Case Report

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# Peripheral Neuropathy Induced by Nitrous Oxide Misuse: A Case Report

**Urgent Message:** Nitrous oxide-associated peripheral neuropathy may present similarly to Guillain-Barré syndrome, and clinicians are encouraged to conduct a careful clinical assessment of patients with neurological symptoms.

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## Abstract

**Introduction:** Although often regarded as "safe," repeated exposure to nitrous oxide can result in serious neurological sequelae, most notably functional vitamin $B_{12}$ deficiency.

**Clinical Presentation:** A 20-year-old male with a 2-week history of paresthesia in all 4 limbs presented to urgent care. He reported recreational nitrous oxide use 1-2 times per week over the previous 18 months, using on average 1 tank per session. For the previous 2 weeks, he noticed paresthesia from knees to toes, which progressed to numbness in response to cold stimuli. He reported some issues with coordination but continued to move around on his own.

**Physical Examination:** On examination, the patient's gait was narrow-based, and he was only able to take 2 steps in tandem gait. The Romberg test was negative. His muscle tone was normal throughout the upper and lower limbs. He had mild weakness in bilateral ankle dorsiflexion. His reflexes were brisk in the upper limbs, but both knee and ankle reflexes were absent bilaterally, even with distraction. His plantar reflexes were equivocal. His sensory examination revealed reduced pinprick sensation up to the superior aspect of both knees and normal pinprick sensation in the upper limbs. His vibration sense and joint position sense were preserved in all 4 limbs. The patient's cranial nerves were intact with no relative afferent pupillary defect and no facial weakness or sensory deficit.

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**Case Resolution:** Following extensive workup, the diagnosis of nitrous oxide-associated peripheral neuropathy was made. Guillain-Barré syndrome (GBS) remained high on the differential diagnosis throughout the patient evaluation.

**Conclusion:** The patient was referred to neurology where a diagnosis of $B_{12}$ deficiency secondary to nitrous oxide use was made. He recovered following administration of $B_{12}$ injections.

## Introduction

Nitrous oxide misuse and abuse have emerged as a significant public health concern, particularly among young adults, where its low cost, ease of access, and perception as a "safe" recreational substance have contributed to rising use.[1] Common street names for nitrous oxide include "hippy crack," "smart whip," and "galaxy gas."[2] Although often regarded as benign, repeated exposure can result in serious neurological sequelae, most notably functional vitamin $B_{12}$ deficiency leading to subacute combined degeneration of the spinal cord and peripheral neuropathy.[3,4,5] Presentations may be insidious and heterogeneous, posing diagnostic challenges in urgent care (UC) settings where early neurological signs can be subtle and overlap with other acute neuropathic conditions.[6]

Frontline clinicians must maintain a high index of suspicion for nitrous oxide-associated neurotoxicity, particularly when evaluating young patients with paresthesia, gait disturbance, or mixed upper and lower motor neuron signs.[4,7] Failure to recognize the condition promptly may delay treatment and risk progression to irreversible neurological deficit.[3,4] Moreover, the differential diagnosis frequently includes time-sensitive and life-threatening conditions such as Guillain-Barré syndrome (GBS), requiring careful clinical assessment and appropriate escalation of care.[6]

## Case Presentation

A 20-year-old male presented to UC with paresthesia in all 4 limbs and instability when walking over the previous 2 weeks. His symptoms were worsening. He stated that he noticed the paresthesia initially starting in his toes, progressing up to his knees. He was also starting to feel some paresthesia symptoms in the tips of his fingers. He reported feeling uncoordinated at times, particularly in the night, but was able to walk without needing the help of additional walking aids (eg, crutches).

