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Asphyxial Deaths from the Recreational Use of Nitrous Oxide

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ABSTRACT: The recreational use of nitrous oxide is widespread. Nitrous oxide for recreational use is usually obtained from anesthesia tanks or whipped-cream machine chargers or cans. Twenty previously described deaths associated with recreational nitrous-oxide use describe anesthesia tanks and whipped-cream machine dispensors as a source. Five deaths associated with nitrous oxide use are presented; two involving whipped-cream cannisters as the source, two involving anesthesia tanks, and one involving a racing fuel tank as a source of nitrous oxide. Autopsy findings in our cases were subtle or negative, but usually suggestive of asphyxia. Through a laboratory simulation, we have confirmed that nitrous oxide displaces oxygen in a closed space, which probably leads to asphyxia. A review of the literature, neuropharmacology, and pathophysiology of nitrous oxide use is also presented.

KEYWORDS: pathology and biology, autopsy, nitrous oxide, asphyxia, sudden death, drug abuse

The recreational use of nitrous oxide is widespread in today's society [*1–3*]. Although nitrous oxide is often promoted as a "safe" substance among users seeking the euphoric effects of "laughing gas," 20 cases of death due to the recreational use of nitrous oxide are found in the literature [*5,6,20*]. In each of these reported cases, the source of nitrous oxide was a gas-filled anesthesia tank. Recently, an alternate form of nitrous-oxide administration has become popular. Whipped-cream cans as well as chargers for whipped-cream dispensers ("Whippets®") are a readily available, less expensive, and more easily concealable source of nitrous oxide [*1,2,4,7–10,20*]. Because it is bacteriostatic, nonflammable, and does not change the taste of the product, nitrous oxide is used to dispense whipped cream [*3*]. We present five cases of death associated with nitrous oxide use; two deaths associated with inhaling nitrous oxide from chargers for whipped-cream dispensers,

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one associated with inhaling gas from a race car super charger tank and two associated with inhaling nitrous oxide from gas-filled anesthesia tanks.

Case Reports

Case 1

A 19-year-old restaurant employee with a history of drug abuse was found dead, lying face up on his bed, with both feet on the floor (Fig. 1). His head was covered with a large plastic garbage bag and a belt was loosely applied around his neck. A spent whipped-cream charger and a charger puncturing device (a "Whippet") was found lying within the bag (Figs. 2 and 3). The belt was apparently used to seal the base of the bag around his neck. The bulk of the bag was behind the head and the remainder was stretched tightly against his face and mouth. The autopsy showed only passive congestion of the lungs. Although the serum alcohol was negative, the subject's urine was positive for cannabinoids. Nitrous oxide was detected in the blood and the left mainstem bronchus.

Case 2

A 29-year-old male was found naked in front of his television. His wife, who found the subject, initially told police that he had been murdered. Later, when whipped-cream nitrous-oxide chargers were found near the body, she admitted she had found him with a plastic bag over his head. It seems he would commonly watch pornographic material

