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NITROUS OXIDE MANUAL

INTRODUCTION

Nitrous Oxide has played a prominent role in medicine and dentistry as an anesthetic for more than 150 years. Even though nitrous oxide was the first inhalation anesthetic agent discovered, it still remains the most popular anesthetic agent used today. Other agents have been discovered through the years but for various reasons, such as the explosive nature of the agent, have fallen out of favor and been replaced by newer agents. Nitrous oxide, despite periods of waning interest, remains the most important and most commonly used tool for sedation in dentistry today.

When nitrous oxide is administered using modern sedation units that are required to have built-in safety features such as oxygen fail-safe mechanisms which limit the nitrous oxide concentration that can be delivered to a patient, nitrous oxide has an enviable safety record.

Nitrous oxide sedation provides advantages to other sedation modalities for many reasons. First of all, NPO (nothing by mouth) guidelines are not required, intravenous access is not necessary and in most cases patients can be discharged home without an escort because of the rapid washout of the gas. Lastly, nitrous oxide administration presently does not require special permits to provide nitrous oxide sedation to any patient age group.

In summary, nitrous oxide because of its safety record, relative ease of use, minimal effect on patient physiological function and the fact that there are no limits on oral intake before procedures results in a very versatile and safe sedative agent.

HISTORY

Joseph Priestly has been credited with both the discovery of oxygen and nitrous oxide gas in the late 1770's. Priestly observed that when plants and animals were exposed to "nitrous air", they soon died. He made the recommendation that "all would be well if the gas were diluted with ambient air."¹ In 1799, Sir Humphrey Davy became the first person to inhale N_2O and noted the experience to be very pleasurable, euphoric, and used the term "laughing gas" to describe N_2O . He also was the first to appreciate the analgesic properties of N_2O as he noted the reduction of his toothache pain when he inhaled nitrous gas.²

During the years 1800-1844 N_2O was mainly used at social gatherings and sideshows for entertainment. The medical community however, largely ignored N_2O as a tool to control pain/suffering. During the early 1800's surgeries mainly consisted of short procedures due to the inability to control pain and patients often died from either shock or infection if they survived the procedure.

In 1844 Gardner Colton, an itinerant "professor" presented an exhibition in Hartford Connecticut demonstrating the effects of N_2O which was attended by a dentist named Horace Wells. One of the volunteers who attended the demonstration severely gashed his leg after inhaling N_2O gas and Wells astutely noticed that he felt no pain. Wells had long been interested in pain control and was impressed by what he saw and invited "professor" Colton to his office the next day. With Colton administering the nitrous oxide, Wells colleague, Dr Riggs, extracted Wells abscessed tooth and according to Wells he felt no pain and proclaimed "It is the greatest discovery ever made."³ This was the first documented case of clinical anesthesia! In 1864, the American Dental Association officially recognized Wells as discoverer of anesthesia and in 1870 the American Medical Association awarded him the

honor as well. Unfortunately, in the early days of medical research, experiments were often done on oneself, which in the case of Wells led to addiction. Wells became a victim of his own discoveries and took his own life at the age of 33.²

The clinical use of nitrous oxide in dentistry has gone through periods of decline over the years. This was usually coincident with the discovery of other agents or due to problems associated with nitrous oxide such as controlling the concentration of nitrous oxide delivered and more recently, concerns with the health implications of chronic exposure to waste gasses. When it was realized that the anesthetic effect of nitrous oxide gas was mostly due to asphyxia, improvements in the delivery of nitrous oxide were made over the years to guarantee an adequate supply of oxygen was being delivered to the patient to prevent hypoxia. Modern day nitrous oxide sedation units are designed to deliver at least a minimum of 30 % oxygen. The development of effective scavenging systems for nitrous oxide units to minimize waste gas contamination has led to an increase in the utilization of nitrous oxide.

INDICATIONS FOR NITROUS OXIDE SEDATION

As discussed earlier, nitrous oxide initially was used as the sole agent in producing general anesthesia when it was discovered in the mid 1800's. However, unknown to Wells and others was the relatively low potency of the gas which necessitated high concentrations being delivered to the patient to be effective. Also, equally problematic, was the difficulty in delivering high enough concentrations of the gas with the crude delivery systems (Ox bladders) that were available to them. Nose clamps were applied to prevent the entraining of room air which diluted the anesthetic gas breathed by the patient. Today, nitrous oxide when used as the sole anesthetic agent is:

1. **Primarily used to allay the anxiety and fear of patients** who are undergoing procedures such as dental care. Because of its low potency, nitrous is incapable of inducing general anesthesia in most cases, but provides the practitioner with an excellent tool for accomplishing anxiolysis in the anxious patient.
2. **Secondarily, nitrous oxide has analgesic properties** even at fairly low concentrations, which has distinct advantages when performing traumatic or routine dental procedures.
3. Lastly, though underappreciated, nitrous oxide administration requires the concurrent delivery of oxygen which provides for the medically compromised patient **a continuous supply of relatively high concentrations of oxygen.**

Therefore, in summary, nitrous oxide sedation has wide applications in dentistry ranging from short to long treatment appointments. Listed below are examples of procedures where nitrous oxide sedation has proven to be beneficial and the rationale:

1. **Diagnosics** (X-ray films, clinical exams etc) – Sedation, reduces pain and gag reflex
2. **Minor procedures** (impressions, placement of orthodontic bands, suture removal etc) - Sedation, pain control. There are a myriad of short procedures done in dentistry which unfortunately can be the source of significant pain. In many instances, nitrous oxide can provide adequate analgesia to accomplish these treatments without the use of local anesthesia.
3. **Periodontal** (probing, scaling, root planing) – Sedation, raises pain threshold (analgesic effect) which may obviate the need for local anesthesia in the sensitive patient.
4. **Restorative** (fillings, crown and bridge) – Sedation, pain control. In some instances when the carious lesion is small, local anesthesia may be omitted when nitrous oxide is used (especially useful in the pediatric population). However, in most cases, local anesthesia is used to manage pain and nitrous oxide will serve as an adjunct to local anesthetics for pain control as well as providing sedation. Nitrous oxide dulls the sounds (high speed drill) and vibrations that occur during restorative procedures.
5. **Surgical** (periodontal, oral surgery, endodontic, implant placement) – Sedation and pain control. The stimulus during surgical procedures can be intense, therefore, any modality that lessens the patient's awareness of the procedure is beneficial

The use of nitrous oxide is widespread across the healthcare industry. Below is a partial list of the various disciplines that take advantage of the sedative/analgesic properties of nitrous oxide.

1. **Cardiology** - used as a safe and efficient way to reduce anxiety and discomfort caused by invasive cardiac procedures⁴ and transcutaneous cardiac pacing.⁵
2. **Dermatology** - Used as a safe, easily administered, inexpensive agent that provides pain control in various procedures such as liposuction, hair transplantation and skin cancer removal.⁶
3. **Emergency Medicine** - Nitrous oxide use in the emergency department is extensive; reduction of fractures, suturing of facial lacerations, relief of severe pain during ambulance transport, pain relief during acute myocardial infarctions to name a few.^{7,8,9,10} Nitrous is ideal for these emergency situations as IV access is not necessary, fasting (NPO) guidelines do not apply; clinical effect (pain relief) and recovery are rapid and ease of administration make nitrous oxide an attractive option for use.
4. **Gastroenterology** - The addition of self-administered nitrous oxide offered significant benefits in the area of patient discomfort during flexible sigmoidoscopy¹¹ as well as endoscopy.¹²
5. **Obstetrics** - Entonox (Nitrous oxide 50%) is used extensively in other countries (Great Britain, Australia, Canada etc) for the control of pain during labor and delivery. Nitrous oxide is administered when needed (intense contractions) and discontinued when labor pain wanes. This method of pain control results in almost immediate pain relief (< 1 minute) and is associated with fewer complications (shorter hospital stay, low blood pressure, complications of epidural block etc).¹³
6. **Radiology** - Nitrous oxide has been found to be effective for behavior (sedation) and pain control for imaging studies, especially in the pediatric population.¹⁴ Radiological imaging techniques oftentimes require invasive procedures which are painful or result in claustrophobia (MRI's). Nitrous oxide has been used with good results in these scenarios.
7. **Urology** - found to significantly reduce pain associated with minor invasive procedures such as cystoscopy.¹⁵

CONTRAINDICATIONS TO NITROUS OXIDE USE

There are few contraindications for the use of nitrous oxide sedation. Below is a list of these contraindications (relative and absolute) with a more detailed discussion to follow in the pharmacodynamics section of this manual.

Relative:

1. **Psychiatric disorders** - Nitrous oxide has been used successfully in patients with personality and psychiatric disorders, however, should be used with caution in schizophrenic, bipolar and moderate to severe mental delay (retardation) disorders. These patients are often treated with many psychotropic agents and the addition of nitrous oxide may further alter disposition leading to unpredictable results¹⁶ (E.g., combative, uncooperative)
2. **Drug abuse** - a history of drug abuse (including alcohol) presents a conundrum for the practitioner. The patient may request nitrous oxide sedation as a means of obtaining a "high". However, these patients develop a tolerance and may insist on high levels of nitrous oxide or may be unsatisfied with the results ("I didn't feel any effect"). In any case, these patients should be carefully screened and strict guidelines for the sedation should be laid out.
3. **COPD (chronic obstructive pulmonary disease)** - Use with caution (discussed in detail in the pharmacodynamics section)
4. **Pregnancy** - generally considered to be the safest agent available (quick onset, quick washout) if sedation is needed (E.g., extreme anxiety). However, elective dental treatment (including nitrous sedation) should be avoided during pregnancy, especially the first trimester. (discussed in detail in the pharmacodynamics section)^{17,18}
5. **Bowel obstruction** - Nitrous oxide will expand gas-containing spaces in the case of an obstructed bowel. These patients will not likely be seen in an outpatient setting except for possible emergency care. The expansion of the enclosed space (air pocket) would not likely expand the intestine appreciably to impair lung function when using nitrous oxide for short periods of time (< 1 hour).¹⁹

Absolute:

6. **Inability to use a nasal mask** – This includes a wide spectrum of clinical scenarios which include; severe mental disease (see above), pre-cooperative children, severe claustrophobics and those with obstruction to airflow. These conditions are in large part seen in the nasal passages and result as either an anatomical or disease-induced nasopharyngeal obstruction. These conditions include; deviated septum, nasal polyps (benign growths in nose), upper respiratory infections, allergic rhinitis and severe sinusitis.¹⁶ In any case, these obstructions prevent the intake of nitrous oxide into the lungs.
7. **Inner ear infection or recent inner ear surgery** - Middle ear disturbances, such as ear infections or recent surgery, would contraindicate the use of nitrous oxide sedation as nitrous gas diffuses into closed spaces resulting in increased pressure in the middle ear. This increased pressure can result in headaches, rupture of the tympanic membrane, hearing loss as well as surgical graft displacement.^{20,21,22}
8. **Pneumothorax** - As mentioned previously, nitrous oxide diffuses into closed or air filled spaces. In the case of a patient with a pneumothorax (air in the pleural cavity), 75% nitrous oxide can double the size of the air pocket in 10 minutes.²³ It is doubtful that this patient would present to the dental office for routine care, but in the remote chance that they do, the practitioner must appreciate the sequelae of using nitrous on this patient (further collapse of the lung).
9. **Patient refusal** - The patient ultimately consents to treatment and it is an absolute contraindication to use nitrous oxide for a patient that does not want it. This can result from either a prior unpleasant experience with nitrous oxide, concerns with side effects of the drug or may be simply a lack of desire by the patient to undergo sedation.

ADVANTAGES OF INHALATION SEDATION

When considering the administration of medications to patients for the purpose of anxiolysis, the practitioner needs to examine the state regulations regarding the use of sedative agents. Certification (sedation permit) by the Dental Board is required when conscious (moderate) sedation is intended. Nitrous oxide sedation, however, when used as the sole agent, does not require a special permit from the Dental Board. The ADA in its guidelines for teaching pain control and sedation to dentists and dental students, states that competency in nitrous oxide sedation can be accomplished at the pre-doctoral level provided the course fulfills the clinical and didactic requirements (14 hours of didactic and clinical exposure). Therefore, one of the major advantages to nitrous oxide administration is the minimal regulation by the Dental Board. Therefore, it should be readily apparent that this is not an oversight on the part of the Dental Board, but a testimony to the safety record of nitrous oxide sedation. With this background in mind, an outline of the advantages of nitrous oxide sedation will be laid out.