He was previously fit and well, worked in retail and was in school part-time. He denied any family history of neurological issues. He denied any chest pain, shortness of breath, fevers, or other infectious symptoms. He had not traveled abroad (outside the United Kingdom) in the previous few months. He reported no other sensory symptoms, back pain, weakness, diplopia, visual changes, or bladder or bowel continence issues. On social history, he denied smoking or using any other illicit substances. However, he did state that he would inhale nitrous oxide from canisters when partying with his friends. He reported using nitrous oxide 1–2 times a week and used 1 tank per session for the last 18 months. He stated that he stopped using nitrous oxide when his symptoms started.

*"Given the presentation of lower limb paresthesia and reduced sensation after excessive nitrous oxide use, the differential diagnosis included nitrous oxide-associated myeloneuropathy and GBS."*

Physical examination revealed his gait to be narrow based, and he could only take 2 steps in tandem. The Romberg test was negative. His muscle tone was normal throughout his upper and lower limbs with full strength (5/5) in all muscle groups—except for mild weakness in bilateral ankle dorsiflexion. His reflexes were brisk in his upper limbs; however, both knee and ankle reflexes were absent bilaterally, even with distraction. The sensory examination revealed reduced pinprick sensation up to the superior aspect of both knees, with normal sensation in his upper limbs. His vibration sense and joint position sense were preserved in all 4 limbs. His cranial nerves were intact with full extraocular movements, and his pupils were equal and reactive to light with no relative afferent pupillary defect, facial weakness, or sensory deficit.

## Medical Decision Making

Given the presentation of lower limb paresthesia and reduced sensation after excessive nitrous oxide use, the differential diagnosis included nitrous oxide-associated myeloneuropathy and GBS. As such, his case was discussed with both the emergency department (ED) phys-

**Table 1. Key Features Of Nitrous Oxide Neuropathy and Guillain-Barré Syndrome[5,6]**

| Feature | Nitrous Oxide Neuropathy | Guillain-Barré Syndrome |
|---|---|---|
| **Cause** | Functional vitamin $B_{12}$ deficiency due to nitrous oxide inactivating the vitamin. | Autoimmune response, often triggered by a prior infection. |
| **Typical Age** | Younger adults (mean age around 22 years). | Older adults (mean age around 51 years). |
| **Cranial Nerve Involvement** | Rare or absent. | Common (over 50% of cases), causing issues like facial weakness or swallowing difficulties. |
| **Respiratory Weakness** | Rare. | More frequent (around 21% of cases). |
| **Vitamin $B_{12}$ Levels** | Often low, or normal but functionally deficient (high homocysteine and methylmalonic acid levels). | Usually normal (though some studies note potential correlation with $B_{12}$ deficiency in GBS severity). |
| **Electrophysiology** | Typically shows axonal or mixed axonal-demyelinating neuropathy, with absent or very rare conduction blocks. | Usually a primary demyelinating polyneuropathy with frequent conduction blocks. |
| **Cerebrospinal Fluid Analysis** | Albumin cytologic dissociation (high protein with normal cell count) is less common. | Albumin cytologic dissociation is a classic finding. |
| **Treatment** | Immediate cessation of nitrous oxide use and parenteral (intramuscular) vitamin $B_{12}$ supplementation. | Intravenous immunoglobulin or plasmapheresis. |

ician and a neurologist. They both agreed that the patient required additional same-day work-up, and he was sent to the ED for further assessment.

## Differential Diagnosis and Final Diagnosis

Given the progressive, ascending pattern of sensory disturbance, the top 2 diagnoses considered were nitrous oxide-associated myeloneuropathy and GBS. Diagnoses also considered were diabetes mellitus, which can cause chronic or acute-onset peripheral neuropathy, and nutritional deficiencies, particularly of vitamins $B_6$ and $B_{12}$, due to his symmetrical distal paresthesia and sensory loss.[8] Additional considerations included alcohol-related neuropathy, hereditary neuropathies such as Charcot-Marie-Tooth disease, and infectious causes, notably HIV/AIDS, which can manifest with a range of neuropathic syndromes.[9]

Blood tests done in the ED revealed a complete blood count that was normal with normal renal and liver function tests. However, the patient had low vitamin $B_{12}$ levels of 179 pg/mL (normal range 200–900 pg/mL), low folate levels of 2.7 µg/L (normal range 3.1–20.5 µg/L), and an elevated homocysteine at 120 µmol/L (normal range 5–15 µmol/L). An urgent whole spine magnetic resonance imaging (MRI) demonstrated no evidence of myelopathic signal change.

