivery system was an MDS Matrx portable continuous flow inhalation sedation unit (Orchard Park, NY) with a 3 liter reservoir bag.

Prior to the study, the authors calibrated the gas delivery system and determined that the $N_2O/O_2$ concentrations in the mask equaled flowmeter settings. After proper adjustment of the scavenging power to -5 mm/Hg (45 L/minute), a disposable adult nasal mask (Porter Slimline, Hatfield, Pa) was positioned over the subject's nose and 100% $O_2$ was administered for 2 minutes at a flow rate of 6 L/minute. Subsequently, $N_2O$ was added to $O_2$ in 10% increments every 2 minutes until a final concentration of 50% $N_2O$/50% $O_2$ was reached. At the final 50% concentration, $N_2O$ was delivered for 2 minutes and then the concentrations were decreased by 10% incrementally in the same manner. At the end of the study period, the subject was dismissed after a 3-minute 100% $O_2$ flush through the nasal mask. The subjects were visually monitored during the entire procedure. Because pulse oximetry monitoring is not mandated for level I conscious sedation by current American Academy of Pediatric Dentistry guidelines, it was not part of the study's protocol.[14]

An anesthesia gas monitor and capnograph (POET, CSI Criticare Systems Inc, Waukesha, Wis) continuously measured and analyzed respiratory rate (RR), inspired and expired concentrations of $N_2O$ and $O_2$, as well as endtidal $CO_2$ concentration ($P_{ET}CO_{2)}$ that were obtained from the nasopharyngeal sampling site. During the 22-minute study period, data were measured every 20 seconds, electronically transferred to a computer, and stored using Hyperterminal software. A second gas monitor analyzed inspired and expired [$N_2O$] in the nasal mask. Those measurements were manually recorded every 20 seconds. A file conversion program converted the Hyperterminal text file into spreadsheet format (MS Excel, Microsoft Corp, Richmond, Wash) for data analysis. Each variable yielded 133 data readings, 1 for each 20-second time period during the 22-minute experiment.

From the nasopharyngeal probe, measurements were obtained for 8 variables for each subject: (1) inspired and expired [$N_2O$] and [$O_2$] (2) RR; and (3) $P_{ET}CO_2$. From the nasal mask, inspired and expired [$N_2O$] were recorded. Each subject's corresponding data for a variable (eg, inspired [$N_2O$] or $P_{ET}CO_2$) were combined into a single spreadsheet. Up to 2 missing data points or zeros—due to recalibration of the gas monitor with at least 4 valid preceding or following readings—were filled in as the average of the values before and after the missing data points to avoid precipitous drops to 0 within a graph. For each of the variables, the median data values for each of the 133 time points were obtained. Therefore, each variable was expressed as the median value for all 15 subjects at each time point. The median was chosen over the mean to account for outlying random "0" readings. The data were subsequently transformed to line graphs and plotted against the flowmeter's [$N_2O$] settings.

Data were statistically analyzed using the SAS system version 8e (SAS Institute, Cary, NC). Using distribution-free multiple comparisons test based on the Friedman rank sums, the areas under the curves for each subject were calculated using the trapezoidal rule. They were then compared to test for significant differences between any of the curves and to determine the average differences in [$N_2O$].