1. **No special permit required by Dental Board** (check individual State Dental Boards for regulations)
2. **Special monitoring equipment is not mandatory** - However; there is value to the use of monitors such as pulse oximetry, and EKG's in the case of medically compromised patient. But, when nitrous oxide is used as the sole sedative agent this is optional and basic understanding of the data output is necessary for interpretation. However, this does not excuse the practitioner from vigilant visual monitoring of the patient throughout the procedure.
3. **Rapid onset of action and peak clinical effect** - Compared to other routes of administration, nitrous oxide sedation approaches IV sedation in speed of onset (<30 secs). Other routes (oral, rectal, IM) of administration have prolonged latency periods (>30 mins). Also, nitrous oxide due to its insolubility in tissues reaches maximal clinical effect in less than 5 minutes. This equals and surpasses most commonly used IV administered sedative medications.
4. **No venipuncture required** - A much underappreciated advantage of inhalation sedation. This is especially valuable in the pediatric and needle phobic patient.
5. **Rapid reversal of sedation** - As mentioned above, due to its insolubility in tissues, nitrous oxide levels in the body can be altered rapidly. This is invaluable in the unfortunate occurrence of an oversedated patient as the depth of sedation can quickly be decreased. This one characteristic alone results in the remarkable safety record of nitrous oxide. No other drug administered for sedation has this characteristic. Reversal of sedation requires the administration of "reversal agents" (drug antagonists) specific for that drug class and some classes of drugs (barbiturates) lack a reversal drug.

6. **Ability to titrate** - As described previously, sedation depth can be increased or decreased rapidly. This attribute allows for the depth of sedation to correspond to the level of stimulation (intensity) of the procedure. For example, if the most dreaded part of the dental experience for the patient is the administration of local anesthetic, the level of sedation can be deepened just prior (60 seconds) to injection and then decreased after its completion.
7. **Analgesic effect** - In addition to its primary purpose of anxiety reduction, nitrous oxide also possesses analgesic properties. It must remain clear that this in no way precludes the use of local anesthetics. However, in minor procedures such as scaling, minimal restorations and suture removal, nitrous oxide may provide sufficient pain control.
8. **NPO (nothing by mouth) not required** - Almost all other methods of sedation require that the patient adhere to a fasting protocol (no food intake for 8 hours). This limits the option of sedation for patients that arrive at the dental office having not fasted. Nitrous oxide provides the opportunity to sedate the emergency patient as well as patients for whom fasting is often difficult to carry out (E.G., pediatric, diabetics).
9. **No escort necessary** - In most cases patients recover rapidly (<5 minutes) and can safely drive a motor vehicle 30 minutes after nitrous oxide sedation.⁵⁶ Of course, it is imperative that vital signs are close to baseline values and that psychomotor and cognitive function be at pre-sedation levels.

DISADVANTAGES OF INHALATION SEDATION

There is no sedation technique without shortcomings; however, the disadvantages associated with nitrous oxide sedation compared to other alternatives are few. The main obstacle to setting up nitrous oxide sedation in the office is the acquisition of equipment and plumbing the office if a central supply of gasses is desired.

1. **Initial set up cost** - Historically it has been more costly to set up an office for nitrous oxide sedation than for other alternate techniques such as IV sedation. However, with increased monitoring requirements (expensive monitors) for the other techniques becoming mandatory, the cost differential is narrowing. If the intent is to utilize nitrous oxide only occasionally (2-3 times/week) then it might be best to purchase a portable unit (< 6000 \$). However, if nitrous oxide is to be used in multiple operatories, a central supply of gasses reduces cost (large volumes of gas cost less) and is more convenient.
2. **Nasal mask obstruction** - The nasal mask (hood) can obstruct the view and working field for the dentist in the anterior areas.
3. **Patient cooperation essential** - The continuous uptake of nitrous oxide gas is required for optimal effect. Therefore, it is imperative that the patient be able to continuously breathe through their nose. This of course can be a challenge with certain groups of patients (mentally handicapped, pediatric). And then there is a small segment of the population who do not tolerate the mask due to claustrophobia.
4. **Concerns with exposure to waste gasses** - The debate over the biological effects of long term exposure to nitrous oxide is far from over. However, the preponderance of evidence seems to indicate that the concern over biologic adverse effects secondary to scavenged nitrous oxide is unfounded. (see section on potential hazards from long-term exposure to nitrous oxide)

RESPIRATORY PHYSIOLOGY/ANATOMY

A basic understanding of respiratory anatomy and physiology is important in nitrous oxide administration as the lungs are responsible for the uptake and elimination of the agent. Nitrous oxide, if used correctly, fortunately has minimal effect on respiratory function. However, as with all agents that depress the central nervous system, that is not always the case.

The primary purpose of respiration is the exchange of gasses across the alveolar-capillary membrane (most importantly oxygen and carbon dioxide). It is vital that this process take place within narrow physiologic parameters to maintain acceptable concentrations of each gas in the body.

ANATOMY

In humans the respiratory system can be conveniently subdivided into an upper respiratory tract and lower respiratory tract. The upper respiratory tract consists of structures beginning at the nares (nose) to the vocal cords.

- Nasal cavity
- Nasal pharynx
- Oropharynx
- Laryngopharynx
- Larynx (voice box)

The lower respiratory tract consists of all structures below the vocal cords:

- Trachea (windpipe)
 - Bronchi (left and right)
 - Bronchioles (multiple divisions)
 - Respiratory bronchioles
 - Alveolar ducts
 - Alveoli
- } *Respiratory zone*
(Gas exchange occurs)

PHYSIOLOGY

Mechanics of Pulmonary Ventilation

Inhalation - The expansion of the lungs (taking a breath) during quiet breathing, results mainly from two processes:

1. Downward movement of the diaphragm (muscle contraction)
2. Outward and upward movement of the rib cage (mainly external intercostal muscles)

During exercise (or stress), recruitment of accessory respiratory muscle groups occurs to facilitate and meet the demands of increased oxygen need both for inspiration and expiration.

Exhalation - Exhalation (breathing out) essentially is the result of the opposite process. Inspiration requires the expenditure of energy, whereas expiration during quiet breathing is a passive process requiring little if any energy. Breathing at rest only requires 3-5% of the total energy expended by the body. But during heavy exercise, the energy required increases as much as 50 fold.

Regulation of Respiration

Respiration is under control of the autonomic nervous system (also voluntary control) from the respiratory center found in the medulla oblongata and pons (lower and upper part of the brain stem respectively). There is an interconnected series of neurons which coordinate respiratory movements. These neurons are divided into three major collections:

1. **Dorsal respiratory group** - signals inspiration
2. **Ventral respiratory group** - signals both inspiration and expiration during heavy respiration - i.e., exercise (there is no signal from this group during quiet respiration)
3. **Pneumotaxic center** - primarily functions to limit the duration cycle of inspiration (short breaths)

Respiratory drive

Respiration as mentioned above is mainly controlled by specialized regions in the brainstem. **The ultimate goal of respiration is to maintain proper concentrations of oxygen, carbon dioxide and hydrogen ions in the body tissues.** It should be no surprise that even slight alteration in the concentration of either of these results in changes in breathing patterns. Respiratory control ultimately occurs in the respiratory center in the brain stem (medulla, pons). However, either the respiratory center can be stimulated directly by chemical stimulation (CO_2) or indirectly by nerve impulse from peripheral chemoreceptors.

Direct (central)

- $\uparrow\text{CO}_2$ is the primary stimulus for breathing!!! Actually it is H^+ ions that stimulate the sensors ($\text{CO}_2 + \text{H}_2\text{O} = \text{H}^+ + \text{HCO}_3^-$), but it is the carbon dioxide that crosses the blood brain barrier and combines with water to produce the hydrogen ions.

Indirect (peripheral)

Another mechanism for controlling respiration is the peripheral chemoreceptor system located in areas outside the brain. They are most sensitive to changes in oxygen levels in the blood, however they do respond to a lesser extent to changes in carbon dioxide and hydrogen ions as well.

- **Carotid bodies** - located at the bifurcation of the common carotid arteries (send signals to the brainstem via the Glossopharyngeal nerve [IX])
- **Aortic bodies** - located along the aortic arch (send signals to the brainstem via the Vagus nerve [X])

In summary, the primary respiratory drive to breath is an increase in carbon dioxide (and subsequently H^+) levels in the blood. Hypoxia (low oxygen) is a backup mechanism for respiratory drive should the primary mechanism fail. This is seen in certain medical conditions such as chronic obstructive pulmonary disease.

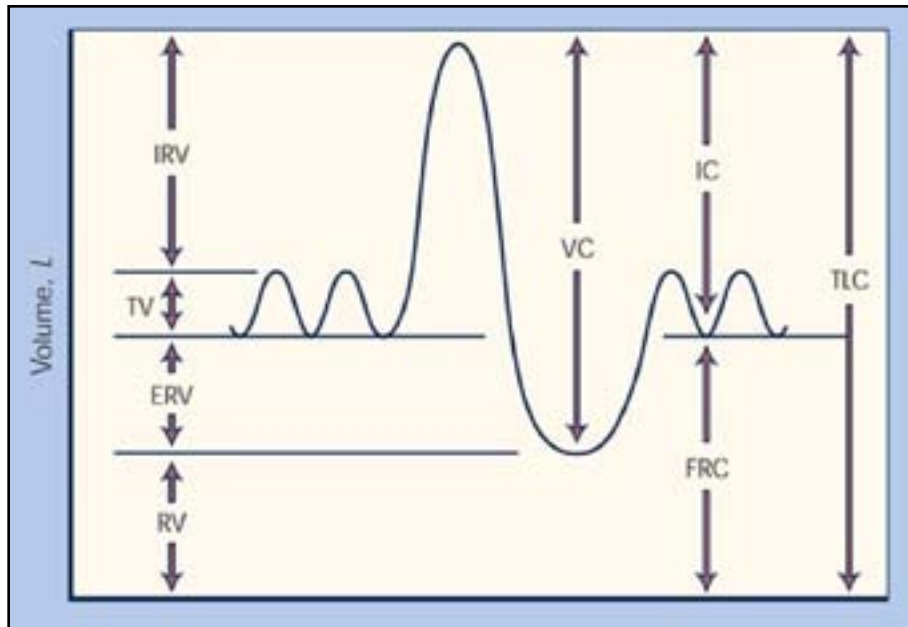
Pulmonary Capacities (lung volumes)

Figure 1.

(Approximate lung volumes for the average 70 kg male in parentheses)

- TV—tidal volume, that is, volume of gas inspired or expired during quiet respiration (500 ml)
- IRV—inspiratory reserve volume (3000 ml)
- ERV—expiratory reserve volume (1100 ml)
- RV—residual volume, that is, volume of gas remaining in the lung after a maximal expiration (1200 ml)
- VC—vital capacity, that is the total volume of gas that can be expired after a maximal inspiration (IRV, TV, ERV) (4600 ml)
- IC—inspiratory capacity (3500 ml)
- FRC—functional residual capacity, that is, volume of gas within the lungs at the end of expiration during normal tidal breathing pattern (ERV, RV) (2300 ml)
- TLC—total lung capacity (5800 ml)

Alveolar ventilation

The ultimate importance of respiratory ventilation is to bring gasses (i.e., air, nitrous oxide, oxygen) into close proximity to the pulmonary blood. The respiratory tree (trachea, bronchi etc) serves this purpose of conveying gasses to the respiratory zone (see above) where this process takes place. The most important gas exchange site is the alveolus. Some of the gasses that are breathed in never reach the alveoli and remain in the conducting areas (e.g., trachea, bronchi, bronchioles) of the respiratory tree. These conducting areas are called **anatomic dead space**. **Dead space volume in a 70 kg adult is about 150 ml**. Therefore, dead space results in the inefficient exchange of gasses as this volume occupies approximately 30 % of a normal tidal volume. Hence, alveolar ventilation is one of the major factors determining the concentrations of oxygen and carbon dioxide (and other gasses) in the alveoli. Alveolar ventilation is computed by subtracting the anatomic dead space from the tidal volume and minute alveolar ventilation is the alveolar ventilation multiplied by the respiratory rate/min:

$$\text{Tidal Volume} - \text{Dead Space} = \text{Alveolar Ventilation}$$

$$\text{Alveolar Ventilation} \times \text{Respiratory Rate/Minute} = \text{Minute Alveolar Ventilation}$$

Example (alveolar ventilation): $500 \text{ ml} - 150 \text{ ml} = 350 \text{ ml}$ (volume of gas that reaches the alveoli)

Example (minute alveolar ventilation): $350 \text{ ml} \times 12 \text{ breaths/min} = 4200 \text{ ml/min}$

It should be immediately apparent from the above example that large tidal volumes result in more efficient exchange of gasses (alveolar ventilation) than do smaller tidal volumes (shallow breaths).

