

The Use and Abuse of Nitrous Oxide: No Laughing Matter

Erica Helfer

Title

The Use and Abuse of Nitrous Oxide: No Laughing Matter

Motivation

The goal of this project is to use the topic of nitrous oxide (N_2O , or laughing gas) to engage high school students in inquiry-based activities that allow them to more deeply explore a number of topics typically taught in first-year chemistry.

North Carolina Standard Course of Study Objectives Addressed

- 1.01 Design, conduct, and analyze investigations to answer questions related to chemistry.
- 2.03 Apply the language and symbols of chemistry.
- 2.05 Analyze the basic assumptions of kinetic molecular theory and its applications:
 - Ideal Gas Equation
 - Dalton's Law of Partial Pressures
- 3.02 Apply the mole concept, Avogadro's number, and conversion factors to chemical calculations.
- 3.03 Calculate quantitative relationships in chemical reactions (stoichiometry).

Outline of Module

I. Background information

This will be provided by the instructor in the form of a short didactic presentation. Ideally this presentation would be interactive with an emphasis on eliciting students' prior knowledge about (and personal experiences with) anesthetic drugs such as nitrous oxide. Topics included in this presentation will include a brief history of anesthetic drugs, a comparison of different methods of administration (inhaled vs. intravenous), and an explanation of the basic mechanism of action of nitrous oxide.

II. Chemical principles of nitrous oxide administration

During this inquiry-based activity, students will explore the properties and behavior of gasses using nitrous oxide as an example. Key concepts will include the solubility of gases in liquids, Dalton's Law of Partial Pressures, and the Ideal Gas Law. I envision an activity in which students are provided with some basic information about how nitrous oxide is administered and are then presented with a problem-solving task in which they have to design a detailed procedure (as if they were the anesthesiologist) for different real life scenarios such as dental sedation (using nitrous oxide-oxygen) and general anesthesia (using nitrous oxide-halothane). For example, students might use Dalton's Law of Partial Pressures to calculate the pressure of various gasses used given the percent composition of the anesthetic mixture and then use a given flow rate and the Ideal Gas Law to calculate how many molecules of nitrous oxide/minute are being administered to the patient. Questions would also be designed to encourage students to think critically about the advantages and disadvantages of this drug, including possible complications involved in using nitrous oxide as an anesthetic (e.g. Based on what you know about the MAC value of nitrous oxide, why would using nitrous oxide alone for general anesthesia pose a risk of anoxia?) Ideally students would also have the opportunity to see and manipulate a real-life nitrous oxide administration set-up (gas tank, valves, hoses, face mask, etc.) in order to provide a concrete picture of science in action.

III. Nitrous oxide abuse

Students will research nitrous oxide abuse, either independently or by reading articles/case studies provided by the instructor. After students have gathered the facts, the instructor will guide students in a discussion about the effects of inhalant abuse and addiction.

IV. Assessment

One possibility for a cumulative assessment would be to have students construct concepts maps using key terms from the module such as nitrous oxide, halothane, anesthesia, analgesia, amnesia, CNS (central nervous system), GABA (gamma-aminobutyric acid), MAC (minimum alveolar concentration), Dalton's Law of Partial Pressures, Ideal Gas Law, solubility, blood:gas partition coefficient, alveoli, drug abuse, addiction, whippets, etc.

References

- Brody's Human Pharmacology: Molecular to Clinical, 4th ed. Chapter 28.
- Integrated Pharmacology, 3rd ed. Chapter 23.
- Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th ed. Chapters 13 and 14.
- Abraini, et al. (2003) *Gamma-aminobutyric acid neuropharmacological investigations on narcosis produced by nitrogen, argon, or nitrous oxide*. Anesthesia and Analgesia.
- Malamed & Clark (2003) *Nitrous oxide-oxygen: a new look at a very old technique*. Journal of the California Dental Association.
- Balster (1998) *Neural basis of inhalant abuse*. Drug and Alcohol Dependence.
- Rosenberg, et al. (1979) *Abuse of nitrous oxide*. Anesthesia and Analgesia.