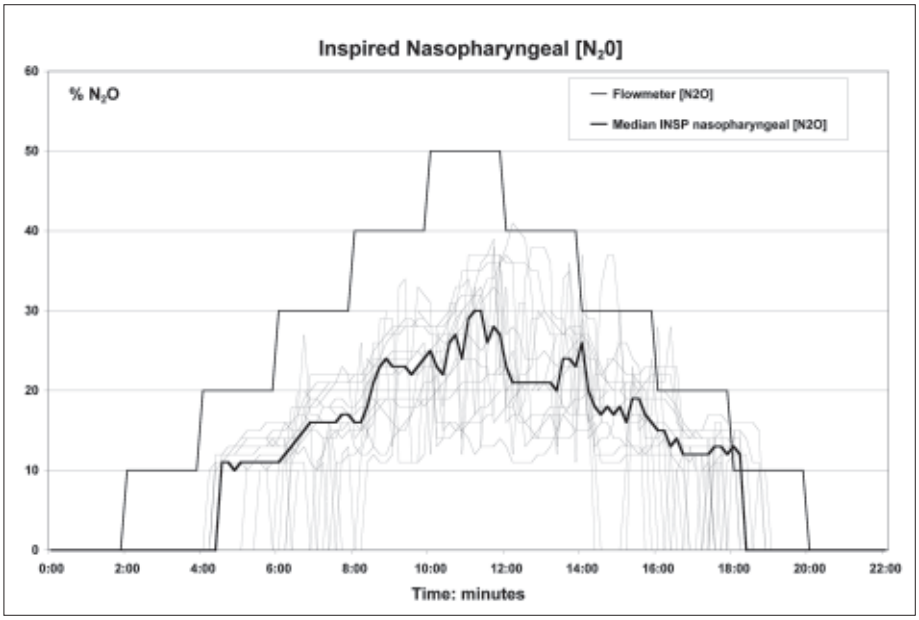


Figure 1. Inspired nasopharyngeal [$N_2O$] of all subjects and median expired [$N_2O$] vs flowmeter [$N_2O$].

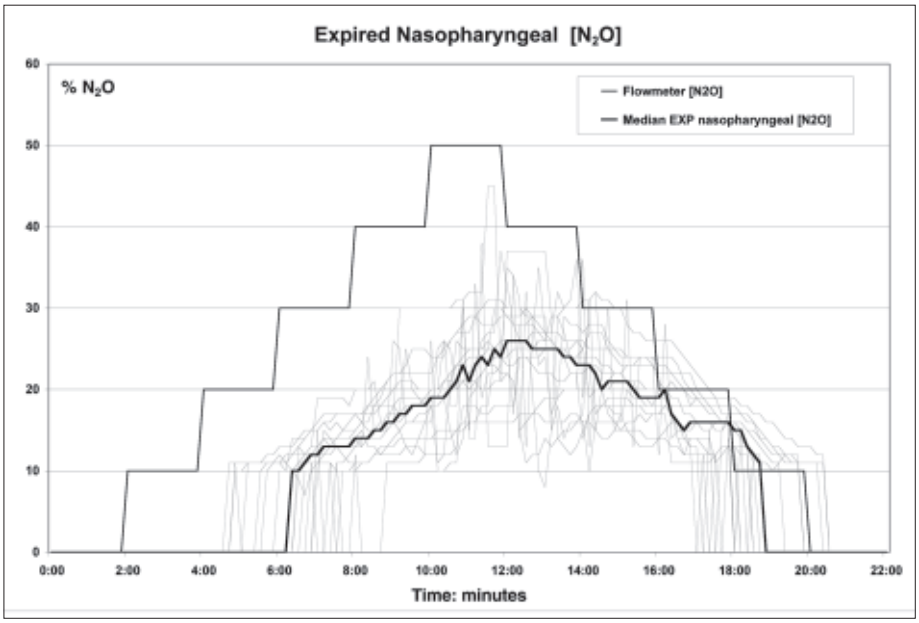


Figure 2. Expired nasopharyngeal [$N_2O$] of all subjects and median expired [$N_2O$] vs flowmeter [$N_2O$].

## Results

Figures 1 and 2 display the data of inspired and expired [$N_2O$]of all 15 subjects as well as the median summary graphs. There were considerable interindividual differences in nasopharyngeal [$N_2O$] at identical flowmeter settings. Inspired and expired [$N_2O$] were consistently lower than the corresponding flowmeter settings during the phase of increasing $N_2O$. During the phase when [$N_2O$] were decreased, clearing of dissolved $N_2O$ frequently increased expired [$N_2O$] above flowmeter values. At the beginning of each experiment, $N_2O$ could only be measured after the unit delivered concentrations greater than or equal to 20%. During the final period of $N_2O$ washout, expired $N_2O$ could not be detected in any subject 30 seconds after 100% oxygen was delivered.

