

## CLINICAL VIGNETTE

# Laughing Gas (Nitrous Oxide) Is No Laughing Matter

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A 24-year old female with no prior medical issues presented to the emergency department with 2 weeks of progressive numbness that started in the lower extremities and had progressed to the upper extremities. Two weeks earlier, she woke up with numbness in the lateral aspects of her knees and legs, which progressed to her feet over the next few days. She also developed “pins and needles” sensation in her feet as her symptoms progressed. One week prior to admission, she developed tingling and burning sensations in her hands and had difficulty performing fine tasks with her hands. Three days prior to admission, she complained of difficulty walking and had three ground level falls. She did not report any head injury or loss of consciousness. She denied any bowel or bladder incontinence or any significant extremity pain. She denied taking any medications and denied smoking, alcohol, and, initially, the use of any recreational drugs.

On exam, her vital signs were normal except for slight tachycardia. Her gait was ataxic with a positive Romberg’s. She had upper and lower extremity proximal and distal muscle weakness. She also had symmetric upper and lower extremity sensory loss in a stocking and glove pattern. Sensation to pinprick, light touch, proprioception, and vibration were all absent bilaterally below her knees. Her reflexes were brisk.

On further history, she admitted to the use of nitrous oxide recreationally in the form of “whip-its,” which are small pressurized canisters containing nitrous oxide used in whipped cream dispensers. She was using about 80 grams (10 whip-its) per day for the last 3 months.

Her labs showed a macrocytic anemia with a hemoglobin of 10g/dL and mean corpuscular volume (MCV) of 110  $\mu\text{m}^3$ . Her vitamin B<sub>12</sub> level was low at 150 pg/mL (normal 210-950 pg/mL). Homocysteine and methyl malonic acid levels were elevated at 60  $\mu\text{mol/ml}$  (normal 5-15  $\mu\text{mol/ml}$ ) and 2520 nmol/ml (87-318 nmol/ml) respectively. Folate levels were normal.

An MRI of the spine did not show any significant abnormalities. The patient was admitted to the hospital and started on intramuscular vitamin B<sub>12</sub> in addition to physical therapy. Over the next three months, her sensory and motor symptoms improved; however, she required a cane for mobility.

### Discussion

Nitrous oxide, popularly referred to as laughing gas, is an inhalant that is commonly used as an anesthetic in the medical and dental fields. It is also used as a propellant in the food industry and in the car racing industry to boost horsepower.<sup>1</sup> The gas is also readily available in grocery stores in small canisters called “whip-its” used by caterers and chefs as a propellant for whipped cream and foams.

Nitrous oxide has become a popular drug of abuse. Large quantities of nitrous oxide intended for the medical/dental field or the racing industry have been diverted to underground parties, commonly known as raves, where it can be dispensed in balloons for inhalation.<sup>2</sup> In one study, nearly 16% of adolescents reported nitrous oxide abuse, making it one of the most commonly abused inhalants in the United States.<sup>3</sup> Figure 1 shows the general set-up for inhalation of the gas.

The toxicity related to nitrous oxide is mediated through oxidation of cobalt ions in vitamin B<sub>12</sub> causing its inactivation.<sup>4</sup> The deactivation of vitamin B<sub>12</sub> leads to inability of homocysteine to be converted to methionine. Lack of methionine prevents methylation of myelin proteins causing demyelination within the peripheral and central nervous system. Myelopathies affecting the dorsal columns can result in issues with fine touch, proprioception, and vibration as exhibited in this patient.<sup>5,6,7</sup>

The presence of neurologic dysfunction associated with nitrous oxide abuse is usually associated with low serum vitamin B<sub>12</sub> levels, low hemoglobin, and high MCV as depicted in the laboratory profile of the case patient. However, all the above listed tests can be normal in some patients. When there is a high index of suspicion but the initial findings of serum vitamin B<sub>12</sub>, hemoglobin, and MCV are normal, substrates needed in reactions catalyzed by vitamin B<sub>12</sub>, namely homocysteine and methyl malonic acid, can be measured. When these substrates are elevated in the presence of a normal vitamin B<sub>12</sub>, hemoglobin, and MCV, it becomes an example of “functional vitamin B<sub>12</sub>” deficiency.<sup>8</sup>

Neurological complications from nitrous oxide abuse can be improved with high dose intramuscular vitamin B<sub>12</sub>. Homocysteine and methyl malonic acid will normalize within a short period of time after initial supplementation. However, recovery from the neurologic injury is usually slow and may

take several months. In some patients, neurologic damage may be irreversible.<sup>9,10</sup>

It is imperative that healthcare providers recognize the dangers and debilitating effects of short- and long-term inhalant abuse. Patients presenting with unexplained neurologic complaints should be screened for nitrous oxide abuse. Appropriate laboratory evaluation, rapid treatment, and proper counselling can only be accomplished if the provider is aware of the more uncommon drugs of abuse.

### Figures

**Figure 1:** “Whip-it” cannisters containing nitrous oxide, a balloon and an aluminum cracker.



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