CARDIOVASCULAR ANATOMY/PHYSIOLOGY

The purpose of the cardiovascular system (circulatory system) is to circulate blood throughout the body. This serves as a transport system for supplying each cell with metabolic substrate (e.g., oxygen, nutrients) and many other functions such as removal of waste products and carbon dioxide. The cardiovascular system is broken down into three main components:

1. Heart
2. Vasculature
3. Blood (plasma and cells)

The cardiovascular system consists of two parallel series of blood vessels. The left side of the heart pumps blood through the systemic (peripheral) circulation and the right side of the heart pumping blood through the pulmonary system. The effectiveness of this process relies mainly on:

1. A well conditioned heart
2. Adequate blood volume (and red blood cells)
3. Intact nervous system

BLOOD FLOW SEQUENCE:

Pulmonary Circulation

Venous return (SVC, IVC) → Right Atrium (Tricuspid Valve) → Right Ventricle (Pulmonic Valve) → Pulmonary Artery → Lung

Systemic Circulation

Lung → Pulmonary vein → L Atrium (Mitral Valve) → Left Ventricle (Aortic Valve) → Aorta → Systemic Vasculature

CARDIAC OUTPUT

Cardiac output is the most important factor that we have to consider in relation to the circulation. Cardiac output is defined as the quantity of blood pumped into the aorta each minute by the heart and can be calculated by the following equation:

Formula: Cardiac output = heart rate x stroke volume (volume pumped by each beat of the heart)

The average cardiac output for the average adult (70 kg) is about 5 L/min at rest and can reach levels of 30-40 L/min in the elite athlete during maximum effort. As mentioned above, cardiac output is dependent on many factors:

1. Heart - a compromised heart (ischemia, valvular dysfunction, cardiomyopathies, arrhythmias etc), results in decreased stroke volume and therefore cardiac output. In the most severe cases, the heart is incapable of meeting the body's metabolic demands.
2. Adequate blood volume - decreased blood volume is usually not seen in routine outpatient settings such as the dental office. Loss of blood volume is usually seen in the trauma or surgical patient. However, it must be understood that dehydration is a common cause of inadequate blood volume in the outpatient. Therefore, it should be intuitive that inadequate blood volume results in low cardiac output.
3. Nervous system - the autonomic nervous system maintains tight control over systemic arterial pressures. Any impairment in this system can affect cardiac output mainly by impairing venous return to the heart (less blood to fill the heart). Optimal cardiac output also requires organized contraction of the myocardium through electrical potentials developed in the cardiac conduction system. An electrical impulse spontaneously generates in the sinus node which then spreads throughout the heart resulting in an efficient, organized contraction and subsequent expulsion of blood into the aorta and pulmonary artery.

CARDIAC CYCLE

Systole

Systole is the contraction phase of the heart cycle where the heart muscle (myocardium) contracts and propels blood into either the lung or the peripheral circulation. This is represented by the top number of the blood pressure recording. This is the period when tissues are perfused with blood except the heart itself which is perfused during the diastolic phase.

Diastole

Diastole is the resting phase of the heart and it is during this time that the heart fills with blood in preparation for the next contraction (systole). Diastole corresponds to the denominator in blood pressure readings.

Mean Arterial Pressure (MAP)

Mean arterial pressure is a time weighted blood pressure average of the cardiac cycle. The formula for calculating MAP is:

$$\text{MAP} = 1/3 \text{ Pulse pressure (SBP-DBP)} + \text{DBP}$$

Example

Calculate the MAP of a patient with a blood pressure reading of 100/70 mmHg.

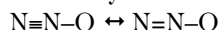
$$(100-70)/3 + 70 = 80 \text{ mmHg}$$

The importance of this number is that a MAP of at least 60 mmHg is usually necessary for the adequate perfusion of the tissues (most importantly the vital organs). Therefore, assessment of blood pressure before dismissal of the patient after nitrous oxide sedation should be mandatory to ensure adequate cardiac function.

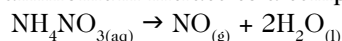
Reference: Guyton AC and Hall JE; Textbook of Medical Physiology, 10th edition, Philadelphia, 2000. WB Saunders

PHYSICAL PROPERTIES AND MANUFACTURE OF NITROUS OXIDE

Nitrous oxide is a colorless, odorless, non-irritating gas. This is fortunate as these properties allow clinicians to use nitrous oxide as an inhalant without patient objection. It is the only inorganic anesthetic agent routinely used in clinical practice today with the molecular configuration shown below:



It is a linear compound that is approximately 1½ times as heavy as air. Nitrous oxide is manufactured commercially by heating the raw ingredient ammonium nitrate to a temperature of 245 to 275 degrees celcius⁴:



Ammonium nitrate is very explosive at high temperatures and pressures; therefore great care is necessary when heating this substance for the manufacture of nitrous oxide. More than 25 major explosions involving ammonium nitrate over the last 100 years have killed at least 5000 people.²⁴ The gas is then cooled and a series of steps are completed which results in a final product which is nearly 99.9 % pure nitrous oxide.

Nitrous oxide is a gas at room temperature and ambient pressure. However, when nitrous oxide is stored under pressure (750 psi) at room temperature it exhibits biphasic properties (exists both as a liquid and gas). Thus as gas is used; nitrous oxide is converted from the liquid into the gaseous phase therefore maintaining a constant pressure in the tank until the liquid is entirely depleted. At the point when all the liquid is converted into the gas phase, the pressure in the cylinder begins to fall in proportion to the volume of gas remaining in the cylinder. Although nonexplosive and nonflammable, nitrous oxide is as capable of as oxygen of supporting combustion.²⁵

PHARMACOLOGY OF NITROUS OXIDE

When medications are administered to patients regardless of the route (E.g., Oral, Inhalation, IM, IV) it is important for the clinician to have a thorough understanding of the drug that is being delivered to the patient. It is important to know the mechanism of action or simply stated, how the drug works as well as the pharmacokinetics (what the body does to the drug) and the pharmacodynamics (what the drug does to the body) of the particular medication. Armed with this information, we can better select treatment modalities which are best suited for the patient's level of anxiety, psychological condition and medical history.

Mechanism of action

Nitrous oxide exhibits both sedative and analgesic properties. Recent evidence points to release of endogenous opioid peptides (dynorphins) by N₂O which then bind to kappa opioid receptors (Table 1.) as the mechanism for analgesia.^{27,28} It is estimated that delivery of 30% N₂O is equianalgesic to 10-15 mg of morphine.²⁶

Table 1: Classification of opioid receptors

1. μ 1 (Mu): Supraspinal analgesia
2. μ 2 (Mu): Respiratory depression, decreased heart rate, euphoria, physical dependence
3. Δ (Delta): Modulation of μ receptor activity
4. κ (Kappa): Analgesia, sedation, respiratory depression, miosis
5. Σ (Sigma): Dysphoria, hypertonia, tachycardia, tachypnea, mydriasis, hallucination

The mechanism for sedation (anxiolysis) is not quite as clear. Current theory states that N₂O produces its effects by either direct (agonist) or indirect activation of the Gamma-aminobutyric acid (GABA) receptor complex through the benzodiazepine binding site (see figure 2.).^{29,30,31} The GABA receptor is a prototypic ligand-gated receptor that inhibits the generation of new action potentials when bound by a variety of substances such as the inhibitory neurotransmitter GABA, benzodiazepines (E.g., valium) barbiturates and alcohol. To simplify this concept, binding of the GABA receptor complex with any number of substances, results in a decrease in central nervous system activity which produces clinical sedation.

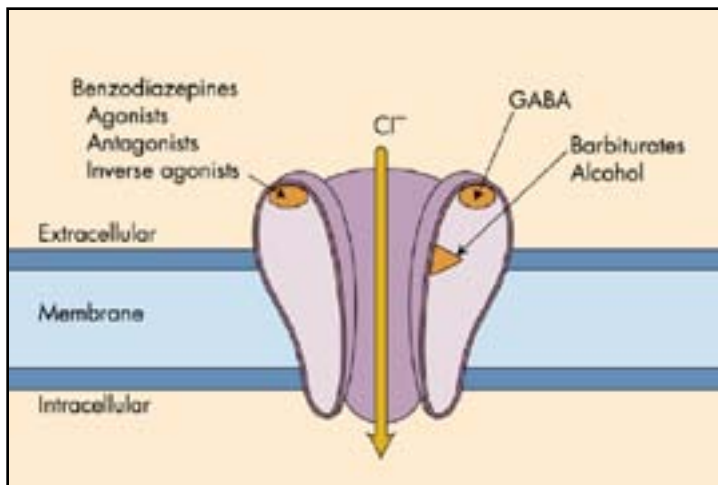


Figure 2.

Pharmacokinetics

Pharmacokinetics is a term that defines what the body does to the drug, in other words, its absorption, its distribution, biotransformation (metabolism) and elimination from the body. Let's take a look at each on of these individually:

- **Absorption (uptake)** - N_2O is inhaled into the lungs where it is rapidly absorbed from the alveoli into the pulmonary capillaries. This process is driven by N_2O moving down its concentration gradient from regions of high concentration (alveoli) to areas of low concentration (blood).
- **Distribution** - N_2O is distributed throughout the body dissolved as a free gas (not bound to carrier protein such as hemoglobin) in the blood. N_2O is a relatively insoluble gas in blood which just means that small amounts of nitrous oxide can be taken up into the bloodstream. This characteristic results in the rapid filling of the blood compartment which then allows the nitrous oxide to be driven across the blood brain barrier where the nitrous oxide has its effect. Nitrous oxide also has low solubility in other tissue beds such as fat and muscle which are reservoirs for other drug groups.
- **Metabolism** - Nitrous oxide does not undergo appreciable biotransformation (metabolism) in the liver and an insignificant amount is metabolized in the GI tract.
- **Elimination** - 99% of nitrous oxide is eliminated through the lungs unchanged.³²

Pharmacodynamics

Pharmacodynamics tells us what the effects of the drug are on the body including its therapeutic as well as its toxic effects. Listed below is a brief (by no means complete) summary of how nitrous oxide affects various organ systems in the body:

- **Central Nervous system** - Nitrous oxide administration results in the depression of the central nervous system (sedation) and psychomotor (movement or muscular activity associated with mental processes) impairment. Reaction times on cognitive processing speed tests do not increase significantly until approximately 10-20% nitrous oxide levels are breathed. Short term memory loss, tinnitus, nausea, paresthesias and disorientation may occur at 20-30% nitrous oxide levels.³³
- **Respiratory system** - Nitrous oxide decreases tidal volume in humans, but this decrease is offset by an increase in respiratory rate which results in an increased minute ventilation.³⁴ Even though there is some debate as to the respiratory effect of nitrous oxide on the CO_2 response curve (primary respiratory drive) it seems that at subanesthetic (patient remains conscious) doses (35-67%), nitrous oxide does not depress the respiratory response to increasing levels of CO_2 .^{35,36} However, subanesthetic doses of nitrous oxide depress the ventilatory response to hypoxia (secondary respiratory drive) significantly.^{36,37} This is not of concern in most clinical situations, but in the case

of a patient diagnosed with severe chronic obstructive pulmonary diseases (COPD) that rely almost exclusively on hypoxic drive to stimulate respiration, administration of nitrous oxide/oxygen sedation to these patients can create problems for two reasons:

1. Nitrous oxide depresses the hypoxic drive to low levels of oxygen significantly.
2. Secondly, simultaneous administration of high levels of oxygen (>30 %) further suppresses the hypoxic drive (due to high levels of arterial oxygen).

However, patients undergoing nitrous oxide sedation have voluntary control (they are conscious) of their breathing and therefore can initiate a breath at any time. Also, in the case of apnea (no breathing), the respiratory centers (medulla) will be stimulated when the oxygen levels fall in the body.