Inspired [$N_2O$] in the nasal mask were, on average, 31% lower than those dispensed by the gas delivery unit and decreased by another 19% on the way to the nasopharyngeal sampling site (Figure 3). This represents an overall average 50% decrease in $N_2O$ delivery from the flowmeter to the nasopharyngeal sampling site. These 3 curves were significantly different at the $P$=.01 level. The inspired nasal mask concentrations were significantly different ($P$=.05) from the inspired nasopharyngeal concentrations in the interval between 8 and 14 minutes.

During the phase of increasing $N_2O$, average expired nasopharyngeal [$N_2O$] were 22% lower than inspired concentrations. In this time period, it took approximately 2 minutes longer for expired [$N_2O$] to reach the same level as inspired [$N_2O$]. When $N_2O$ was decreased, the effect was reversed, with half the lag time and average expired [$N_2O$] 18% higher than inspired (Figure 4). During the entire study period, expired nasopharyngeal $N_2O$ concentrations were, on average, 51% lower than the flowmeter readings suggested.

Differences during expiration were small and occurred mainly during the phase of increasing $N_2O$. Mean $P_{ET}CO_2$ was 39.7±1.4 mm Hg and mean RR 13.4±1.2 breaths/min.

## Discussion

The literature provides ample recommendations for the therapeutic [$N_2O$] needed to produce a clinical effect.[2-6,13,15] They vary for ambulatory settings between 10% and 70% and are titrated to the desired effect. The range for achieving ideal sedation in 70% of all patients lies between 30%

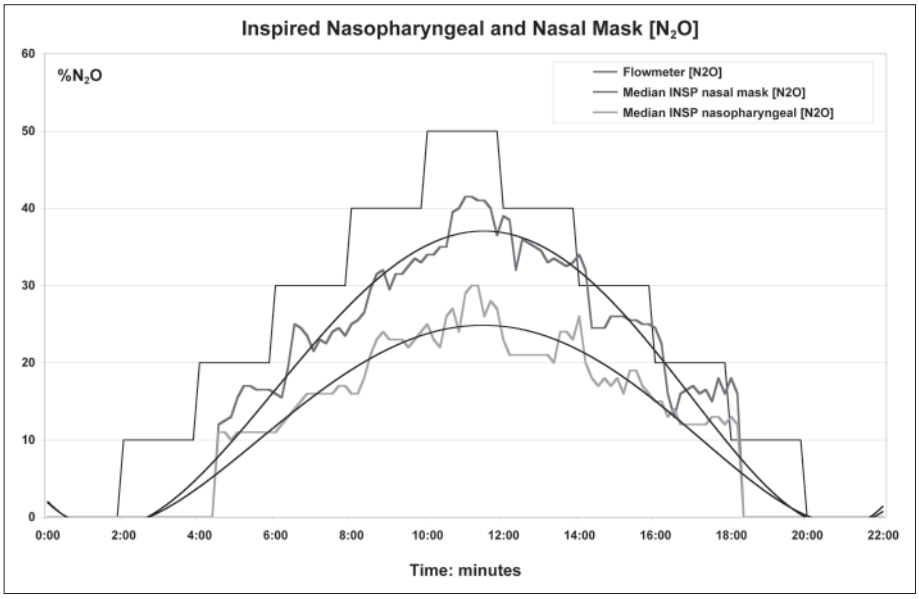


Figure 3. Median inspired nasopharyngeal and nasal mask [$N_2O$] vs flowmeter [$N_2O$]. Dotted lines represent sixth order polynomial trendlines.

