

# INDC Inland Northwest Dental Conference

April 24 - 25, 2025 Spokane, WA



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## Nitrous Oxide and Dental Personnel Concerns

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### Our Clinician:



**Dr. Mark Donaldson BSP, RPH, PHARMD, FASHP, FACHE** received his baccalaureate degree from the University of British Columbia and his Doctorate in Clinical Pharmacy from the University of Washington. He completed a residency at Vancouver General Hospital, and has practiced as a clinical pharmacy specialist, clinical coordinator and director of pharmacy services at many healthcare organizations in both Canada and the United States. He resides in Whitefish, Montana and is currently the Associate Principal of Pharmacy Advisory Solutions for Vizient.

Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, and Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last 25 years focusing on dental pharmacology and dental therapeutics, and is a leader in the field.

Dr. Donaldson has published numerous peer-reviewed works and textbook chapters. He currently serves on the Editorial Board for the Journal of the American Dental Association, is board certified in healthcare management and is the Past-President of the American College of Healthcare Executives' Montana Chapter. Dr. Donaldson was named as the 2014 recipient of the Bowl of Hygeia for the state of Montana and is the 2016 recipient of the Dr. Thaddeus V. Weclaw Award. This award is conferred upon an individual who has made outstanding contributions to the art and science of dentistry and/or enhanced the principles and ideals of the Academy of General Dentistry. This year, Dr. Donaldson was conferred by the Canadian Dental Association (CDA) in Ottawa with the, "Special Friend of Canadian Dentistry Award for 2019." This award is given to an individual outside of the dental profession in appreciation for exemplary support or service to Canadian dentistry and/or to the profession as a whole.

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April 24, 2025

Spokane, WA

# Nitrous Oxide – Oxygen Administration: Contamination and Scavenging

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Introduction to potential health hazards of trace anesthetics and proposed techniques for limiting occupational exposure.

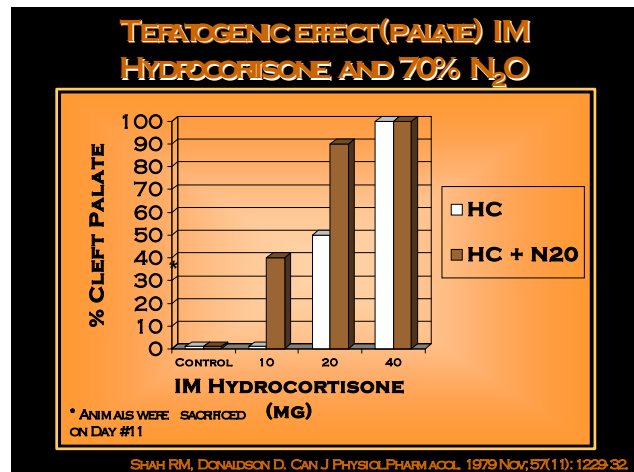
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## Animal Studies

Several studies have examined the effects of nitrous oxide on the development of animal embryos with inconsistent results. Discrepancies between these conclusions are due to:

- Different animals
- Different gas concentrations
- Different times during pregnancy of exposure
- Different durations of exposure

*Mutagenicity tests of other inhalational anesthetics have also provided no evidence of carcinogenicity or organ toxicity, although some animal studies indicated that chronic exposure to nitrous oxide concentrations of 1000 ppm or higher can result in teratogenicity.*



## Human Studies

**Cohen 1975:** Retrospective Questionnaire defined

Levels of Exposure as:

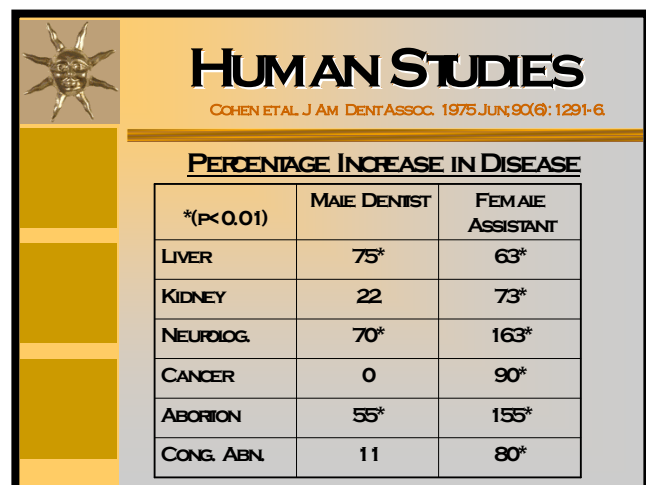
0	None
1-2999 hours	Light
≥ 3000 Hours	Heavy