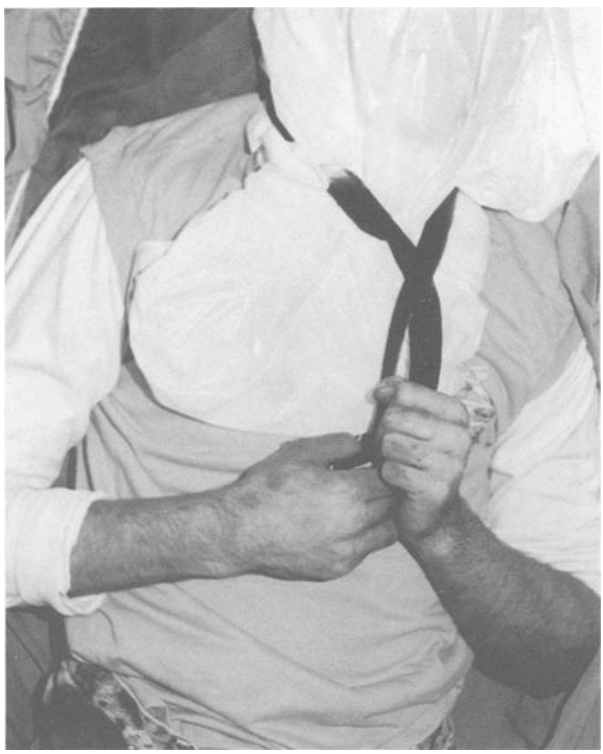

FIG. 1—*Case 1. Victim with plastic bag around neck secured by belt.*

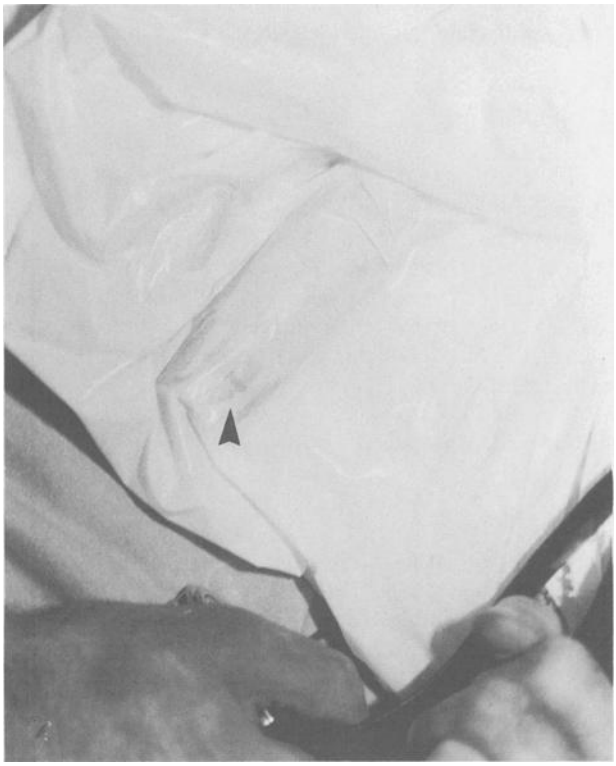

FIG. 2—*Case 1. Note "Whippet" with N_2O cartridge (arrow) inside bag.*

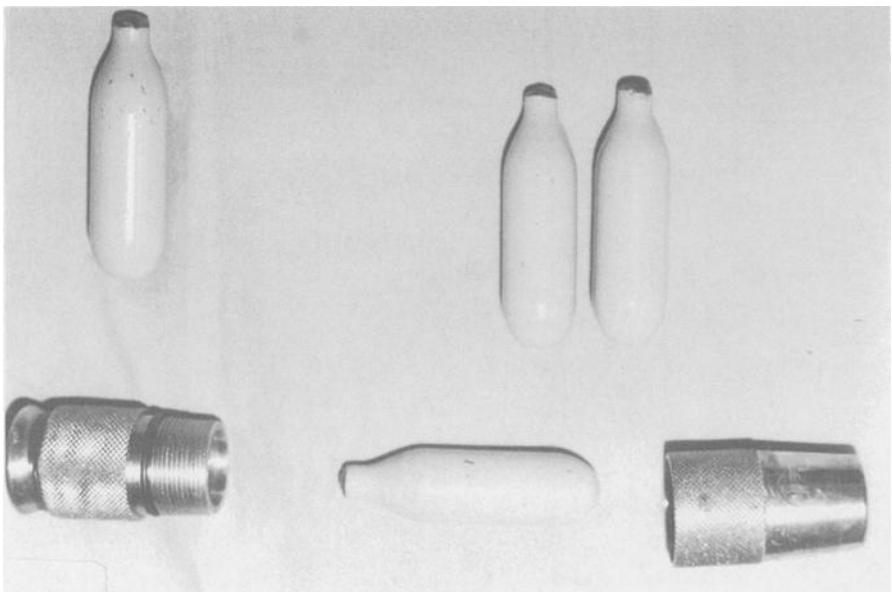

FIG. 3—*Whippet discharge device with empty N_2O cartridges.*

and masturbate while inhaling nitrous oxide. He also used a bag to aid in the inhalation of the gas and then presumably removed it. At autopsy, evidence of asphyxial death was found, including suffusion of livor in the face and neck as well as subgaleal petechiae. Toxicologic analysis was negative for nitrous oxide and other drugs of abuse.