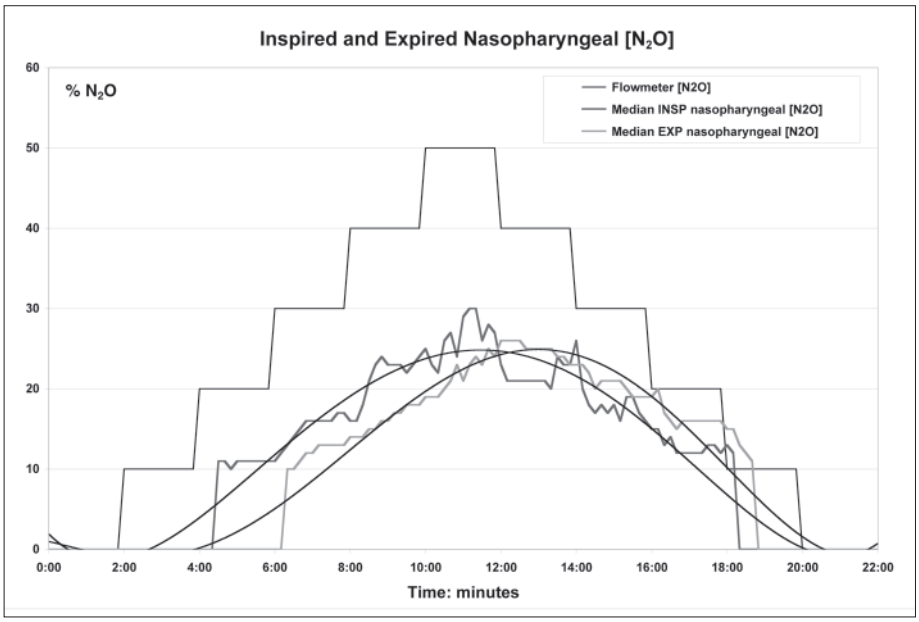


Figure 4. Median inspired and expired nasopharyngeal [$N_2O$] vs flowmeter [$N_2O$]. Dotted lines represent sixth order polynomial trendlines.

and 45% [$N_2O$].[2,6] The threshold for $N_2O$-induced behavioral effects begins at 10%, and memory is affected at concentrations of 20% to 30%.[16] MAC awake (the minimum alveolar $N_2O$ concentration at which 50% of patients do not respond to commands) equals 55% to 75% $N_2O$ and is age dependent.[17] Despite these observations, it has not been precisely described if these concentrations reflect flowmeter settings or true alveolar concentrations.

The advantages of $N_2O$ include a high MAC (minimum alveolar concentration for an inhaled anesthetic at 1 atmosphere that prevents movement in response to a noxious stimulus) that produces a sufficiently high margin of safety. Its low blood-gas solubility coefficient allows rapid induction and recovery.

In contrast to general anesthetics, measurement of [$N_2O$] during conscious sedation for dental procedures is limited by the open delivery system and by presence of airway reflexes, making proper sampling probe placement in alert, nonintubated individuals difficult. During conscious sedation procedures, a variety of probe designs and loci for probe placement as well as capnographic measurements have been published. Sample lines were either inserted inside the nasal mask with a Luer lock attachment mechanism or into foam inserted into a nostril.[18-20] Prong-shaped $O_2$ delivery or $CO_2$ sampling devices, that reach approximately .5 inch into both nostrils, have also been described.[21] Although ease of placement was an advantage of these measurement techniques, dislodgment, clogging, suction-induced attachment to nasal mucosa, or underestimation of $P_{ET}CO_2$ occurred. Because such measurement techniques yield erroneous data when the mouth is open or breathing is irregular, they are impractical for monitoring during dental treatment in sedated or uncooperative patients. In contrast, this measurement system allows the determination of average [$N_2O$] during dental treatment.

Both in vivo and in vitro studies have measured the gradients between dispensed [$N_2O$] and airway dilution. The authors of an in vitro study[22] applied a 50% $N_2O$/50% $O_2$ mixture to an analog lung model with a tight sealing breathing mask and measured [$N_2O$] at the subglottic level. At a flow rate of 6 L/minute, the mask delivered concentrations of 34% $N_2O$/44% $O_2$. In an in vivo study in a dental setting, $N_2O$ was administered to 25 adult subjects with a nasal mask to reach a "pleasant and adequate" level of sedation.[23] With an average 45% $N_2O$ flowmeter setting, $N_2O$ concentrations declined from 23% in the mask to 16% in the pharynx at the tonsillar level.

Others[24,25] have described that $N_2O$, $O_2$, and sevoflurane concentrations as well as $P_{ET}CO_2$ were measured and recorded every 5 minutes through a probe in the nasal mask,

but failed to validate their findings with $P_{ET}CO_2$ measurements. Therefore, it remains unclear whether these reported values represent true end-expired alveolar concentrations or those dispensed by the vaporizer.