- **Cardiovascular system** - At subanesthetic concentrations of nitrous oxide there is no major physiologic change in cardiovascular function. Nitrous oxide does depress the myocardium but cardiovascular function remains stable because of an accompanying increase in sympathetic tone (activation). Therefore, it is reasonable to assume that the use of subanesthetic doses (conscious sedation) of nitrous oxide should not result in increased blood pressure. Eger³⁸ et al noted that blood pressure readings to be lower when nitrous oxide was used. Whether this effect was due to depression of the cardiovascular system or simply a benefit of decreased stress is debatable.
- **Hematopoietic system** - In the early fifties, the prolonged use (days) of nitrous oxide was employed to treat certain disease states (E.g., tetanus). These patients developed bone marrow suppression resulting in mild leukopenia (low white cell count) followed by anemia (low red blood cell count) and much later (12 days) by thrombocytopenia (low platelet count). The underlying mechanism for bone marrow suppression is an interference of Vitamin B12 metabolism which affects enzymes (methionine synthetase) that are dependent on this process for proper function. Methionine synthetase is necessary for DNA synthesis required to form blood cells.³⁹
- **Endocrine, renal, GI, system** - No effect
- **Hepatic system** - No effect (Nitrous oxide does not rely on the liver for metabolism) However, nitrous oxide does interfere with methionine synthetase (mentioned above) which is present in the liver.³⁹
- **Reproductive system** - Early studies reported an increased incidence of spontaneous abortions and congenital abnormalities in both females and wives of males chronically exposed to nitrous oxide. This body of evidence was obtained by sending out questionnaires to all members of the ADA encompassing a time period of 11 years (1968-1978).⁴⁰ However, several flaws are evident in this report; first there was no data on whether scavenging systems were used or not, and secondly, data was collected relying on individual recall (which is at best a rudimentary method of data collection!). Furthermore, not all questionnaires were returned which means that the data is incomplete and also it is not known if abuse of nitrous oxide occurred (this results in chronic exposure of high concentrations of nitrous oxide) as this was not a controlled study. More recent studies have shown that there is no evidence that a direct causal relationship exists between reproductive health and scavenged low levels of nitrous oxide.^{41,42}

ARMAMENTARIUM

Compressed Gasses

Nitrous oxide and oxygen are stored in pressurized tanks (cylinders). In the typical dental office setting, supply cylinders are available in two sizes. When gasses are stored in a central supply area, larger G or H cylinders are typically used and smaller E cylinders are used for portable units. (see Table 2 below.) Oxygen and nitrous oxide are stored in high pressure cylinders or tanks as described above. The tanks are color-coded for easy identification and safety. The tanks are constructed of alloy steel (heavy), aluminum (lightweight) or wrapped fiber-glass (feather weight and expensive). The cylinders are imprinted with important information about the cylinder including serial number, size, maximum psi, manufacturer, origin, date of original test etc. (see figure 3.)



Figure 3.

Table 2

Cylinder	Color	Pressure	State	Volume G/H cylinder	Volume E cylinder
Oxygen	Green	2000 psi	Gas	(H) 5500 L	625 L
N ₂ O	Blue	750 psi	Liquid/gas	(G) 16000 L	1600 L

Oxygen

It must be appreciated that oxygen, although not being a flammable agent, does support combustion. Therefore, it is imperative that pressurized oxygen should not come in contact with combustible materials such as oil, grease etc at any time. Violent reactions, with catastrophic results, have occurred when oxygen under high pressure comes in contact with these materials. With this in mind, any fitting or connection (especially high pressure connections) that comes in contact with oxygen should be free of these materials.

A full oxygen cylinder is pressurized to approximately 2000 psi, but is able to withstand pressures up to 3500 psi before a pressure relief valve releases. As shown in table 2 above, an H and E cylinder of oxygen contains approximately 5500 and 625 Liters of oxygen gas respectively. It is vitally important to track the amount of gas used and approximate time remaining before depleting the oxygen supply. These calculations are simplified with oxygen gas as the volume remaining is in direct proportion to the pressure in the cylinder. In other words, as the oxygen is used, the pressure in the cylinder will fall in proportion to the amount of oxygen used. The following formula can be used to estimate the volume in liters remaining:

Formula E Cylinder (Volume)

$$625 \text{ liters/cylinder (full)} \times \frac{\text{Pressure in Cylinder (psi)}}{2000 \text{ psi}} = \# \text{ of liters in cylinder}$$

Formula H Cylinder (Volume)

$$5500 \text{ liters/cylinder (full)} \times \frac{\text{Pressure in Cylinder (psi)}}{2000 \text{ psi}} = \# \text{ of liters in cylinder}$$

Example

How many liters are in an oxygen E cylinder with a pressure reading of 750 psi?

$$625 \text{ liters/cylinder} \quad \times \quad \frac{750 \text{ psi}}{2000 \text{ psi}} \quad = \quad 234 \text{ liters}$$

It is also equally important to be able to estimate the time lapse before the oxygen supply is depleted. A simple calculation before the beginning of a nitrous oxide sedation predicts the amount of time available before the supply is exhausted. Oxygen depletion before the end of the treatment session can be both frustrating for the practitioner and upsetting for the patient. The simple formula below can be used to estimate the time before the contents of the oxygen cylinder are depleted:

Time Estimate Formula

$$\frac{\text{\# of Liters in cylinder}}{\text{Rate of delivery in liters/min}}$$

Example

You have scheduled a patient for a 3 hour treatment plan and are planning nitrous oxide administration. You want to be sure that you have an adequate supply of oxygen for the entire treatment period. The pressure gauge on the E cylinder reads 2000 psi and after you adjust the flow rate to accommodate the patient's tidal volume and titrated the nitrous oxide level to adequately sedate the patient, you note that the oxygen flowmeter is set at 4 L/min and the nitrous oxide level is at 2 L/min. How long do you have before you deplete your oxygen supply given that your preoxygenation (100% oxygen) period lasted 4 minutes at 6 L/min?

Step 1 Calculate how much oxygen used (rate= 6 L/min) during the preoxygenation period

$$4 \text{ min} \times 6 \text{ L/min} = 24 \text{ liters of oxygen used}$$

Step 2 Total volume – volume used in preoxygenation period

$$625 \text{ L} - 24 \text{ L} = 601 \text{ L remaining (after preoxygenation period)}$$

Step 3 Time remaining before depletion of oxygen (rate = 4 L/min)

$$\frac{601 \text{ L}}{4 \text{ L/min}} = \sim 150 \text{ min}$$

Nitrous oxide

Nitrous oxide, like oxygen, is not flammable but does support combustion. Therefore, the same precautions should be practiced with nitrous oxide as with oxygen. Nitrous oxide differs from oxygen in that at room temperature, under pressure, it exists as a liquid and a gas. Therefore, it is difficult to estimate the amount of nitrous oxide remaining in the cylinder. The only reliable way to determine residual volume of nitrous oxide is to weigh the cylinder and subtract the weight of an empty cylinder. When the nitrous oxide cylinder is full the pressure gauge will measure 750 psi and will exist predominately (95%) in the liquid form.⁴³ The pressure

will remain constant as liquid is converted to the gaseous phase. The vaporization process is an endothermic process which draws heat from ambient air, thus if high flows are used, frost may appear on the cylinder and the pressure gauge may freeze.

When the pressure begins to fall, this indicates that all the liquid has been converted to the gas phase and generally indicates that less than 20% of the original volume of nitrous oxide remains. Fortunately, if the supply of nitrous oxide is depleted during a case, this presents more of an embarrassment to the office rather than a catastrophe. Therefore, an ample supply of nitrous oxide should always be available. In general, 2.5 cylinders of oxygen are used for every cylinder of nitrous oxide.

If the pressure gauge reads more than 750 psi this indicates gauge malfunction, overfill, or a cylinder containing a gas other than nitrous oxide.⁴⁴

NITROUS OXIDE UNITS

There are two basic types of nitrous oxide delivery systems: wall and portable nitrous oxide units. The units are similar in design; however, the portable unit differs in that it contains its own supply of the compressed gases nitrous oxide and oxygen and the wall mounted unit receives gasses from a central supply.

Cylinders and Pin Index Safety System

The portable nitrous-oxide machines are set up with the oxygen tank color coded green on the right, and the nitrous oxide tank color coded blue on the left. The nitrous oxide and oxygen tanks are attached to the unit by a yoke assembly. To prevent the mix-up of gasses, a safety feature known as the pin index safety system was developed. A specific configuration of two pins protruding from the yoke is unique for each gas. When attaching the cylinder to the sedation unit, the pins on the sedation unit must be aligned with the corresponding holes on the valve stem of the cylinder (figure 4A/4B). Thus, it is almost impossible to attach the wrong cylinder to the wrong portal site on the unit. A Teflon spacer is placed on the interface between the cylinder and the sedation unit which serves to create an airtight seal. The yoke system should then be tightened securely to avoid leakage of gasses.



Figure 4A.



Figure 4B.

Valves

After the tanks are securely fastened to the machine, the valve on the cylinder is opened by turning the valve wrench counterclockwise. Only one cylinder of nitrous oxide and oxygen should be opened at a time. When the contents of the first cylinder have been depleted, the second cylinder should then be opened. As mentioned previously, it is extremely important to remember that it is absolutely contraindicated to lube, grease or oil any of the valves, fittings, hoses, etc that come in contact with the compressed gases. (see figure 5.)



Figure 5.

Pressure gauges

Pressure gauges measure the pressure within the cylinder and usually are color coded to their corresponding cylinder. (see figure 6.)



Figure 6.

Pressure regulators

Pressure regulators (reducing valves) are positioned between the cylinders and the flowmeters and function to reduce the high pressure within the cylinders to a line pressure of about 50 psi. After passing through the pressure regulator, low pressure hosing delivers the nitrous oxide and oxygen to the back of the flowmeter. (see figure 7.)



Figure 7.

Diameter Index Safety System

The diameter index safety system prevents the cross plumbing of these low pressure hoses to the flowmeter by using different diameter attachments and threading. When using a wall unit that receives gasses from a central supply, the low pressure hoses connect directly from the wall outlet to the flowmeter unit. At this point, the equipment is the same whether delivering gas from a central supply or a portable unit. (see figure 8.)



Figure 8.

Flowmeter

The flowmeter sits on top of the unit and contains two parallel tapering tubes dedicated for either nitrous oxide or oxygen gas. The tubes are narrow at the bottom and flared at the top. A ball shaped float is often used to measure the flow rate of gas passing delivered through the system with the middle of the ball serving as the reference point. As the flow rate is increased, the ball will rise higher in the flowmeter.

The flow rate in L/min is adjusted by either a single control knob or by dedicated control knobs for each of the gases. In the case of dedicated control knobs, the oxygen control knob is always placed on the right, while the nitrous oxide control knob is always placed on the left. The ratio of nitrous oxide to oxygen can be selected by adjustment of these two knobs. Gas flow is increased by turning the knobs counterclockwise and decreased by turning the knobs clockwise. In the case of a single control knob, selection of differing flow ratios is accomplished by adjusting the knob to preset percentages on the flowmeter. (see figure 9.)



Figure 9.

Reservoir bag, Emergency Air Inlet Valve, Nonbreathing Valve

The reservoir bag is located below the flow-meter unit, but downstream from the flow meters. The reservoir bag is approximately 3L in volume and should remain visible throughout the procedure as it serves as a visual monitor that the patient is breathing. The reservoir bag also provides a reservoir of gas should the patient require more volume than is being supplied through the system. Near the units reservoir bag is an emergency air inlet valve which allows the intake of air in the event that the volume in the reservoir bag is inadequate for the patient's needs or the gas flow fails for some reason. A nonbreathing valve located near the reservoir bag prohibits exhaled gas from the patient back-flowing into the unit. (see figure 10.)

The nitrous oxide and oxygen gas exit the nitrous machine through the common outlet and are delivered to the patient by a corrugated plastic tube that connects to a mask or cannula.



Figure 10.

Oxygen Flush Valve

The oxygen flush valve when activated allows for rapid delivery of 100% oxygen. When activating the oxygen flush valve the oxygen bypasses the flow meter unit and is used to rapidly fill the reservoir bag and can be used in emergency situations. It is claimed that positive pressure oxygen can be delivered to a patient using this system. (see figure 11.)



Figure 11.

Oxygen Fail Safe Mechanism

In the event that the oxygen supply should fail, the oxygen fail safe mechanism is activated. Oxygen flow at 50 psi keeps a valve open that allows nitrous oxide to flow. When oxygen delivery fails or pressure falls, this valve closes and prevents the potential catastrophe of delivering 100 % nitrous oxide to a patient. Central supply systems and some portable units have an audible alarm or flashing lights that are activated when the oxygen fails. (see figure 12.)