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Activity #1 – You Be the Anesthesiologist
Teacher's Guide

Overview of Activity

In this activity students have the opportunity to engage in a real-life problem solving activity that challenges them to use what they know about gases to design a detailed procedure for the administration of nitrous oxide in a dental setting. Questions are designed to encourage students to think critically (and quantitatively) about chemical principles such as flow rate, temperature, pressure, and volume.

Prior to this activity students will need to be introduced to the basic gas laws (combined gas law, ideal gas law, and Dalton's law of partial pressure) and calculations involving these laws. Ideally students would also have the opportunity to see and/or manipulate a nitrous oxide administration set-up (gas tanks, valves, hoses, face mask, etc.).

Introduction

Have you ever had a cavity filled at the dentist or had your wisdom teeth removed by an oral surgeon? If so, it is likely that you have experienced the anesthetic effects of nitrous oxide. Dentists commonly use a mixture of nitrous oxide and oxygen administered by a nasal mask to induce mild sedation and help patients feel more relaxed.

Anesthesiologists must understand the properties and behavior of gasses in order to properly administer inhaled anesthetics like nitrous oxide. Your challenge in this activity is to use what you already know about gases to design a realistic procedure for administering nitrous oxide.

Activity

1. Sketch a drawing of the nitrous oxide/oxygen administration set up you saw in class. Make sure to include and label the following: gas tanks, flow meters, ventilator, gas monitor, mask, and waste gas tube. Use arrows to indicate the flow of gasses through the system. Below your drawing, describe the function of the different parts of the system.
2. A common mix used by dentists is 30% nitrous oxide/70% oxygen. Use the given information and your knowledge of the behavior of gases to answer the following questions.

Tidal volume (volume of one breath)	500 mL
Respiratory rate	12 breaths/min
Room temperature	22° C
Atmospheric pressure	1.00 atm
Volume of nitrous oxide in tank	20.0 L
Pressure inside nitrous oxide tank	135 atm

- a. What total flow (in L/min) to the nasal mask is required in order to maintain a normal respiratory rate?

$$\frac{500 \text{ mL}}{1 \text{ breath}} \left| \frac{12 \text{ breaths}}{1 \text{ min}} \right| \frac{1 \text{ L}}{1000 \text{ mL}} = 6 \text{ L/min}$$

- b. What would the flow rates of nitrous oxide and oxygen be in this mixture (in L/min)?

$$6 \text{ L/min} \times 0.30 = 1.8 \text{ L/min } N_2O \quad 6 \text{ L/min} \times 0.70 = 4.2 \text{ L/min } O_2$$



- c. What would the mole fractions (and partial pressures) of nitrous oxide and oxygen be in this mixture?

$$x_{N_2O} = 0.30, P_{N_2O} = 0.30 \text{ atm}, x_{O_2} = 0.70, P_{O_2} = 0.70 \text{ atm}$$

- d. How many moles of nitrous oxide are in your tank? (Assume that the tank is at room temperature.)

$$PV = nRT$$

$$n = PV/RT$$

$$n = (135 \text{ atm})(20.0 \text{ L}) / (0.0821 \text{ L}\cdot\text{atm}/\text{mol}\cdot\text{K})(293 \text{ K})$$

$$n = 112 \text{ moles}$$

- e. What volume would this amount of nitrous oxide occupy at room temperature and atmospheric pressure?

Using the combined gas law

$$P_1V_1/T_1 = P_2V_2/T_2$$

$$(135 \text{ atm})(20.0 \text{ L}) = (1.00 \text{ atm})(V)$$

$$V = 2700 \text{ L}$$

Using the ideal gas law

$$PV = nRT$$

$$V = nRT/P$$

$$V = (112 \text{ moles})(0.0821 \text{ L}\cdot\text{atm}/\text{mol}\cdot\text{K})(293 \text{ K}) / (1.00 \text{ atm})$$

$$V = 2690 \text{ L}$$

- f. Assuming you have an unlimited supply of oxygen, how long could you run your apparatus at this rate before you ran out of nitrous oxide?

$$\frac{2690 \text{ L}}{\text{tank}} \bigg| \frac{1 \text{ min}}{1.8 \text{ L}} = 1490 \text{ min (24.9 hr)}$$

- g. Breathing air that contains less than 20% oxygen can lead to hypoxia (oxygen deficiency) causing serious problems and even death. How might you design safety mechanisms for your oxygen and nitrous oxide tanks to prevent this dangerous scenario?