Return Rate: 70%

Dentists:	21,000/120,000
Assistants:	22,000/150,000

### Epidemiological Errors:

- Retrospective
- Inadequate Control
- Incomplete Return
- Biased Return
- Unknown Exposure
- Unsupported by other studies
- Unsupported Diagnosis of defect



## Other Notes or Questions to Ask:

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**Cohen 1980** (Heavily Exposed is redefined as >8 hours per week):

Heavily Exposed Dentist

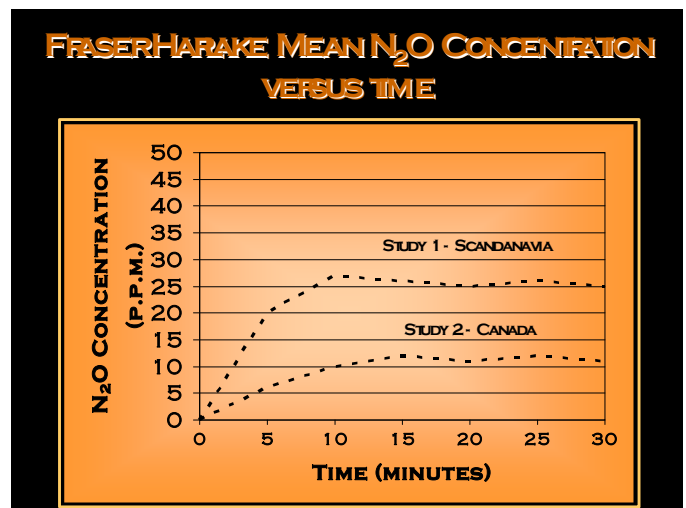
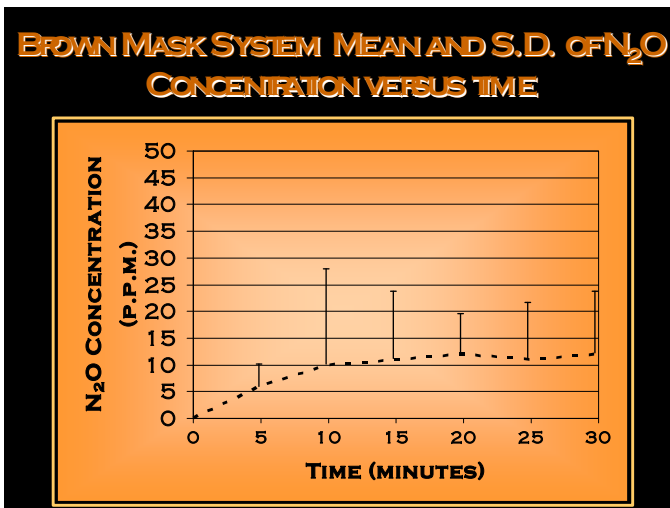
- 1.7 fold increase in liver disease
- 1.2 fold increase in kidney disease
- 1.9 fold increase in neurological disease
- 1.5 fold increase in spontaneous abortions in wives

Female Assistants Exposed

- 1.6 fold increase in liver disease
- 1.7 fold increase in kidney disease
- 2.8 fold increase in neurological disease
- 2.3 fold increase in spontaneous abortions
- 1.5 fold increase in Cancer Rates

**N<sub>2</sub>O Contamination Factors**

- 1. Movement 48%
- 2. Talking 46%
- 3. Mask Leakage 17%
- 4. Poor Suction 13%
- 5. Laughing 11%
- 6. Mouth Breathing 7%
- 7. Moustache 5%