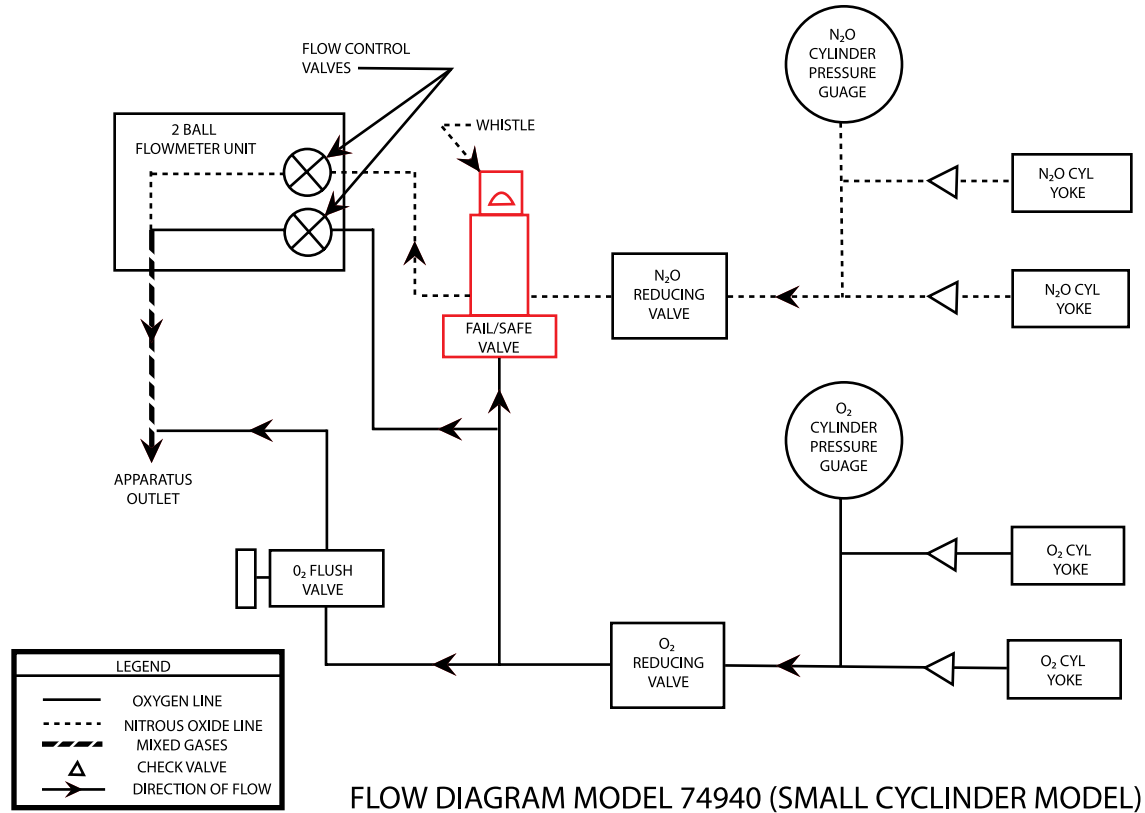


Figure 12.

Scavenger

It is the standard of care to scavenge exhaled and excess nitrous oxide gas. There are several designs of scavenging systems but most of the more popular systems function adequately. One system consists of a smaller mask contained within a larger mask with the smaller mask delivering the nitrous oxide/oxygen to the patient and the larger mask scavenging off the excess. Another type which is used here at LLUSD is a scavenging cone which attaches to the top of the nasal hood with tubing that connects the scavenging cone to the low volume suction device. It is important to optimize the suction volume rate per manufacturer recommendations, as excessive suction will remove excess gas from the system and inadequate suction will allow gas contamination of the operating environment. (see figure 13.)



Figure 13.

PATIENT ASSESSMENT

When treatment is to be rendered to a patient, it is below the standard of care to not complete a thorough patient evaluation before initiating care. Patient assessment evaluates not only the patient's medical status, but also allows the practitioner to determine the patient's level of anxiety as well as their expectations for treatment. Comprehensive patient assessment for dental care under nitrous oxide sedation involves addressing four main areas:

1. **Medical history and ASA classification**
2. **Preoperative vitals**
3. **Medical consultation (if necessary)**
4. **Anxiety level assessment**

Medical history (ASA classification)

The major endpoint of the medical work-up is to determine whether the patient has the physiologic/psychological reserve to undergo the planned treatment with low risk of complication. A system for preoperative risk assessment stratifies patients into categories and was developed by the American Society of Anesthesiologists in the 1940's. Despite its popularity and acceptance among practitioners for preoperative assessment of patients, it still must be realized that this system is only a guide and presents with many shortcomings and every patient will need to be evaluated and categorized individually. Placement of patients into one of these categories listed below, guides decisions by the practitioner for patient care. For example, further information may be needed (medical consultation) or treatment modifications may be considered such as the scheduling of a morning appointment for the diabetic patient or short appointments for medically compromised (ASA III) patients. ASA categories I-VI are summarized below:

Table 3

ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes

Exercise tolerance correlation

- ASA I** No dyspnea, undue fatigue or precordial (chest) pain with normal activity. Normal activity is defined as:
1. climbing one flight of stairs
 2. walking 2 level blocks at a normal pace
 3. mowing lawn for 5 - 10 minutes
- ASA II** Mild dyspnea after normal activity; may rest at top of flight of stairs.
- ASA III** Dyspnea during normal activity. Comfortable at rest in any position. Needs to rest before reaching top of a flight of stairs. Ankles swell as day progresses. Definite risk patient, short appointments ideal.
- ASA IV** Dyspnea and orthopnea at rest. The patient will rest several times when climbing a flight of stairs if he can climb them at all. These patients will experience symptoms of their disease (E.g., chest pain) at rest

Treatment modifications

- ASA I-** Psychological/procedural stress - well tolerated by the patient; no treatment modification necessary (stress reduction?)
- ASA II-** Psychological/procedural stress - tolerated by the patient; no treatment modification (stress reduction?)

- ASA III- Psychological/procedural stress - don't tolerate well
- Alter treatment plan - avoid long complex procedures
 - Stress reduction protocol is good idea
 - Medical consult is advised
- ASA IV- Psychological stress/procedural - may decompensate the patient
- Emergency care only that is simple in nature (i.e., smoothing of a sharp tooth, place temporary filling etc).
 - Invasive procedures such as multiple extractions should be referred to oral and maxillofacial surgery for removal in a hospital setting.
 - Medical consultation required

Medical History Forms

Medical history forms should be designed to address and provide information on the following topics. Health history forms should be unique to each office setting (E.g., pediatrics) and questions should be geared toward the segment of the population that are most commonly seen in the office. Listed below is a sample of topics that are important to cover on the health history form:

- o **Current problem (chief complaint)**
- o **Medications**
 - Prescription
 - Nonprescription
- o **Allergies**
 - Drug, food, latex, drug sensitivities
- o **Previous anesthetics (local, sedation and general)**
 - Adverse reactions
 - Morbidity
- o **Previous surgeries and hospitalizations**
- o **Family history**
 - Familial diseases
 - Causes of premature death
- o **Social history**
 - Alcohol (acute, chronic)
 - Tobacco (lung function, heart disease)
 - Illicit drug use
- o **ROS (review of systems)** The review of systems is a series of questions grouped by organ system. Organ systems that are not relevant to dentistry should be excluded (E.g., reproductive).
 - General (activity)
 - HEENT (Head/ears/eyes/nose/throat)
 - Respiratory
 - Cardiovascular
 - Genitourinary (GU)/reproductive
 - Gastrointestinal (GI)
 - Endocrine
 - Hematologic
 - Neuromuscular

Current problem (chief complaint)

This tells us why the patient is here.

Medications

Recording each medication that the patient is taking and when the physician ordered the prescription is important as it tells the practitioner what the disease process is, how recent the diagnosis (how long the

patient has had the disease) or indicates that prior medications were not working and that new therapies are being attempted. Also, it is important to determine how compliant the patient is with taking the prescribed medication. Proper compliance with medications often results in stabilization of the disease process (E.g., hypertension) and oftentimes, results in patients downgrading from a higher to lower ASA classification (III→II). It is also important to ask if the patient is taking any self-prescribed medicines such as herbal remedies. These drugs may alter physiologic as well as cognitive function and drug interactions are possible with many of these remedies.

Allergies

The medical history must have questions pertaining to drug and latex allergy. There needs to be a clear distinction between true drug allergies (e.g., rash, dyspnea) and intolerances (e.g., gastrointestinal upset). If there is a positive response, an exact account of the event should be elicited including what symptoms the patient experienced as well as what treatment, if any, was prescribed for the reaction.

Latex allergy is becoming more frequent due to the widespread use of latex since the 1980's. It is estimated that 5% of the general population and 15% of health care workers are allergic to latex. This problem is remedied simply by the avoidance of latex products. Latex-free products (gloves) are available and should be kept in supply.

Previous anesthetics (local, sedation and general)

In the dental office setting, history of previous anesthetics especially local anesthetic, allows the practitioner to discover the "difficult to numb" patient and to prepare for that likelihood. Encountering a difficult to anesthetize patient on a busy treatment day can be frustrating and discouraging for both clinician and patient. Prior knowledge of this probability can allow the practitioner to plan and review alternative injection techniques and assure that all necessary armamentarium is on hand to manage these scenarios. Also, gathering information on the patients prior sedation experiences (most importantly, nitrous oxide) is helpful.

Family history

This section alerts us to possible undiagnosed medical conditions in our patients. Examples of disorders might include bleeding disorders, diabetes, cardiac disease etc.

Social history

A positive social history almost always impacts patient care, especially pertaining to pain control and sedation. A patient that abuses alcohol presents with a unique challenge. The recent consumption of alcohol makes the use of sedation such as nitrous oxide unpredictable. The patient will be more sensitive to the effects of the nitrous oxide, as alcohol is classified as a sedative-hypnotic agent and will increase the likelihood of rendering the patient unconscious.

A positive response to smoking requires inquiry into the number of years that the patient has smoked as well how many packs/day. Decades of smoking obviously have more of an impact on health than a few cigarettes smoked in social situations. Long-term abuse often results in pulmonary disease (COPD) as well as being a major risk factor for coronary artery disease.

Patients that have recreationally abused drugs should be questioned carefully. Those that are presently abusing drugs should be denied care **if they have used drugs in last 48 hours** and probably should not be treated electively until they have been treated for their drug abuse problem. The probability of drug toxicity (e.g., heart irritability), drug interactions with sedative and local anesthetic medications and behavior management issues form the foundation for this premise. The recovering addict presents a unique opportunity to help an individual, but realizing that pain control often becomes a problem in this group of patients.

REVIEW OF SYSTEMS (ROS)

General

Questions relating to the patients general state of health and ability to conduct usual activities (exercise tolerance) should be asked. Responses that indicate a decline in health, gain in weight or reduction in exercise capacity should be investigated further (medical consult?). These patients will have difficulty in handling the physiologic and psychological stress of a lengthy dental appointment

HEENT (Head/ears/eyes/nose/throat)

Nitrous oxide comment: *nitrous oxide is contraindicated in the conditions listed below:*

A diagnosis of glaucoma would preclude the use of anticholinergic (atropine, scopolamine and glycopyrrolate) medications as these drugs will increase the pressure in the eye. Middle ear disturbances, such as ear infections or recent surgery, would contraindicate the use of nitrous oxide sedation as nitrous gas diffuses into closed spaces resulting in increased pressure in the middle ear. This increased pressure can result in headaches, rupture of the tympanic membrane, hearing loss as well as surgical graft displacement.^{45,46,47}

Concurrent upper respiratory infections (colds, flu) would contraindicate the use of nitrous oxide mainly for the reason that the nasal passages will be congested and impair the uptake of nitrous oxide through the nose. Also, to be considered is the possibility of cross contamination due to contaminated equipment. This should be considered for any communicable disease, however, the disposal of plastic and rubber goods (these are inexpensive) virtually eliminates this problem.

Respiratory (Pulmonary)

Nitrous oxide comment: *nitrous oxide is indicated for patients with pulmonary diseases with few exceptions (see below). In most pulmonary diseases, administration of supplemental oxygen is beneficial for these patients. Also, pulmonary conditions such as asthma are exacerbated by stress; therefore, alleviation of the stress response by nitrous oxide sedation is advantageous.*

a. Asthma

Asthma is an inflammatory condition of smooth muscle of the tracheobronchial tree. An acute attack is brought on by intrinsic and extrinsic stimuli such as environmental allergens (pollen) as well as exercise, colds, foods, food preservatives and emotional stress. However, most asthmatic attacks are brought on by inhaled allergens, but attacks brought on by food and food preservatives can be life-threatening.

Management:

1. Stress reduction protocol
2. Bronchodilator (B-2 agonist) such as albuterol (preferably the patient's) must be immediately available
3. Avoid local anesthetics containing bisulfites antioxidants in susceptible patients
4. **Nitrous oxide/oxygen is suggested if sedation is needed**
5. Patients must not have signs and symptoms of an acute asthmatic attack (wheezing, dyspnea) on day of treatment

b. COPD (bronchitis, emphysema)

Patients with a diagnosis of COPD (chronic obstructive pulmonary disease) have lung disease in which the lungs are damaged making it difficult to breathe. The airways are partially obstructed (bronchitis) and some of the alveolar walls are destroyed (emphysema) making it difficult to move air in and out of the lungs. Treatment options include bronchodilators and inhaled steroids and patients with severe disease are often maintained on supplemental oxygen. In advanced cases of some COPD diseases (bronchitis), patients retain high levels of CO₂ due to the obstructive nature of the disease (In other words, it is more difficult for CO₂ to exit the lungs). The primary drive for respiration in the normal population is increased levels of CO₂, however, in these patients who have chronic elevated levels of CO₂ the primary stimulus for breathing is decreased levels of oxygen (hypoxia). Therefore, theoretically, high levels of oxygen may depress the drive for respiration. Therefore, oxygen flow levels of 4L/minute or less are acceptable to maintain the hypoxic drive.