Design a valve that prevents the flow of oxygen from dropping below 1.2 L/min and prevents the flow of nitrous oxide from exceeding 4.8 L/min.

3. Entonox, a gas mixture containing 50% nitrous oxide in oxygen, is widely used to provide analgesia during labor, for trauma victims, or other emergencies. It is manufactured by bubbling O_2 through liquid N_2O , with vaporization of the liquid to form a gaseous O_2/N_2O mixture. Entonox is supplied in cylinders at a pressure of 137 bar and must be stored above -6°C . Below this temperature the N_2O liquefies and the two gases separate in a process called lamination. Why would this be problematic?

If this occurs, a high concentration of O_2 will be delivered first, but as the cylinder empties the mixture will become progressively more hypoxic as it approaches 100% N_2O . Source: Bovill, J.G. Inhalation Anaesthesia: From Diethyl Ether to Xenon. (2008).

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Activity #1 – You Be the Anesthesiologist
Student Handout

Introduction

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Room temperature	22° C
Atmospheric pressure	1.00 atm
Volume of nitrous oxide in tank	20.0 L
Pressure inside nitrous oxide tank	135 atm

- a. What total flow (in L/min) to the nasal mask is required in order to maintain a normal respiratory rate?
- b. What would the flow rates of nitrous oxide and oxygen be in this mixture (in L/min)?
- c. What would the mole fractions (and partial pressures) of nitrous oxide and oxygen be in this mixture?
- d. How many moles of nitrous oxide are in your tank? (Assume that the tank is at room temperature.)
- e. What volume would this amount of nitrous oxide occupy at room temperature and atmospheric pressure?
- f. Assuming you have an unlimited supply of oxygen, how long could you run your apparatus at this rate before you ran out of nitrous oxide?
- g. Breathing air that contains less than 20% oxygen can lead to hypoxia (oxygen deficiency) causing serious problems and even death. How might you design safety mechanisms for your oxygen and nitrous oxide tanks to prevent this dangerous scenario?

3. Entonox, a gas mixture containing 50% nitrous oxide in oxygen, is widely used to provide analgesia during labor, for trauma victims, or other emergencies. It is manufactured by bubbling O_2 through liquid N_2O , with vaporization of the liquid to form a gaseous O_2/N_2O mixture. Entonox is supplied in cylinders at a pressure of 137 bar and must be stored above $-6^\circ C$. Below this temperature the N_2O liquefies and the two gases separate in a process called lamination. Why would this be problematic?

Overview of Activity

The main objective of this activity is to provide students with the opportunity to better understand nitrous oxide as a commonly abused inhalant drug. Through reading a variety of sources (see “Suggested Resources” list) students learn how and why nitrous oxide is abused and be able to discuss the adverse effects associated with nitrous oxide abuse. Upon completion of their independent research students will be prepared to debate whether or not they feel the distribution of nitrous oxide should be more tightly controlled.

Introduction

“...I felt a high, an extraordinary degree of pleasure, different from that produced by wine...and yet approaching nearer to it than any other sensation I am acquainted with.”¹

The euphoric effects of nitrous oxide were first described by Humphrey Davy in 1800. Today, people that abuse nitrous oxide as a recreational drug seek this same “high”. Nitrous oxide is becoming increasingly popular as an inhalant drug of abuse. Compared to other illegal drugs, nitrous oxide is relatively easy to obtain because it is used legally in medicine and industry. Most recreational users consider this fast-acting drug relatively harmless; however, nitrous oxide can have many serious short- and long-term effects on the human body.

In this activity you will conduct your own research to learn more about the abuse of nitrous oxide. Use the resources provided to you by your instructor to investigate the questions below.

Questions to Investigate

1. Why do people use and abuse nitrous oxide?

Feelings of euphoria, a “high”, sense of well-being.

2. What are some possible short-term negative effects of nitrous oxide use?

Slurred speech, difficulty maintaining balance, difficulty walking, slow response times, unconsciousness, nausea, etc.

3. Directly inhaling nitrous oxide from a tank or whippit can result in frostbite. How does this happen?

Rapid expansion of compressed nitrous oxide gas causes the metal container to get very cold.