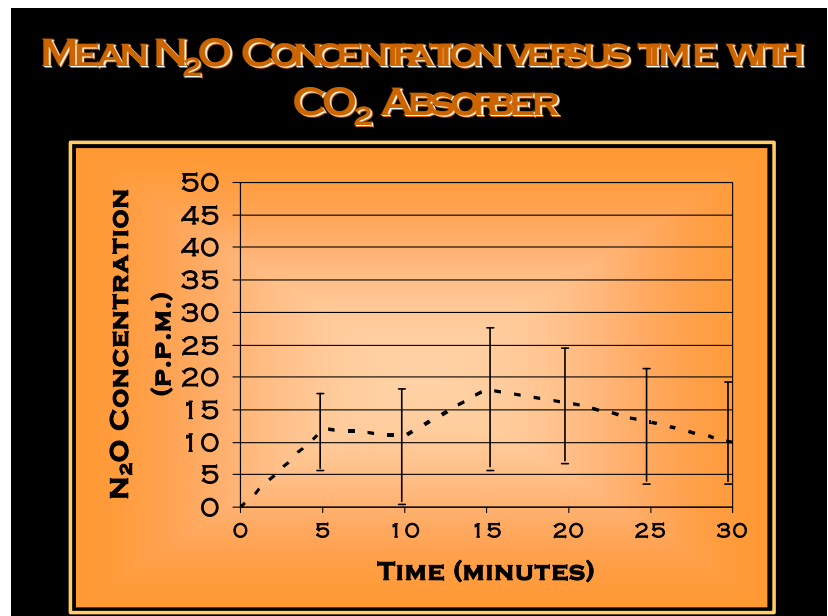
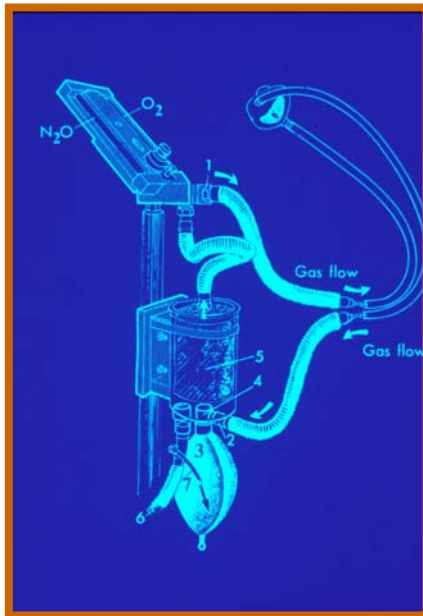
**Comparison of the Tested Masks**

<u>N</u>	<u>Mask Type</u>	<u>Mean ppm N<sub>2</sub>O</u>
35	Brown	43.4
29	Porter	48.2
24	Parkell	54.4
23	Dupaco	61.2
33	Fraser- Harlake	62.7

**Other Notes or Questions to Ask:**

## Carbon Dioxide Absorber

How can we minimize occupational exposure?



**Tomaszewski L, Nadworny J, Zmudzka B. Vitamin B-12 and sterility. Pol Tyg Lek. 1964;19:1915-8.**

- ↑ Vit B12 = increases human sperm motility
- ↓ Vit B12 = increases human infertility

**Shah NK, Kripke BJ, Sanzone CF, Cosman EB. Histological evaluation of cutaneous wound healing in presence of nitrous oxide in rats. Anesth Analg. 1978;57(5):527-33.**

- Effect of 20% N<sub>2</sub>O on rat spermatogenesis after 5-week exposure:
- Decreased sperm count
- Abnormal multinucleated giant cells
- Total recovery after 3 days

**Volchansky A, Viera E. Some extrinsic factors in the aetiology of periodontal disease I. J Dent Assoc S Afr. 1983 Mar;38(3):192-5.**

“Concentrations at which there were no longer significant effects of nitrous oxide on rat litter size over a 10-day exposure period were between 3250-3500 ppm”

**Brodsky JB, Baden JM, Serra M, Kundomal Y. Nitrous oxide inactivates methionine synthetase activity in rat testis. Anesthesiology. 1984 Jul;61(1):66-8.**