Case 3

A 54-year-old dentist was found dead in his office with a plastic bag over his head and an empty nitrous oxide anesthesia tank nearby. The tank was connected to a hose that ran into the bag. He had been depressed recently and was known to use nitrous oxide during periods of depression. The autopsy showed pulmonary congestion and edema. There was also mild cardiac dilitation and hypertrophy. Nitrous oxide determinations were not done; ethanol and other drugs of abuse were not detected.

Case 4

A 20-year-old college student driving his automobile crossed the center line on an interstate highway, hitting a semi-tractor trailer "head-on." Autopsy showed extensive blunt force injury of the head and abdomen. A blue nitrous-oxide tank was found at the scene (Fig. 4). This type of tank is used to supercharge racing engines. Survivors of the crash had balloons in their pockets. The occupants of the car were probably passing around nitrous oxide-filled balloons. Nitrous oxide was detected in the blood at a concentration of 14.6 mg/dL. A test for blood alcohol was negative and other drugs of abuse were not detected in the urine.

Case 5

An 18-year-old male college student was found dead by his roommate in his bunk bed cupping an anesthesia mask over his face. The mask was connected to a nitrous oxide anesthesia tank stolen from the anesthesia department of a local hospital. Cardiopulmonary resuscitation was attempted, but was unsuccessful. The autopsy revealed mod-

FIG. 4—*Tank of N_2O used in automobile racing found at scene of fatal motor vehicle accident in Case 4.*

erate pulmonary edema, cardiac petechiae and generalized visceral congestion. Blood nitrous oxide concentrations were measured at 12.3 mg/dL.

Analytical Methods

Blood nitrous oxide levels were determined using the method of Molloy, et al. [*11*]. Accordingly, nitrous oxide was measured by an equilibration method in which known volumes of air were equilibrated under standard conditions. The nitrous-oxide concentration of the overlying air was analyzed by gas chromatography and compared to a standard curve. In case one, the left mainstem bronchus was clamped and sealed immediately after the chest was opened. The bronchus was sealed with paraffin film, as was the container. The air in the bronchus was analyzed by gas chromatography.

Laboratory Simulation of Apparatus in Case One

In an attempt to recreate and analyze the nitrous oxide and oxygen environment present in the plastic bag covering the head of Case 1, we assembled an apparatus from a plastic bag, a belt, an anesthesiologists' end-tidal nitrous oxide and oxygen analyzer, and the original whipped-cream charger with an unopened nitrous-oxide cartridge. The plastic bag was held upright while the cartridge puncture device (Fig. 3) was used to release the nitrous oxide into the bag. The bag was loosely sealed around the arm of the investigator with a belt. Oxygen and end-tidal nitrous oxide electrodes (Ohmeda 5200 CO_2 Monitor {capable of analyzing nitrous oxide} and Ohmeda 5120 Oxygen Monitor) were placed in the center of the bag. The volume of the bag was similar to that depicted in Fig. 1. The nitrous-oxide cartridge was punctured using the charging device and its contents discharged into the bag over a period of approximately 3 s. Percent oxygen and percent nitrous oxide in the bag were then measured.

The nitrous-oxide cartridge (EZ Whip®, manufactured in Hungary), when weighed analytically before and after discharge, contained 7.787 grams of nitrous oxide. This is the equivalent of approximately 8 L of nitrous oxide at standard temperature and pressure. At the beginning of the simulation, the oxygen sensor read 21%. Ten s later, the percent concentration of oxygen in the bag was only 13%. The percent concentration of nitrous oxide was zero initially and in 10 s had increased to 59%. At 1 min, the percent oxygen concentration had decreased to 10% while the nitrous oxide percent remained essentially unchanged (59%) (Fig. 5). The results of a second simulation trial were similar to that of the first.

Discussion

Case 1 illustrates the most immediate danger of nitrous oxide use—the displacement of oxygen which, in an enclosed space, can lead to hypoxia and asphyxiation [*12*]. As we have shown, even a small nitrous oxide charger (Whippet) can rapidly change the percent oxygen available for inspiration from 21% to 9%. With respiration, the percent concentration of oxygen within the bag would most likely decrease further as oxygen is consumed. The hypoxia and subsequent asphyxia was probably further enhanced by the bag becoming tight over the victims' face. It is unclear whether hypoxia or the anesthetic effect of nitrous oxide led to the loss of consciousness in case one, but it is likely that the two are synergistic. It has been reported that some individuals lose consciousness when inspiring 30% nitrous oxide in oxygen while most become unconscious with 80% [*12*].