Valid $P_{ET}CO_2$ measurements were reported in an experimental study in which breathing patterns in children, who received 40% $N_2O$ for 15 minutes after oral midazolam administration, were evaluated.[26] Nitrous oxide and $O_2$ concentrations could be continuously measured and recorded from a sample line inserted into a tight-sealing facemask that was applied over the nose and mouth. This technique is not applicable to dental practice, however, because it makes the oral cavity inaccessible.

Others have described postoperative long-term $P_{ET}CO_2$ measurements with a nasal catheter in 19 adult patients who were undergoing major surgery.[27] The authors recorded meaningful capnograms even from somnolent or mouth-breathing patients, validating this methodology and confirming a favorable sample line location in the posterior nasopharynx. They found a correlation coefficient of $r$=0.82 between clinical $P_{ET}CO_2$ and $PaCO_2$ obtained from simultaneous arterial blood samples.

In contrast, falsely low $P_{ET}CO_2$ readings were reported in 2 somnolent, predominately mouth-breathing patients when modified nasal prongs were used as a probe.[21] After they were asked to close their mouths and breathe nasally, $P_{ET}CO_2$ increased immediately to physiologic values. These authors also reported no significant differences between arterial $PaCO_2$ and $P_{ET}CO_2$ tensions, whether sampling was done with nasal cannulae or endotracheal tubes.

Unlike previous studies that either failed to confirm their findings with valid $P_{ET}CO_2$ data or used clinically inapplicable methods, this study demonstrated that continuous monitoring of [$N_2O$] and [$O_2$] as well as $P_{ET}CO_2$ in conscious adult subjects with a sampling probe seated in the posterior nasopharynx is possible and yields reproducible data. Such an objective measurement method meets demands for evidence-based dental practice. The authors used this technique initially in adult volunteers to validate the methodology and ensure cooperation.

Although none of this study's subjects was given instructions on breathing techniques to obtain normal $P_{ET}CO_2$ measurements, this study yielded a $\pm P_{ET}CO_2$ of 39.7, with a low standard deviation of 1.4 for all subjects and an average respiratory rate of 13.4±1.2 breaths/minute. These results indicate a consistently well-functioning sampling probe in proper position. Its placement in the nasopharynx appears to be the closest possible approximation to measuring gases in an endotracheal tube. This study's modified probe tip design elevates and prevents the distal end from curving towards the nasal mucosa, thus avoiding contamination with normal quantities of mucus or adherence to the nasal mucosa. By taping the sampling line to the upper lip, it followed the patient's head movements and did not dislodge nor interfere with the nasal mask. With this methodology, [$N_2O$] can be continuously measured during dental treatment.

These findings demonstrate that, even under well-controlled circumstances with cooperative subjects, alveolar [$N_2O$] differs significantly from flowmeter settings. Air entrainment reduces [$N_2O$] delivered by the gas delivery unit on average by 31% in the nasal mask and by another 19% on the way to the nasopharynx (Figure 3). Inspired nasopharyngeal [$N_2O$] was, on average, 50% lower than that suggested by flowmeter settings ($P$=.01). Due to the small sample size and considerable intersubject variation, nasal mask and nasopharyngeal concentrations were significantly different only in the period from 8 to 14 minutes ($P$=.05).

When equating expired nasopharyngeal [$N_2O$] as the closest approximation to alveolar concentration, the authors found that alveolar [$N_2O$] was, on average, 51% lower than that dispensed by the gas delivery unit. Expired nasopharyngeal [$N_2O$] was 22% lower during the first half of the experiment when $N_2O$ was incrementally increased. During the second half, however, when $N_2O$ was decreased, expired concentration exceeded inspired concentration by 18% (Figure 4). It took approximately 2 minutes longer for expired [$N_2O$] to reach the same as inspired [$N_2O$]. During the phase of decreasing [$N_2O$], the effect was reversed with a 1-minute time difference. These time lags can be interpreted as the time periods needed to saturate the blood with $N_2O$, followed by the time of $N_2O$ washout. No $N_2O$ could be detected in any subject after 30 second of 100% oxygen delivery. During expiration, nasopharyngeal and mask readings were not significantly different, because air entrainment plays a role only during inspiration, when subatmospheric airway pressures exist.