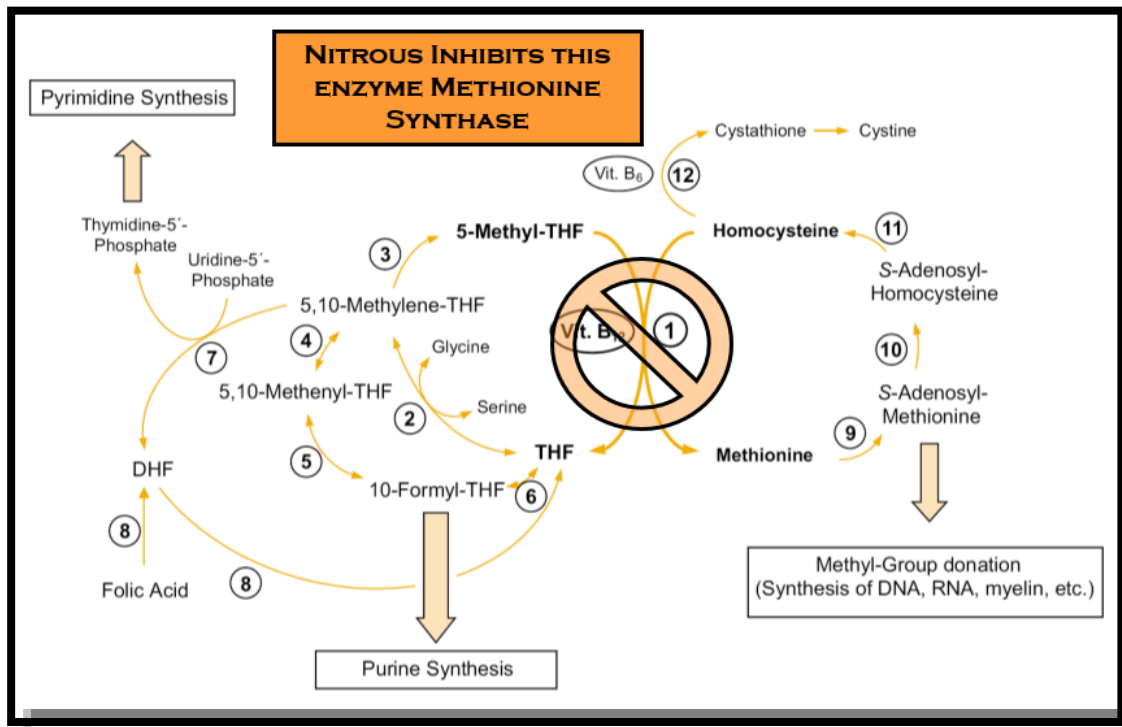
### Effect of N<sub>2</sub>O on rat testicular methionine synthetase activity after 1 hour exposure

Level	Exposure	Reduction	Recovery
10%	1 hour	29%	48 hours
50%	1 hour	63%	72 hours

**Other Notes or Questions to Ask:**

**Sweeney B, Bingham RM, Amos RJ, Petty AC, Cole PV. Toxicity of bone marrow in dentists exposed to nitrous oxide. Br Med J (Clin Res Ed). 1985 Aug 31;291(6495):567-9.**

- Deoxyuridine suppression test on dentists using nitrous oxide suggest 400 ppm as a safe level
- Provided the first direct evidence that occupational exposure to N<sub>2</sub>O can result in altered vitamin B<sub>12</sub> metabolism and impaired synthesis of methionine synthase (a crucial enzyme for DNA formation)



The MTHFR gene provides instructions for making an enzyme called **methylenetetrahydrofolate reductase**. This enzyme plays a role in processing amino acids, the building blocks of proteins. Methylenetetrahydrofolate reductase is important for a chemical reaction involving forms of the vitamin folate (also called vitamin B9). Specifically, this enzyme converts a molecule called 5,10-methylene-tetrahydrofolate to a molecule called 5-methyltetrahydrofolate. This reaction is required for the multistep process that converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds. A study in 2000 had identified only 24 cases of severe MTHFR deficiency (from nonsense mutations) across the whole world (*Sibani, Sahar; Christensen, Benedicte; O'Ferrall, Erin; Saadi, Irfan; Hiou-Tim, Francois; Rosenblatt, David S.; Rozen, Rima (2000). "Characterization of six novel mutations in the methylenetetrahydrofolate reductase (MTHFR) gene in patients with homocystinuria". Human Mutation. 15 (3): 280.*)

**Yagiela JA. Health hazards and nitrous oxide: a time for reappraisal. Anesth Prog. 1991 Jan-Feb;38(1):1-11.**

- Evidence is overwhelming that prolonged exposure to clinical concentrations of N<sub>2</sub>O inhibits cellular proliferation of the formed elements of the blood and can lead to megaloblastic anemia, leukopenia and thrombocytopenia.
- A time-weighted average of 100ppm for an eight-hour workday and/or a time-weighted average of 400ppm per anesthetic administration would provide adequate protection of dental personnel.