Although nitrous oxide does not depress the respiratory drive significantly, the normal physiologic response to hypoxia is blunted when 50% nitrous oxide is given [*12*]. An

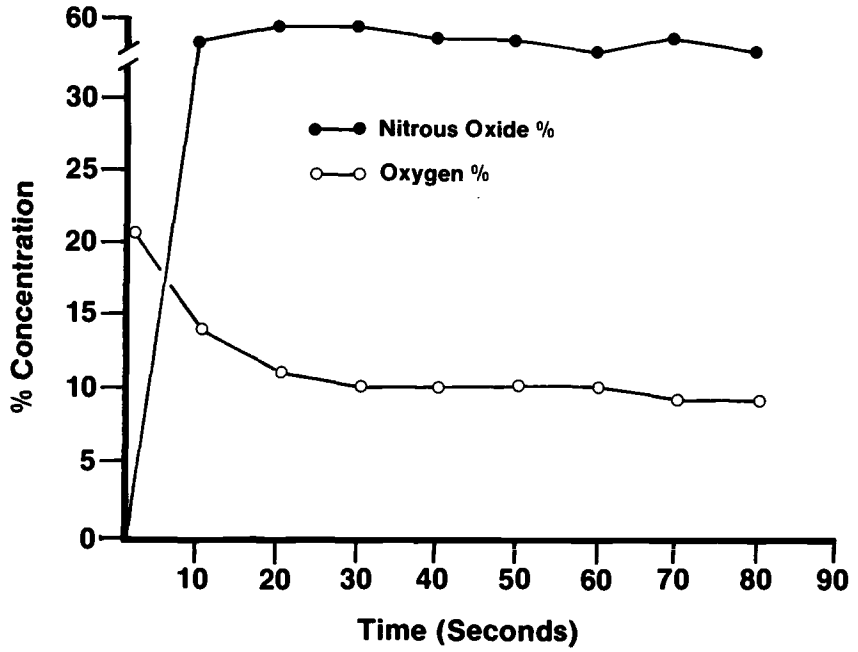

FIG. 5—*Laboratory simulation of environment from Case 1.*

environment of 60% nitrous oxide was produced in our simulation. The discharge of a nitrous oxide cartridge into the plastic bag may not have only displaced oxygen, but may also have blunted the normal hypoxic response mechanism, making the victim even more susceptible to a positional type of asphyxia.

Autopsy findings in all cases were those seen in asphyxial deaths, that is, acute passive congestion of the lungs and other viscera, subgaleal petechiae, cardiac petechiae, and suffusion of livor in the face. Blood and/or bronchial nitrous oxide is usually positive, but may be negative as in case two, where the scene had been altered. Since most centers probably do not routinely test for nitrous oxide, and the anatomic findings of asphyxial deaths are often subtle, many nitrous oxide related deaths may be overlooked. For example, had we not been presented with the history of a race car supercharger tank at the scene in Case 4, we would not have investigated nitrous-oxide blood levels. Obviously, nitrous oxide poisoning should be considered as a potential cause of death in asphyxial deaths, especially when other studies are negative.

Nitrous oxide is used in hot-rodding and drag racing to boost horsepower. By forcing nitrous oxide into the combustion chambers of the engine, the oxygen content of the gaseous combustion mixture is increased [*22*]. Oxygen is released when N_2O is heated to 572° Fahrenheit. Also, the release of the gas cools the engine, producing roughly a 1% increase in horsepower with each degree Fahrenheit of cooling. Large tanks of nitrous oxide, usually mixed with small amounts of sulfur dioxide, are widely available at racing supply stores.