Management:

1. Consultation with physician to determine if patient is medically optimized
2. If supplemental oxygen is given, keep oxygen flow levels below 4L/min
3. **Avoid nitrous oxide/oxygen sedation for severe COPD patients, however, it is okay for early stages of disease (mild-moderate)**
4. Position semi-supine or upright
5. Avoid bilateral mandibular blocks and local anesthesia of the soft palate

Cardiovascular

Nitrous oxide comment: nitrous oxide is indicated for patients with various cardiovascular diseases for several reasons: first of all, oxygen is concurrently being administered with nitrous oxide which increases the supply of oxygen. Secondly, nitrous oxide reduces the workload on the heart (decreased anxiety) which results in less oxygen demand as a result of a lowered stress response.

a. HTN

Hypertension is very prevalent in our society. The clinician should seek to understand the significance and extent of the hypertensive end organ disease (heart, kidney, cerebral) as well compliance with proscribed medical regimens. At LLUSD, it is appropriate to provide elective treatment for a patient that has a BP reading of <180/110 provided that this patient does not have a co-diagnosis of cardiac and cerebrovascular disease and is asymptomatic (chest pain, headache etc). However, it is assumed that the patient has controlled hypertension and the high blood pressure reading is the direct result of the patient's anxiety.

Management:

1. Stress reduction protocol (gentle technique, profound local anesthesia, short appointments)
2. Minimize use of vasoconstrictors (2 cartridges of 1:100000 epinephrine)
3. **Sedation (Nitrous Oxide, oral, IV)**

b. Ischemic heart disease/angina

Ischemic heart disease or angina is a condition in which there is a myocardial oxygen supply and demand imbalance. Atherosclerotic plaque is the most common cause of this condition. Anginal attacks (chest pain) are the clinical manifestations of this disease. It is important to question the patient with regards to the following:

- **Nature and frequency of the anginal attack.** In other words, is the angina brought on by strenuous exercise, while climbing one flight of stairs or at rest (sitting on the couch).
- **Effectiveness of treatment.** When the anginal episode occurs, what is done to relieve the pain? Rest, oxygen, nitrates?

If the patient experiences chest pain while doing minimal exercise (washing dishes) or at rest, the patient is considered to have unstable angina. Also, if the patient requires multiple doses of nitrates before symptoms resolve places them at risk for a myocardial infarction. All of these clinical situations are poor risks for elective dental care and require medical consultation and follow-up before care is provided to them.

Management:

1. Stress reduction protocol (gentle technique, profound local anesthesia, short appointments)
2. **Sedation (Nitrous Oxide, Oral, IV),**
3. Pre-op nitroglycerin sublingually 5 min (1 tablet) before starting local anesthesia. Use patient's tablets if possible.
4. Consider administering oxygen (nasal cannula) during treatment
5. Minimize use of vasoconstrictors (2 cartridges of 1:100000 epinephrine)
6. Remember patient is a definite risk. (ASA Class III)

c. Myocardial infarction

Myocardial infarction is the actual death and necrosis of myocardial cells. The long term prognosis of these patients hinges on the extent and location of the damaged cardiac muscle.

Management:

1. No elective dental treatment for 6 months.
2. Consultation with patient's cardiologist.
3. Routine dental care can then be provided utilizing the same protocol as the patient with ischemic heart disease.

d. Congestive heart failure

Congestive heart failure defined in its simplest terms is a pump (heart) that is failing due to any number of underlying causes (i.e., ischemia, infarction, valvular disease, cardiomyopathy). This condition results in decreased cardiac output and a backing up of blood behind the failing heart. This manifests clinically as peripheral edema (swollen ankles) and pulmonary edema (fluid filled lungs) for right and left sided heart failure respectively.

Management:

1. No treatment until patient has been optimized medically (minimal evidence of edema, good exercise tolerance etc)
2. Stress reduction protocol (gentle technique, profound local anesthesia, short appointments)
3. **Sedation (Nitrous Oxide, Oral, IV)**
4. Position patient semi-supine or upright to avoid fluid overload in patient's lungs
5. Minimize use of vasoconstrictors (2 cartridges of 1:100000 epinephrine)

e. Valvular heart disease

Patients with a history of valvular heart disease must be evaluated for the nature and hemodynamic significance of the condition. Basically, patients with a positive history of valvular heart disease have as an underlying pathology the inability to either open or close the heart valve properly which results in impeded forward blood flow or a significant regurgitation (backflow) of blood. In the cases of severe stenosis or regurgitation cardiovascular hemodynamics (cardiac output, BP) can be significantly altered. Also, valvular heart disease carries the risk of bacterial endocarditis.

Management:

1. Medical consultation with the patient's physician to determine the need for antibiotic prophylaxis and the hemodynamic significance of the valvular disease
2. Maintain patient's heart rate and blood pressure as close to baseline as possible to avoid hemodynamic derangements
3. Provide antibiotic prophylaxis if indicated

f. Cardiac pacemaker, implanted cardioverter/defibrillator

Cardiac pacemakers are most commonly placed in patients with symptomatic arrhythmias and heart blocks that are unresponsive to medical therapy. The device is implanted under the skin and leads are fed through blood vessels into the right atrium or ventricle. Implanted cardioverter/defibrillator (ICD's) is placed in a similar fashion to pacemakers. These devices detect life threatening arrhythmias and deliver a shock in these susceptible patients.

Management:

1. Consultation with the patient's physician to determine if the patient is medically optimized and evaluation of the device to check for proper function is vital
2. There is no need for antibiotic prophylaxis as the device is not placed into the heart
3. Extreme caution when using electrocautery units
4. No contraindication for administration of local anesthetic

g. Cerebrovascular

Stroke (cerebrovascular accident)

A stroke is the end result of a disruption of oxygenated blood flow to a part or parts of the brain. The most common causes of stroke are hemorrhage and occlusion of a vessel (thromboembolism). The outcome of a stroke is at the worst death and if the patient survives there is a high probability that the patient will suffer long term neurologic and motor deficits depending on the area of the brain affected. As in myocardial infarction, the most common cause of a stroke is hypertension and atherosclerosis.

Management:

1. No elective dental care for 6 months (post CVA)
2. Consultation with physician to determine patient's recovery and to manage anticoagulants (see hematology section)
3. Avoid treatment in patient experiencing transient ischemic attacks (TIA's)
4. Limit local anesthetic with vasoconstrictor (2-3 cartridges of 1:100000 epinephrine)
5. Stress reduction protocol

Genitourinary

Nitrous oxide comment: As stated earlier, nitrous oxide is eliminated almost entirely through the lungs, therefore making nitrous oxide an attractive sedation option for the patient presenting with kidney disease. The problem of delayed drug elimination is a concern in these patients, but nitrous oxide completely circumvents this problem.

Sexually transmitted disease much like infectious diseases discussed above, require meticulous “universal precautions” (infection control) protocol (Gloves, mask, use of disposable items etc). Aside from that there is no contraindication for nitrous oxide use.

Gastrointestinal (GI)

Nitrous oxide comment: for the most part, gastrointestinal diseases (ulcers, hepatitis, cirrhosis, etc) do not contraindicate the use of nitrous oxide sedation.

Nitrous oxide is not metabolized in the liver or eliminated in the GI tract to any significant degree and therefore is a good choice of agent when sedation is required for patients with these diseases. However, nitrous oxide is contraindicated in patients with bowel obstruction. Nitrous oxide will diffuse into closed spaces and expand air pockets in the intestines which result in increased pressure (pain).

Endocrine

a. Diabetes Mellitus

Nitrous oxide comment: The long-term effects of diabetes on organ systems, most notably the heart, vasculature and kidneys, are well known. Damage to these organs (especially in the poorly controlled diabetic) includes coronary artery disease, peripheral vascular disease and kidney failure. Nitrous oxide is indicated for these patients for several reasons: first of all, oxygen is concurrently being administered with nitrous oxide which raises the inspired concentration of oxygen and secondly, nitrous oxide reduces the stress response (decreased anxiety) which lowers the oxygen demand. Lastly, patients with end stage renal disease (renal failure), nitrous oxide elimination is not affected as nitrous is metabolized minimally by the body.

Diabetes is a metabolic disorder in which there is a derangement in carbohydrate metabolism. This results from either insufficient or a complete absence of insulin secretion or there is a lack of receptor response to circulating insulin. Patients are typically classified as type 1 or 2 diabetics. Type 2 diabetics are usually managed with diet modifications or by an oral medication regimen (some require insulin). Type 1 diabetics have an absolute lack of insulin and therefore require exogenous insulin. Patients with diabetes develop long term complications such as cardiovascular disease, blindness (retinal damage), renal failure, nerve damage (neuropathy) and gangrene. Diabetics that have tight control over their blood glucose levels have less long term complications and can lead a relatively normal life. On the other hand, those with poor control of their plasma glucose levels have more serious end organ disease.

Management:

1. Avoid hypoglycemia
2. Stress reduction protocol
3. No treatment modification necessary provided there is no evidence of end organ disease (cardiac, kidney, neuropathy). In other words, it is okay to administer routine doses of local anesthetic with vasoconstrictor to patients with controlled disease
4. Elective dental treatment is contraindicated in the poorly controlled diabetic (brittle diabetes)

b. Hyperthyroidism (thyrotoxicosis)

Nitrous oxide comment: nitrous oxide is indicated for these patients mainly for its stress reduction properties.

Patients with a diagnosis of hyperthyroidism that are not being treated are at risk for developing a thyrotoxic crisis (“thyroid storm”) the most severe form of thyrotoxicosis. Infection, trauma, dental procedures and stress may precipitate the crisis.

Management:

1. No elective treatment until medical consultation and treatment of hyperthyroidism completed
2. Important to manage dental infections
3. **Avoid epinephrine** and other sympathomimetic drugs in the uncontrolled hyperthyroid patient

c. Adrenal gland insufficiency (Addison's disease)

Nitrous oxide comment: nitrous oxide is indicated for these patients as physiologic stress is reduced.

Normal function of the adrenal gland allows for the body to cope with stress. Glucocorticoids (cortisol), mineralocorticoids (aldosterone) and epinephrine are produced by the adrenal gland for this purpose. Therefore, in scenarios where the adrenal gland is suppressed either by **primary causes** (Addison's) or **secondary causes** (corticosteroid therapy), there is a theoretical chance that under certain conditions (extreme stress) the patient could suffer cardiovascular collapse. However, it is unlikely that routine dental treatment with local anesthesia will precipitate a cardiovascular collapse. There is considerable controversy in management of the patient with adrenal insufficiency and whether it is appropriate to increase the steroid dose or not and if so, for how long.

Management:

1. No additional dosing of steroid for minor procedures (dental treatment), however, should take daily dose of steroid
2. Consider additional steroid coverage for major surgical procedures (abdominal, thoracic surgery) for patients taking steroids for systemic inflammatory diseases (rheumatoid arthritis, asthma, lupus)
3. Consult with physician if unsure how to manage steroid coverage

Hematology

Nitrous oxide comment: nitrous oxide is indicated for patients with hematopoietic disorders. As mentioned previously, long-term exposure to nitrous oxide depresses the bone marrow resulting in decreased blood cell production. Nitrous oxide administered in clinical situations (< 12 hours) produces no such effect. Nitrous oxide does not bind to hemoglobin and thus does not displace oxygen and as with other diseases, the concurrent administration of high concentrations of oxygen is beneficial.

a. Hemophilia

Patients at risk for bleeding during a dental procedure have either an inherited defect in the coagulation pathway, an acquired form of hemophilia observed in patients taking anticoagulation medications (coumadin, aspirin, NSAIDS, heparin) or patients with some types of cancer (leukemia). In the dental office, bleeding abnormalities are usually elicited from the health history and **should raise concern on the part of the practitioner** and requires further questioning and consultation with the patient's physician.