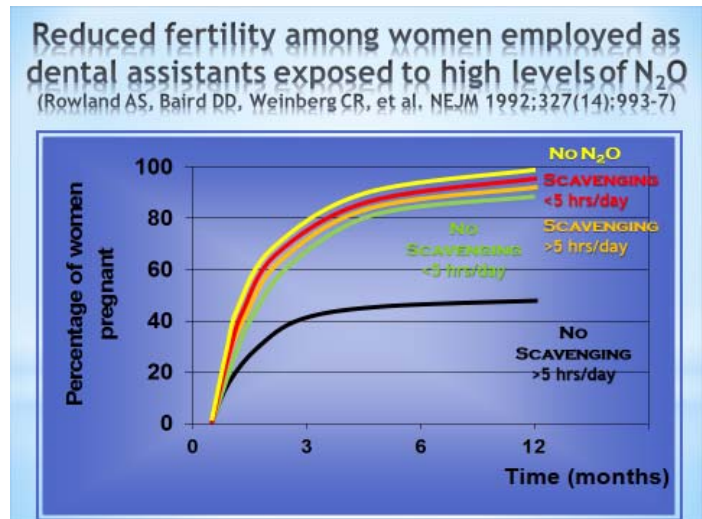
**Other Notes or Questions to Ask:**



**ADA guidelines are 50 ppm TWA for offices,  
25ppm TWA for hospital settings**

**ADA Workshop Panel Conclusions**

1. N<sub>2</sub>O/O<sub>2</sub> is a very valuable tool for pain and anxiety control and it should continue to be taught at all levels of dental education.
2. Chronic occupational exposure to N<sub>2</sub>O/O<sub>2</sub> in offices without scavenging units may be associated with deleterious neurological and reproductive effects on the health of dental personnel.
3. Where scavenging systems are used there has been no such evidence to date. Appropriate scavenging systems and methods of administration should be adopted.
4. It should be clearly indicated that potential health hazards of N<sub>2</sub>O do not apply to the patient.
5. N<sub>2</sub>O levels vary significantly among offices using scavenging systems. Therefore a protocol should be implemented.
6. State dental boards regulate certification programs requiring evidence of satisfactory completion of educational programs.

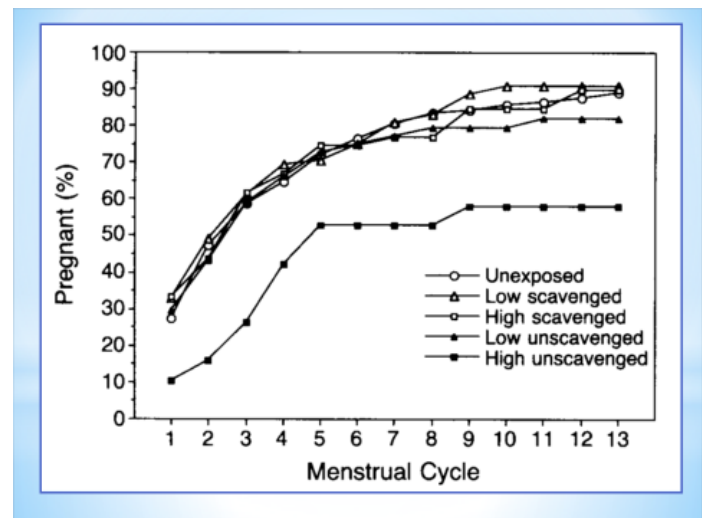


**Recommended Checklists**

On Installation - Whole system (spectrophotometer)

- Daily
- Rubber hoses
  - Nasal masks
  - Connectors (high and low pressure)
  - Reservoir bags (visual)

Quarterly - Whole system (spectrophotometer)



**Other Notes or Questions to Ask:**

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## Other Notes or Questions to Ask:

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# Nitrous oxide – Oxygen Administration When Fail-Safe Isn't Safe

*“There has never been a reported mortality in a dental office while using nitrous oxide – oxygen sedation as the sole sedative and dentistry is being performed.”*

*John A. Yagiela, DDS, PhD (1948-2012)*

Early attempts to use nitrous oxide as a sole anesthetic were not successful because of its low potency. With a minimum alveolar concentration (MAC50) of 104% in humans, N2O by itself would require high volume percentage and hyperbaric conditions to achieve anesthesia in 50% of subjects. This scenario is unlikely in any dental office: a characteristic that gives the gas its large, inherent margin of safety.