Nitrous oxide is designated by the U.S. Food and Drug Administration as Generally Recognized as Safe (GRAS). In fact, many manufacturers ignore the internationally recognized blue color code for whipped-cream chargers [*13*]. Nitrous oxide is used by the dairy industry because it is inexpensive, bacteriostatic, and does not change the taste of food [*13*]. Two common forms of "grocery store" or "Whippet®" nitrous oxide are available. These are chargers for whipped cream machines and pre-mixed aerosol cans

of whipped cream. The aerosol cans, if held upright, can be used to obtain nitrous oxide without dispensing whipped cream as long as the aerosol can is not shaken [*4*]. A standard charger generally contains 4 to 5 L of 90 to 95% pure nitrous oxide while the aerosol cans hold around 3 L of nitrous oxide. The EZ Whip® charger used in Case 1, according to the manufacturer's product information, contained pure nitrous oxide. According to our analysis, one cartridge contains approximately 8 L of nitrous oxide, capable of producing an environment of 60% N_2O in our laboratory simulation. The aerosol cans and chargers can be purchased by anyone at local drug stores, supermarkets, or restaurant-supply houses [*7,10,13*].

Aside from sudden death, there are other harmful effects, both chronic and acute, associated with nitrous oxide use. The cold gas escaping from the source of administration can freeze the oropharynx [*4*] and polyneuropathy has also been described as a result of chronic use [*8,14*]. Heavy exposure has been associated with seizures and coma [*14,16*]. Bone-marrow suppression has also been associated with nitrous oxide use [*12*].

Respiratory distress and acute bronchiolitis have been reported in a patient who inhaled a third potential source of nitrous oxide—"homemade" production of gas from the combustion of ammonium-nitrate fertilizer [*8*]. The respiratory distress induced by the inhalation of nitrous oxide in this case was probably a result of contamination with nitric oxide [*15*]. Two cases of "spontaneous" pneumomediastinum associated with nitrous oxide abuse have also been reported [*21*]. Instructions for making nitrous oxide at home as well as various devices for using nitrous oxide are available in drug paraphernalia stores, that is, "head shops" [*1,2,4*].

Nitrous oxide is an inexpensive, readily available recreational "drug" that is currently undergoing a resurgence in popularity. For example, it is common knowledge among drug abusers that nitrous oxide cannot be detected in routine urine drug screens. Therefore, the gas may be chosen for use instead of narcotics, which are notoriously easy to detect in the urine. Although "laughing gas" has been used recreationally for over a century, little has been known concerning its pharmacodynamics. It is a well known fact that nitrous oxide produces analgesia equivalent to that of morphine. Nitrous oxide also decreases cortisol and increases prolactin without changing adrenocorticotrophin hormone (ACTH) levels in a manner similar to that of exogenously administered opiates [*17*]. A recent study has shown that nitrous-oxide analgesia is stereospecifically reversed by (−)-nalozone, a pure narcotic antagonist, but not by its enantiomer (+)-naloxone [*18*].

It seems likely, therefore, that nitrous oxide-induced euphoria and analgesia is a result of interaction with endogenous opioid system(s), either through direct interaction with opiate receptors or with endogenous opioid neurotransmitters/neuromodulators. In addition to the difficulty in detection, euphoria and analgesia created by nitrous oxide, other reasons for its popularity probably include the fact that nitrous oxide can be legally and easily obtained and that it does not produce a "hangover" or other untoward effects for the most part. As one college student described his experience, "It came on fast and totally wipes you out . . . and in five minutes you are ready to do your homework" [*13*].

In one study, the dose of nitrous oxide (percent N_2O) required to produce subjective pleasant effects such as warmth, tingling, "floating" and relaxation without significant or observable reduction in consciousness, ranged from 33 to 60% (mean 49%) [*17*]. If indeed, the endogenous opioid system were involved and tolerance were to develop to nitrous oxide in a manner similar to that of exogenously administered opiates, users of nitrous oxide would probably need to seek higher doses, that is a higher percent N_2O in the form of prolonged inhalation of pure nitrous oxide or the use of plastic bags to cover the head in order to achieve the same pharmacological effect.

When properly used, nitrous oxide is a safe, non-toxic adjunct to anesthesia and propellant for whipped cream. We have shown that when nitrous oxide is used in a closed

space, a lethally low oxygen tension environment develops. The autopsy may show signs of asphyxial death, or anatomic findings may be absent. The death scene may be altered. Nitrous oxide, therefore, should be considered as a potential cause of death in unexplained asphyxia or in cases of "no anatomic cause of death."

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