4. What are some possible long-term negative effects of nitrous oxide use?

Anemia, neuropathy, ataxia (gross incoordination of muscles), etc.

¹ Description of nitrous oxide inhalation by Mr. James Thomson in the classic monograph of Sir Humphrey Davy (from Rosenberg, et al., 1979.)

5. How is vitamin B12 involved in the long-term effects of nitrous oxide?

“The neuropathic effects of nitrous oxide are thought to be due to the gas’ ability to inactivate vitamin B12 by oxidizing the cobalt moiety of the vitamin. Deficiency of vitamin B12 inhibits methylation processes specifically important for efficient hematopoiesis and membrane lipid formation.” (Miller, 2004)

6. Can you die from inhaling nitrous oxide? Explain.

Yes! Death could potentially result from hypoxia or aspiration of vomit.

7. **THE BIG QUESTION:** Based on what you have learned, do you feel that the distribution of nitrous oxide should be more tightly controlled? Why or why not?

One possibility would be to have students “debate” this issue. Hopefully most students will come to the ultimate conclusion that the brief high provided by nitrous oxide is not worth the risk of serious adverse effects or even death.

Suggested Resources

1. The Compressed Gas Association’s “Nitrous Oxide Abuse Hotline”. <http://www.cganet.com/N2O/>

This website provides a very readable fact sheet about nitrous oxide as well as a page specifically about nitrous oxide abuse. It is a good place to start in order to learn some basic information about nitrous oxide use and abuse.

2. Michael Miller, et al. Nitrous Oxide “Whippit” Abuse Presenting as Clinical B12 Deficiency and Ataxia. American Journal of Emergency Medicine. Volume 22, Number 2. March 2004.

This brief (less than 1 page) article provides a recent case study of a 39-year old man presenting with multiple symptoms as a result of chronic nitrous oxide abuse. The article provides a good overview of the negative effects of nitrous oxide abuse as well as a short discussion of how some of these effects are tied to vitamin B12 deficiency. Although it contains some challenging vocabulary, advanced high school students should be capable of comprehending this article with some assistance.

3. Henry Rosenberg, et al. Abuse of Nitrous Oxide. Anesthesia and Analgesia. Volume 58, Number 2. March-April 1979.

This article reports the results of a study on nitrous oxide abuse in medical and dental students. The results of an anonymous questionnaire showed that up to 20% of students surveyed had used nitrous oxide in a social setting! The article discusses some of the adverse effects reported by the students as well as other potentially more dangerous effects. Various sources of nitrous oxide for recreational use are also discussed.

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Activity #2 – Nitrous Oxide Abuse
Student Handout

Introduction

“...I felt a high, an extraordinary degree of pleasure, different from that produced by wine...and yet approaching nearer to it than any other sensation I am acquainted with.”²

The euphoric effects of nitrous oxide were first described by Humphrey Davy in 1800. Today, people that abuse nitrous oxide as a recreational drug seek this same “high”. Nitrous oxide is becoming increasingly popular as an inhalant drug of abuse. Compared to other illegal drugs, nitrous oxide is relatively easy to obtain because it is used legally in medicine and industry. Most recreational users consider this fast-acting drug relatively harmless; however, nitrous oxide can have many serious short- and long-term effects on the human body.

In this activity you will conduct your own research to learn more about the abuse of nitrous oxide. Use the resources provided to you by your instructor to investigate the questions below.

Questions to Investigate

1. What kinds of “positive” effects do recreational nitrous oxide users report? In other words, why do people abuse nitrous oxide?
2. What are some possible short-term negative effects of nitrous oxide use?
3. Directly inhaling nitrous oxide from a tank or whippit can result in frostbite. How does this happen?
4. What are some possible long-term negative effects of nitrous oxide use?
5. How is vitamin B12 involved in the long-term effects of nitrous oxide?
6. Can you die from inhaling nitrous oxide? Explain.
7. **THE BIG QUESTION:** Based on what you have learned, do you feel that the distribution of nitrous oxide should be more tightly controlled? Why or why not?

² Description of nitrous oxide inhalation by Mr. James Thomson in the classic monograph of Sir Humphrey Davy (from Rosenburg, et al., 1979.)