Management:

1. Consultation with the patient's physician to determine how to manage anticoagulants.
2. The target INR (international normalized ratio) should be less than 3.0 before dental treatment. This corresponds to a PT (prothrombin time) of about 1.5 - 2.0 of normal value.
3. If a patient is on coumadin and the physician elects to reduce the anticoagulant, then a period of 3 days is required before a change in the INR will be reflected. A repeat INR should be done on the day of surgery to determine if the desired therapeutic level has been reached.
4. Infiltration, PDL and intraosseous injection techniques are suggested when administering local anesthesia to any patient with an increased risk for bleeding. Avoid block anesthesia if possible due to risk of damaging blood vessels.
5. Local measures such as pressure packs, sutures, gelfoam etc should be used if postop bleeding is encountered.

Neuromuscular

Nitrous oxide comment: nitrous oxide is indicated in patients with a diagnosis of neuromuscular disorders such as multiple sclerosis, Parkinson's, cerebral palsy, muscular dystrophy etc. Nitrous oxide does not produce muscle weakness (most importantly respiratory muscles) and actually increases skeletal muscle function in higher doses.⁵⁰

Pregnancy

Nitrous oxide comment: *The pregnant patient presenting for dental treatment presents a unique challenge. The clinician not only has to be concerned with the well being of the female patient but also that of the fetus. It is general knowledge that elective dental treatment for the pregnant patient should be postponed if possible. This is also true for the use of nitrous oxide. However, it is also clearly evident that emergency dental care and accompanying sedation is often needed. Emergency surgeries (i.e., appendectomy) in pregnant patients are common and nitrous oxide is often administered (along with other agents) to achieve general anesthesia. Retrospective studies have failed to reveal any adverse outcomes to patient or fetus.^{48,49} Nitrous oxide crosses the placenta readily and produces significant blood concentrations in the fetus. Fetal cardiac output is slightly reduced, but critical organ blood flow is unaffected.⁴⁹ However several points need to be considered before administering nitrous to the pregnant patient:*

1. **Avoid treatment if possible**
2. **Obtain medical consultation and patient consent before proceeding**
3. **Avoid hypoxia (prevention against spontaneous abortion)**
4. **Minimize treatment time (decreased exposure to the fetus)**

ANXIETY ASSESSMENT

Anxiety is defined as “an abnormal and overwhelming sense of apprehension and fear often marked by physiological signs (as sweating, tension, and increased pulse), by doubt concerning the reality and nature of the threat, and by self-doubt about one's capacity to cope with it.”⁵⁰ Fear of going to the dentist or more specifically “fear of pain” is one of the most common reasons that people avoid dental care. Therefore, it is important that we as dental healthcare providers be aware and sensitive to this issue. Although it is true that most patients anxiety can be effectively managed with a stress reduction protocol (gentle technique, caring attitude, profound local anesthesia etc), there is a significant segment of the population that need pharmacological intervention to manage their fears. Below is a list of available pharmacological modalities for managing fear and anxiety in the dental office:

- Enteral Sedation (oral, rectal, transmucosal)
- Inhalation (Nitrous Oxide)
- Intravenous Conscious Sedation
- Intravenous Deep Sedation
- General Anesthesia

Although it is difficult to accurately assess a patient's anxiety and place them into defined categories, we nonetheless attempt to categorize patients into 3 main anxiety groups: **mild, moderate and severe**. Once again it is difficult to determine what modality will be effective for each patient as many variables present, such as the pediatric patient that won't allow placement of the nitrous mask or an individual that abuses drugs that results in a high tolerance for medications. But in general, variability aside, listed below are guidelines for levels of anxiety and treatment modalities that in most cases would be appropriate for this class of patients:

Mild to Moderate Anxiety

Enteral Sedation
Inhalation Sedation (Nitrous Oxide)
 Intravenous Conscious Sedation

Severe Anxiety

Intravenous Deep Sedation
 General Anesthesia

In summary, we can expect to be able to effectively treat a significant number of patients that present with a positive history of fear and anxiety of dental treatment with one simple, easy to use and learn modality - **Nitrous Oxide sedation**.

STAGES OF ANESTHESIA

The induction of inhalation **general anesthesia** is divided into four stages. These stages and the body's physiologic reaction in each phase are explained below:

Stage 1 (Induction) - Beginning of administration until loss of consciousness. Analgesia accompanies this stage without amnesia (recall). Therefore, the patient is conscious during this phase.

Stage 2 (Excitatory) - Stage of struggling, breath-holding, delirium: From loss of consciousness to onset of surgical anesthesia. **(This is bad!!!)**

Stage 3 (Surgical) - is called the surgical or operative stage; Characterized by deep, regular, automatic breathing.

Stage 4 (Overdose) - Depression of vasomotor and respiratory centers, dilated pupils that no longer reacted to light (impending death)

With these stages of anesthesia laid out, we can better plan our sedation titration to avoid any level of anesthesia above stage 1. There is also a considerable range of sedation depth within stage 1 using the above defined levels. The American Dental Association (ADA) in their guidelines for the use of sedation and general anesthesia for dentists define four levels of sedation and anesthesia⁵¹ These defined levels of sedation and anesthesia further describe differing levels of central nervous system depression during stage 1 (conscious state) on the continuum to general anesthesia:

- Minimal sedation
- Moderate sedation
- Deep sedation
- General anesthesia

These levels are further explained as follows:

Minimal sedation – a minimally depressed level of consciousness produced by a pharmacological method that retains the patient's ability to independently and continuously maintain an airway and respond normally to tactile stimulation and verbal command. Although cognitive function and coordination may be modestly impaired, ventilatory and cardiovascular functions are unaffected.⁵²

Moderate sedation – a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. (Note: reflex withdrawal from a painful stimulus is not considered a purposeful response.) No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.⁵²

Deep sedation – a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.⁵²

General anesthesia – is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.⁵²

Because sedation and general anesthesia are a continuum, it is not always possible to predict how an individual patient will respond. Hence, practitioners intending to produce a given level of sedation should be able to diagnose and manage the physiologic consequences for patients whose level of sedation becomes deeper than initially intended. For all levels of sedation, the practitioner must have the training, skills drugs and equipment

to identify and manage such an occurrence until either assistance arrives (emergency medical service) or the patient returns to the intended level of sedation without airway or cardiovascular complications.⁵²

Goals of Nitrous Oxide Sedation Levels

Nitrous oxide being a weak inhalation agent requires high concentrations to produce unconsciousness. When using modern nitrous oxide sedation units which limit the maximum concentration of nitrous oxide delivered to the patient (< 70%), the likelihood of inducing the unconscious state (general anesthesia) is unlikely. However, individual response to the effects of any sedative agent must be appreciated.

Example:

1. In the case of the **hyporesponder** (resistant to effect); the level of sedation produced by nitrous oxide (even at high levels) does not effect adequate clinical sedation.
2. In the case of the **hyperresponder** (sensitive to effect); moderate to high levels of nitrous oxide result in oversedation or may result in unconsciousness.

Therefore a careful titration sequence (see table 4.) allows the practitioner to reach the optimal level of sedation for individual patients consistently. Listed below are signs and symptoms of desirable and undesirable levels of sedation/anesthesia:

Desirable

1. Patient is **CONSCIOUS** and muscles relaxed (absence of white-knuckle phenomena).
2. Feeling of well-being, euphoria
3. Vital signs are stable (Respiration, BP, and Pulse).
4. Tingling in toes, finger tips, tip of tongue, lips.
5. Warm sensation (due to vasodilatation)
6. Voice “throaty” due to effect of nitrous on tympanic membrane
7. Pain “disappears” but recognition of touch and pressure is still present.
8. Heaviness in lower extremities or lighter floating feeling, loses control of fine motor movements.
9. Sensation of flying, falling or spinning may be a signal that the patient is “too deep.” Be prepared to lower the level of sedation if the patient does not like this sensation.

Undesirable

1. Laugh, cries, becomes giddy
2. Becomes uncooperative, restless, agitated
3. Becomes uncomfortable
4. Falls asleep, jerks, mouth repeatedly closes
5. Doesn't respond rationally or very sluggishly
6. Talks incoherently, mentions dreams (including sexual)
7. Complains of nausea
8. Vomiting
9. Non-responsive, unconscious

When signs and symptoms of oversedation occur, the level of sedation should be reduced. This can be accomplished by reducing the concentration of nitrous oxide by approximately 10-15% or reducing the nitrous oxide flow rate by ½ L/min (and increasing oxygen flow by ½ L/min). In the case of more significant signs and symptoms of oversedation (vomiting, unconsciousness), the nitrous oxide flow should be stopped and 100 % oxygen delivered to the patient.

It is important to realize that oversedation may occur at any time during the procedure. This usually corresponds to periods of minimal stimulus (temporary crown fabrication, making of impressions etc) which results in the patient reaching deeper sedation levels. This can be avoided by anticipating these stress-free periods and reducing the nitrous oxide levels accordingly. Also, it is good practice to turn off the nitrous oxide gas during long periods of clinical down-time and then retitrate to previous levels of sedation.

To facilitate recovery, nitrous oxide can be turned off toward the end of treatment when the stressful part of the procedure is over (e.g., tooth preparation). This allows the patient to be discharged immediately after the procedure has ended as the patient will have already eliminated nitrous oxide from the body and breathed 100 % oxygen for the required amount of time.

ADMINISTRATION OF NITROUS OXIDE SEDATION

EQUIPMENT CHECK

All equipment should be checked to make sure that it is functioning properly before arrival of the patient.

Oxygen and nitrous oxide cylinders

1. One oxygen and nitrous oxide cylinder valve are opened very slowly counterclockwise to permit the slow rise of pressure in the system.
2. Once maximum pressure has been reached and confirmed, the valve should be closed and the pressure checked on the second set of cylinders as it is important to verify an adequate quantity of gasses available before the start of treatment. This is especially important for oxygen. Since nitrous oxide exhibits biphasic properties at room temperature, it is difficult to determine the volume of nitrous oxide remaining in the tank. However, it is important that the pressure gauge read 750 psi on both tanks before proceeding.
3. A full tank of oxygen will register approximately 2000 psi and unlike nitrous oxide, the pressure in the oxygen tank will drop in proportion to the amount of oxygen used. It is good practice to always use the less full cylinders first as this prevents wasting of the gasses.

Check for leaks

4. The tubing and reservoir bag must be properly connected to the machine and inspected for leaks. A more thorough evaluation of leaks can be made by applying a soap/water solution to pressure connections on the machine paying special attention to the cylinder/valve interface (high pressure connection). In the presence of a leak bubbles will be apparent and measures can be taken to stop the leak which might include tightening a connection or replacing deteriorated tubing and rubber materials.

Scavenging equipment

5. The scavenging equipment must be checked to ensure proper function and attached to the mask. The evacuation (scavenging) system setting should be set according to manufacturers recommendations.

CLINICAL PROCEDURE

1. The patient should visit the restroom before commencing treatment as it is time consuming and difficult to accomplish once the sedation has begun.

Preoperative vitals

2. Review the patient's medical history and record the patient's pulse, respiratory rate and blood pressure in the chart before beginning administration of nitrous oxide sedation. It is essential to obtain preoperative vitals before beginning nitrous oxide sedation as these will be used as baseline values and as a guide for discharge criteria. (see figure 14.)



Figure 14.

Pre-oxygenation period, tidal volume adjustment and trouble shooting

3. If the patient wears contacts, have the patient remove them as gas leaks around the mask may dry out the eyes.
4. Place the patient in a reclining, comfortable position. (see figure 15.)
5. Turn on at least six liters/minute flow rate of 100 % oxygen for the adult patient before placing the mask on the patient. A 4 liter/min rate is usually acceptable for most children.
6. Position the mask over the patient's nose adjusting the straps behind the patient's head to stabilize the mask while the patient adjusts the mask fit to their nose. The straps should be adjusted so that the mask fits snugly to the face and should form a relatively tight seal around the nose to prevent leakage of gasses to the environment as well as to prevent room air from leaking in and diluting the nitrous oxide. (see figure 16.)
7. Usually, leaks occur around the bridge of the nose and if attempts to properly fit the mask fail, 2x2 gauze can be fitted around the mask to prevent gasses from leaking into the patient's eyes. (see figure 17.)
8. 100% oxygen should be administered for three to five minutes to allow the patient to adjust to the apparatus. During this period, adjustments should be made in flow rates to meet the patient's tidal volume demands, making sure that the reservoir bag is neither too distended on expiration nor too empty on inspiration. The patient should be questioned to determine if they are comfortable with the volume of gas being delivered. (see figure 18.)
9. A reservoir bag that inflates and deflates only partially with each breath indicates an adequate flow rate. If the reservoir bag remains deflated this usually indicates either an inadequate minute volume of gas, large leaks in the system or excessive vacuum settings on the scavenging system. However, if the bag remains distended, this indicates too great a minute volume or a kink in the tubing. In either case it is essential that the problem be remedied before proceeding with the sedation. (see figure 19A and 19B.)