**Two Main Types of Systems:** Installed (Central) Systems and Portable Systems.

## The 12 Safety Features of Nitrous Oxide – Oxygen Sedation

1. Alarms
2. Color coding
3. Diameter index safety system (DISS)
4. Emergency air inlet
5. Locks
6. Minimum oxygen liter flow
7. Minimum oxygen percentage
8. Oxygen fail-safe
9. Oxygen flush button
10. Pin index safety system
11. Quick-connect for positive-pressure oxygen
12. Reservoir bag

### #1 Alarms (Audible and visual)

- Ritchie whistle
  - Low oxygen pressure alarm
  - Oxygen Failure Warning Device (OFWD)
  - Oxygen failure protection device – Dräger
  - Pressure sensor shut off valve – Datex-Ohmeda
- High pressure oxygen alarm
- Low nitrous oxide pressure alarm
- High nitrous oxide pressure alarm

### **Other Notes or Questions to Ask:**

At least one case is reported of hypoxia occurring during anaesthesia in a spontaneously breathing ASA I patient. The patient became cyanotic twice when breathing a gas mixture delivered by a safety mixer. Changing the machine solved the immediate problem. The diagnosis was difficult to make because the rotameters all showed normal delivery of oxygen and nitrous oxide. Oximetry elucidated the cause, which was found to be a defective rapid oxygen control. Because these machines do not appear to be absolutely reliable, the use of gas analysers should become more systematic.

*Michon-Boyer-Chammard F, et al. Ann Fr Anesth Reanim. 1988; 7(2):165-7.*

### **#2 Color coding**

Gas cylinders are often color coded, but the codes are not standardized across different jurisdictions. In the United States, for example, oxygen cylinders are typically green, even though oxygen cylinders internationally are typically white. For this reason, cylinder color alone cannot safely be used for positive product identification; cylinders have labels which identify the gas they contain and the label should be used for positive identification. The original anoxic technique of anesthesia with nitrous oxide alone often made patients cyanotic which is where the term “blue nitrous” originates and one of the reasons why nitrous oxide tanks are easily identified as blue cylinders in the United States.

- Cylinders (tanks)
- Hoses (lines, pipes)
- Wall plates (outlets)
- Machine knobs

### **#3 Diameter-Index Safety System (DISS)**

The Compressed Gas Association (CGA) developed DISS to establish a standard for non-interchangeable, removable connections for medical gases, vacuum (suction), and evacuation service. Each type of gas and connector is assigned a DISS number (1040 for nitrous oxide and 1240 for oxygen). Nitrous oxide has been assigned the 3/4"-16 thread connection; oxygen has been assigned the 9/16"-18 thread connection. Regardless, there have been DISS failures reported in the literature:

*Hospital Liability: negligent administration of nitrous oxide: construction defect in new hospital: wrongful death. ATLAS. Rep. 1977; 20:379-380.*

*Oxygen-nitrous oxide mix up hits another hospital. Malpractice Lifeline. 1977; 2(23):1.*

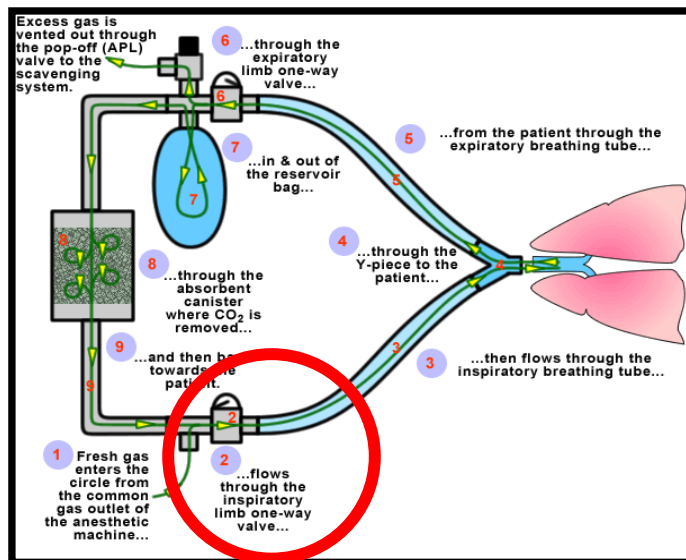
*LeBourdais E. Nine deaths linked to cross-connection: Sudbury general inquest makes hospital history. Dimens Health Serv. 1974 Jun; 51(6):10-2.*

*Robinson JS. A continuing saga of piped medical gas supply. Anesthes. 1979; 34:66-70.*

*Oxygen and nitrous oxide lines reversed: wrongful death: Settlement. ATLAS. Rep. 1978; 21:232.*

### **#4 Emergency Air Inlet**

There is an emergency air outlet that is designed to remain closed as long as gas(es) are being administered to the patient. However, when the oxygen fail safe system turns the gases off, room air is allowed to enter the system so that the patient can continue to breathe through the nasal hood or mask.