This study's results, demonstrating 31% and 19% decreases in [$N_2O$] from delivery unit to the nasal mask and nasopharynx, respectively, fall within the degrees of dilution reported in 2 studies mentioned previously. One such study, using a dental mask delivery system, reported reductions of [$N_2O$] of 49% in the mask and 65% in the pharynx at the level of the tonsils.[23] In the artificial lung model experiment,[22] [$N_2O$] decreased by 32% when measured at the subglottic level. The higher dilution factor in the first study can be explained by methodological constraints, whereas in vitro conditions and the use of a well-fitting, full-breathing mask (Hudson variable performance mask) likely contributed to reduced air entrainment observed in the artificial lung model.

Additional factors that can contribute to inadequate $N_2O$ delivery during daily practice are:

1. incorrectly calibrated flowmeters;
2. improperly adjusted scavenging rates;
3. increased entrainment of room air through ill-fitting standard nasal masks that do not conform well to a patient's facial anatomy.[28]

A nasal mask can further become dislodged by head movements of uncooperative patients or inadvertently by the care providers.

Development of this novel sampling method was undertaken in adults to ensure cooperation and to obtain baseline measurements. It is unclear if these findings can be directly applied to children given the anatomical differences between these age groups. Future studies should be conducted on children to validate this methodology for a younger age group and should include a larger sample size to increase statistical validity.

## Conclusions

Based on this study's results, the following conclusions can be made:

1. Nasopharyngeal [$N_2O$] varied markedly from flowmeter settings and amongst individuals.
2. Close correlation of $P_{ET}CO_2$ with expected physiologic values validates sampling methodology.
3. This novel sampling method obtains accurate, continuous, and real-time measurements of all inhaled and exhaled gases in the conscious dental patient.
4. Suggested probe placement and design provide reliable capnographic measurements and do not interfere with nasal masks or dental treatment. The sampling line does not dislodge nor obstruct easily.
5. During the phase of increasing $N_2O$, expired [$N_2O$] trailed inspired [$N_2O$] by 2 minutes, whereas when $N_2O$ was decreased, the effect was reversed with a 1-minute time difference.
6. During the final period of $N_2O$ washout, expired $N_2O$ could not be detected in any subject 30 seconds after 100% oxygen was delivered.


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## Abstract of the Scientific Literature

### The Significance of Needle Deflection in Success of the Inferior Alveolar Nerve Block in Patients With Irreversible Pulpitis

The purpose of this prospective, randomized, blind study was to compare the efficacy of 2 inferior alveolar injection techniques (conventional technique vs the wand) in adult patients diagnosed with irreversible pulpitis. Sixty-four emergency patients participated in the study and randomly received 2.8 ml of 2% lidocaine with 1:100,000 epinephrine, using either one of the injection techniques. An additional long-buccal anesthesia was provided using the standard syringe technique. Only one operator administered the local anesthetic. Seventeen minutes following injection and after verification of lip numbness as a sign for profound anesthesia, a rubber dam was placed and endodontic access began. Patients assessed pain using a visual analogue scale at 3 different stages: (1) within dentin; (2) entering the pulp chamber; or (3) initial file placement. The success rate was 50% for the conventional technique and 56% for the wand technique, with no statistically significant differences between the 2 groups. These results agree with other studies conducted on irreversible pulpitis patients.

**Comments**: Clinicians must realize that lip numbness does not guarantee successful pulpal anesthesia, and other supplemental techniques such as intraosseous or periodontal ligament are necessary to achieve pulpal anesthesia. It was also important to see that, as with pediatric patients, the use of the wand in adults was not more effective than the traditional syringe technique. **MG**

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**Kennedy S, Reader A, Nusstein J, Beck M, Weaver J. The significance of needle deflection in success of the inferior alveolar nerve block in patients with irreversible pulpitis. *J Endod.* 2003;29:630-633.**
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