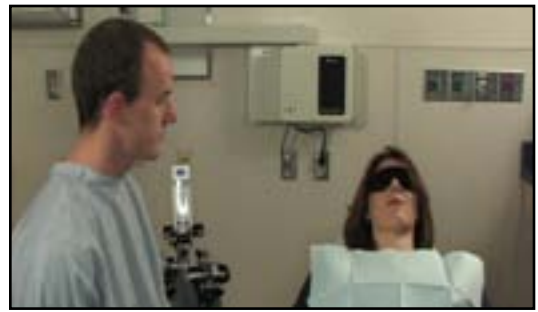


Figure 15.



Figure 16.



Figure 17.

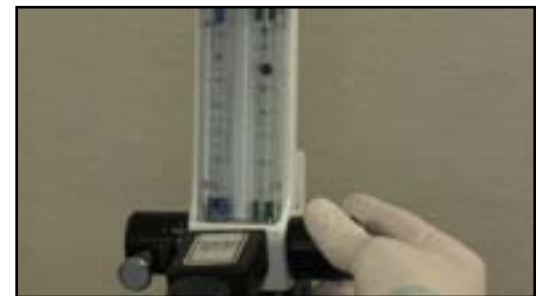


Figure 18.



Figure 19A. - Over-Inflated



Figure 19B. - Under-Inflated

Titration Sequence

10. Once the proper flow rates have been determined the titration of the nitrous oxide can begin. The titration of nitrous oxide in a slow systematic fashion is essential for the success of the technique. The initial titration of nitrous oxide should not exceed 10 -15 %. The concentration of nitrous oxide delivered is easily calculated by dividing the LPM of nitrous oxide by the total flow of gasses.

11. The first titration requires turning on the nitrous oxide gas to 1 L/min and decreasing the oxygen flow by one liter per minute. From this point on the patient should be encouraged to minimize talking and avoid breathing through their mouth as this dilutes the nitrous oxide concentration being taken in by the patient. In the patient that requires 6 LPM of total gas flow, this would result in an initial titration ratio of 5 LPM of oxygen and 1 LPM of nitrous oxide which results in a nitrous oxide concentration of approximately 16 %. The patient should be kept at this titration level for one minute. (see figure 20.)



Figure 20.

12. During the one minute intervals between titrations, the patient should be questioned regarding the symptoms that they are feeling at this level of sedation. Avoid describing sensations or symptoms that the patient might experience as the patient may sense that the sedation is not going well if they are not experiencing any of these symptoms. Questions should be asked concerning what symptoms they are feeling at this level of sedation. At the first titration level, few patients will describe any appreciable change in sensation.

13. After one minute at the first titration level decrease the oxygen flow one half L/min and increase the nitrous oxide flow by one half L/min (see figure 21A.). This sequence should be repeated until the desired level of sedation is reached. (see figure 21B.)



Figure 21A. - 2nd Titration



Figure 21B. - 3rd Titration

14. Titration sequence summary: Example using 6 L/min flow rate

Table 4

	Oxygen	N ₂ O	Concentration (N ₂ O)
1st Titration	↓ 1 L/min= (5 L)	↑ 1 L/min= (1 L)	1 / 6 = 16 %
1 Minute	↓ ½ L/min= (4½ L)	↑ ½ L/min= (1½ L)	1½ / 6 = 25 %
2nd Minute	↓ ½ L/min= (4 L)	↑ ½ L/min= (2 L)	2 / 6 = 33 %
3rd Minute	↓ ½ L/min= (3½ L)	↑ ½ L/min= (2½ L)	2 ½ / 6 = 42 %
4th Minute	↓ ½ L/min= (3 L)	↑ ½ L/min= (3 L)	3 / 6 = 50 %

Assessment of Sedation Depth

15. The ideal nitrous oxide concentration which results in optimal relaxation varies considerably among patients. Also, it is important to realize that the nitrous oxide concentration necessary to achieve this optimal level changes from one appointment to the next.
16. To be most effective, the nitrous oxide level should be adjusted during the procedure according to the intensity of the treatment at that moment. For example, the levels of nitrous oxide can be increased just prior to the administration of local anesthetic if this is considered a stressful part of the appointment for the patient and returned to the pre-established level once the injection is completed.
17. Clinical signs of achieving an adequate level of sedation result in an overall appearance of calmness and relaxation. The patient will no longer appear tense and overall muscle tone will be relaxed. The patient may describe the sensation as a tingling throughout parts of the body, a feeling of heaviness in the legs, a floating feeling or warmth throughout the body. There are many effects that can be experienced by a patient, but the most important end point is conformation from the patient that an adequate level of sedation has been attained and that the patient is ready for treatment to commence. (see figure 22.)



Figure 22.

Maintenance of sedation

18. It takes approximately five minutes for nitrous oxide to reach maximal clinical effect. Therefore, it is prudent to stop just short of the level of sedation that would be appropriate for the patient as the depth of sedation will continue to deepen over the next few minutes.
19. Once the patient has achieved positive signs of relaxation, maintain the patient at this level. **Adequate levels of sedation are usually achieved with a nitrous oxide concentration of 30-40% and 95% of patients can be successfully sedated with nitrous oxide levels at 50 % or lower.** However, levels of nitrous oxide up to 70% may be necessary for some patients.
20. **Permission must be obtained before administering greater than 50% nitrous oxide to any patient at LLUSD.** Newer nitrous oxide machines are designed so that it is impossible to deliver more than 70% nitrous oxide. This is a safety feature which prevents hypoxic mixtures of gasses from being delivered to the patient.

Adverse reactions (oversedation)

21. As nitrous oxide levels are increased, the practitioner should be attentive as levels of sedation change rapidly with nitrous oxide due to its relative insolubility in blood. A patient that was relaxed and cooperative can suddenly become detached and confused. The patient may begin laughing uncontrollably, experience nausea, enter into a dreamlike state, and become agitated or combative. (see figures 23A and 23B.)



Figure 23A.



Figure 23B.

22. At higher levels, patients can begin hallucinating; fantasizing, vomiting and may, in some instances, slip into unconsciousness. In these instances, the nitrous oxide should be turned off and the patient allowed to breathe 100% oxygen. When a patient experiences these adverse events, the sedation experience is unpleasant and in many instances the patient will not consent to nitrous oxide administration again. Careful attention to a regimented titration sequence can prevent this undesirable scenario from occurring. (see figure 24.)



Figure 24. - Unconscious??

Patient recovery, machine shutdown and post-oxygenation period

23. When treatment has been completed, the nitrous oxide is turned off first at the cylinder and then at the flowmeter (after the ball drops). This effectively bleeds the system of nitrous oxide gas. 100% percent oxygen is delivered to the patient at the initial tidal volume flow rate. (see figure 25.)
24. Continue giving oxygen for at least three to five minutes after nitrous oxide is discontinued to enhance recovery and to scavenge the remaining nitrous oxide as it exits the patient's lungs into the mask. This post oxygenation period can be extended if the patient still has lingering signs of sedation.
25. Return the patient to an upright and seated position slowly to prevent postural hypotension.
26. Remove the mask from the patient and turn off the oxygen supply first at the flow meter and then the tank. (see figures 26A and 26B.)

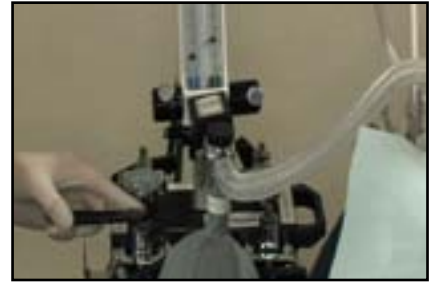


Figure 25



Figure 26A. - Turn off oxygen at flowmeter 1st



Figure 26B. - Turn off oxygen at cylinder valve 2nd

27. Document in the chart the final titration level of nitrous oxide used during the procedure as well as the start and stop time. Documentation of the post-oxygenation period along with any comments or observations that might be helpful for future appointments is essential.

Patient discharge

28. Take the patients pulse and blood pressure and record the values in the chart. The post-op vital signs are an objective sign of recovery from the sedation. These values should be within 20% of the preoperative readings. When it is determined that the patient has returned to baseline levels of cognitive function, it is acceptable to dismiss the patient. Those patients that meet the criteria for discharge are considered safe to operate a motor vehicle and drive themselves home 20-30 minutes post sedation.

ASA classification	I	II	III	IV
Blood Pressure	Pre-op _____			Post-op _____
Pulse	Pre-op _____			Post-op _____
Respirations	Pre-op _____			Post-op _____
N ₂ O start time:	_____			N ₂ O stop time _____
N ₂ O final titration %	_____			Post-oxygenation (minutes) _____
Comments:				

Table 5 - Modified from Handbook of Nitrous Oxide and Oxygen Sedation, Clark and Brunick

COMPLICATIONS ASSOCIATED WITH NITROUS OXIDE ADMINISTRATION

1. Nausea and Vomiting

Causes - the most common complications associated with nitrous oxide administration are nausea and vomiting. However, the incidence is low if proper technique (titration) and nitrous oxide levels of less than 50% are used.

High levels of nitrous oxide (using hyperbaric chamber) have resulted in postoperative nausea and vomiting in 100% of study subjects.⁵³ Nausea and vomiting typically result in insignificant episodes (<0.5%) in large studies conducted in the dental setting.⁵⁴ Other factors include:

- Long appointments (prolonged nitrous oxide administration)
- Eating a large (fatty) meal before appointment
- Empty stomach (fasting before appointment)
- History of motion sickness

Prevention - following these guidelines can reduce the incidence of nausea and vomiting to an almost negligible number:

- The careful titration of nitrous oxide to effect (avoids overdosing)
- Avoid long appointments (if possible)
- Eat a light meal (low in fat) prior to appointment

Management - As long as the patient remains conscious and is not deeply sedated; nausea and vomiting rarely result in adverse outcomes. However, if a patient becomes oversedated, aspiration is more likely and can cause significant morbidity.

- Turn off nitrous oxide and deliver 100% oxygen
- If vomiting occurs, remove nasal mask quickly
- Turn patients head to the side and down as this prevents choking and aspiration of vomitus
- Suction vomitus aggressively (prevents aspiration)
- Attempt to place nasal mask and continue administration of oxygen (patient may refuse mask)

2. Diffusion into closed spaces

Causes - As discussed earlier, nitrous oxide tends to diffuse into closed spaces. The following conditions can result in various signs and symptoms:

- Sinusitis/middle ear infection - Results in increased sinus/inner ear pressure and pain
- Bowel obstruction - diffusion of nitrous oxide into air pockets can result in abdominal distention and discomfort
- Pneumothorax - diffusion of nitrous oxide into a pneumothoraces happens very rapidly and can result in further collapse of the involved lung resulting in difficulty breathing and cyanosis

Prevention - a comprehensive medical history and subsequent review of this form will in most cases uncover these diagnoses.

Management - In the first two scenarios, administration of 100 % oxygen and the “**tincture of time**” (**waiting**) **allows these conditions to resolve on their own. In the unlikely event of an expanding pneumothorax** secondary to nitrous oxide administration, activation of the medical emergency response system (911) is essential.

3. Drying effect of gas

Causes - Leaks around the nasal mask are common due to the fitting of the mask. This produces a continual “air” current blowing into the patient’s eyes with resultant dryness.

Prevention - This is best managed at the beginning of the procedure during the fitting of the nasal mask. The patient should be questioned regarding leaks around the mask and measures taken to prevent leakage such as placement of 2x2 gauze around the edge of the mask (i.e., bridge of the nose). Also, patients who wear contact lenses should remove them prior to the appointment.

4. Delirium/Hallucinations/Sexual phenomena

Causes - Ever since the discovery of nitrous oxide more than 150 years ago, it has been appreciated that the response to nitrous oxide varies widely among individuals. In instances where unsatisfactory reactions occur, it is almost without exception that either excess levels of nitrous oxide (>50%) or rapid changes in concentration levels (neglecting to titrate) were the underlying cause. Jastak and Malamed⁵⁵ reported that greater than 50% nitrous oxide levels were used when allegations of sexual impropriety were brought against dentists. They also noted that there was no third party (dental assistant) present in the room at the time of treatment.

Prevention - Recommendations to avoid these uncomfortable situations (and costly) are:

- **Never be alone in the operatory with a sedated patient!!!! Always have a “chaperon” present throughout the entire procedure**
- Always titrate carefully using the titration sequence as described in this manual
- Charting - document that a third party was present in the room throughout the duration of treatment and levels of nitrous oxide attained

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