### **Other Notes or Questions to Ask:**

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## #5 Locks

Similar to other psychotropic drugs, nitrous oxide may be abused by individuals with access to the drug, including those in the dental profession. According to State fire codes, nitrous oxide and other compressed gases must be kept in locked rooms, but many manufacturers supply additional locks for the machines themselves to dissuade staff from accessing nitrous oxide inappropriately. Examples of some of these locking mechanisms are occur at the tanks themselves, the manifold, or at the level of the mixer.

## #6 Minimum Oxygen Liter Flow

Nitrous oxide – oxygen machines are required to provide a minimum oxygen liter flow of 2.5-3 liters per minute. Since oxygenation of the patient is paramount, this safety feature ensures that the patient always has access to 100% oxygen when the machine is turned on. Regardless of the percentage of gas mix that the patient is receiving, if the nitrous oxide tank were to become empty, this minimum amount of oxygen would continue to flow while the nitrous alarm was alerting the clinician to attend to the tanks.

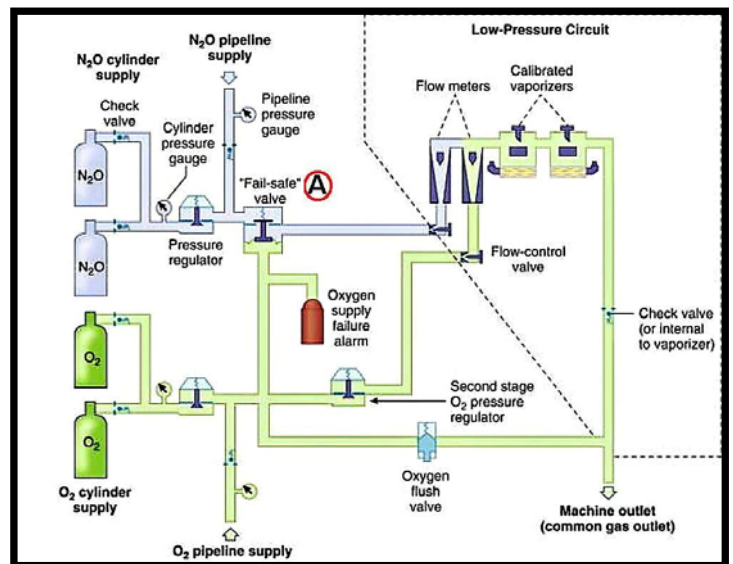
## #7 Minimum Oxygen Percentage

This was one of the initial safety features employed by all manufacturers of nitrous oxide machines to ensure that during gas delivery concentrations of oxygen never fall below 30%. While earlier machines had the ability to give 100% nitrous oxide, they were more commonly found in oral surgery offices or sold as sedation equipment to general dentists in the 1970s. In the 1700s-1800s, the term “Blue Nitrous” was coined as this was the hypoxic technique used to cause sedation and by giving the patient less oxygen than what was available in ambient air, patients would often turn blue. These early anesthesia machines had both nitrous oxide and oxygen flush valves; currently only oxygen flush valves are permitted. The back-ups to this minimum oxygen percentage safety feature are the low oxygen pressure alarm, the pressure sensor shut off valve (oxygen fail-safe) which stops the flow of any other gas, and the emergency air inlet safety feature. In fact, “nitrous oxide sedation” is a misnomer and is more correctly referred to as “nitrous oxide – oxygen sedation” since these two gases must now be given in combination. During gas delivery concentrations of oxygen never fall below 30%. Room air has 21% oxygen.

## #8 Oxygen Fail-Safe

The oxygen fail-safe is designed so that the nitrous oxide will automatically turn off when oxygen delivery is compromised or is depleted. It senses only pressure and does not check whether the supplied gas is actually oxygen, however. See “A” in the diagram:

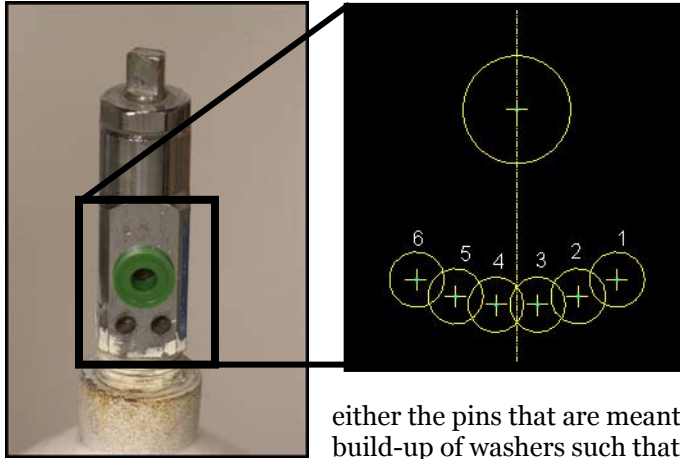
There have been failures of the oxygen fail-safe valve, however, where the internal diaphragm ruptured and the empty oxygen tanks were then back-filled with nitrous oxide. This is perhaps the worst possible scenario since nobody would suspect this flaw, and shutting off the nitrous to give 100% oxygen would actually result in the patient receiving 100% nitrous. This example emphasizes the benefit of simply taking the mask off of the patient thereby allowing them to breathe room air, rather than providing what you believe to be 100% oxygen.



## #9 Oxygen Flush Button

The oxygen flush button is a mechanism that allows for 100% oxygen to be administered through the reservoir in the event of an emergency. It delivers oxygen straight from the pipeline or cylinder regulator at 45-50 psi. The flow rate will be between 35-75 L/min. Unfortunately, there have also been reported failures of this fail-safe mechanism: *Anderson CE, Rendell-Baker L. Exposed O<sub>2</sub> flush hazard. Anesthesiology. 1982; 56(4):328.*

## Other Notes or Questions to Ask:



**#10 Pin Index Safety System**

The Pin Index Safety System uses geometric features on the yoke to ensure that pneumatic connections between a gas cylinder and a machine that uses pressurized gases are not connected to the wrong gas yoke. The units for the pin configurations are in millimeters and for oxygen these pins are at 2 and 5 mm respectively, while they are at 3 and 5mm for nitrous oxide.

Unfortunately, there have also been reported failures of this fail-safe mechanism when either the pins that are meant to engage the holes have fallen off, or if there is a build-up of washers such that the pins cannot engage the holes at all.

**#11 Quick-Connect for Positive-Pressure Oxygen**

Most nitrous oxide – oxygen delivery systems have quick connectors which allow supply hoses to be connected to specific gas connection points. Insertion into an incorrect outlet is prevented by the use of different shapes for mating portions, different spacing of mating portions, or some combination of these: similar in concept to the DISS. In an emergency situation where positive-pressure oxygen is required, perhaps to augment CPR (cardiopulmonary resuscitation) the unique quick-connect compatibility assures immediate access to positive-pressure oxygen anywhere in the office. **Caution** as your caverject may also fit in this connection and the last thing you want to do in an emergency situation is fill an unconscious patients’ lungs with water rather than with air!

**#12 Reservoir bag**

The reservoir bag, also called the breathing bag, is typically an inflatable rubber reservoir bladder where fresh gas entering the circuit is conveyed. The bag is gradually filled as gases enter the circuit and is deflated with inhalation. The reservoir bag is easier for the patient to breathe from than a continuous flow of gas(es). The bag should be maintained partly full. It should not be allowed to overfill as it is difficult for the patient to breathe against this positive pressure. This may also lead to escape of gases around the nose/mouth-piece, causing unnecessary contamination of the ambient office air.

Complete emptying of the bag is also undesirable as this defeats its purpose as a reservoir. An empty bag may indicate that the gas flow is inadequate or a leak is present in the system. Breathing against an empty bag can be very frightening, and this is particularly true for apprehensive patients whom we are trying to relax by administering nitrous oxide – oxygen sedation. With the advent of emergency air inlet valves to allow room air to enter the system if the bag is empty or if the gas flow is inadequate to meet minute volume, this is no longer a problem.

**Best Practices**

Before the initial use of the system for each day, all of the nitrous oxide delivery system components should be inspected for wear, cracks, holes or tears. High-pressure line connections can be tested for leaks quarterly. A portable infrared spectrophotometer can also be used to test for leaks.

*ADA Council on Scientific Affairs, Council on Dental Practice. Association Report: Nitrous Oxide in the Dental Office. J Am Dent Assoc 1997; 128(3):364-5.*

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**Other Notes or Questions to Ask:**

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