A final diagnosis of vitamin $B_{12}$ deficiency secondary to nitrous oxide use was made. The treatment plan was discussed with the patient and involved $B_{12}$ injections 3 times a week. Follow-ups were scheduled at 1 and 2 weeks to ensure symptoms were not rapidly changing. The patient was advised to present to the ED if he was experiencing any rapidly worsening symptoms or weakness.

## Discussion

Nitrous oxide is a colorless gas used medically as an anesthetic and pain reliever. It is also commonly used to create a frothing agent for whipped cream and other cuisine foams. In the last 5 years, recreational use of nitrous oxide has rapidly increased; it is now the second most popular recreational drug in the United Kingdom after cannabis.[1] Following 1 inhalation, usually from a balloon, a euphoric and sometimes hallucinogenic effect is rapidly induced and disappears within minutes.[1] Typical side effects of nitrous oxide use include dizziness, dissociation, disorientation, loss of balance and weakness in the legs.[1] It has been shown that sustained use of nitrous oxide inactivates vitamin $B_{12}$, resulting in $B_{12}$ deficiency. This causes numbness in the fingers and toes which can further progress to peripheral neuropathy and other neurological effects.[3,4,5]

The neuropathy from nitrous oxide use mimics GBS clinically and electrophysiologically, potentially leading to misdiagnosis and incorrect treatment. As the conditions have different underlying mechanisms and treatments, accurate differentiation is crucial.[5,6] While both conditions present with symptoms such as weakness, numbness, and areflexia (absent reflexes), particularly in the lower limbs, several key features help distinguish them **(Table 1).**[5]

Blood tests for homocysteine and methylmalonic acid (MMA) are highly sensitive biomarkers for distinguishing nitrous oxide neuropathy from GBS, with high levels strongly indicating nitrous oxide neuropathy.[3,4] Because of the symptom overlap between these 2 diagnoses, a detailed patient history—including recreational drug use—is vital for proper diagnosis, as patients may initially hide their nitrous oxide use.[1,5] Misdiagnosis can lead to incorrect and expensive treatments (like unnecessary intravenous immunoglobulin for nitrous oxide patients), and delay necessary $B_{12}$ treatment, leading to long-term, irreversible neurologic damage.[1,4,5]

## Disposition, Final Diagnosis and Follow-Up

At the 2-week follow-up visit, the patient reported improvement of symptoms that began about a week after starting $B_{12}$ injections. He had not missed any doses and remained abstinent from nitrous oxide. His paresthesia had resolved in his fingertips and in his lower legs, while still present in his toes. He was still a bit unsteady but was ambulating faster.

Clinical examination revealed slight feet stomping gait and the ability to take 3-4 tandem steps (previously 2). There was normal muscle tone in upper and lower extremities. Strength was unchanged (4+/5 in ankle dorsiflexion bilaterally and otherwise 5/5 throughout). Reflexes remained absent in the lower extremities despite distraction and were present with distraction in the upper extremities. His plantar reflexes were downgoing. There was altered pinprick sensation up to the ankles bilaterally (previously up to knees). Otherwise, a normal sensory exam was noted.

The clinical phenotype was in keeping with nitrous oxide-related peripheral neuropathy. As his symptoms were improving with $B_{12}$ treatment, he was advised to continue injections for an additional 2 weeks.

## Ethics Statement

The patient was unable to be contacted as he was lost to follow-up in the urgent care system. Therefore demographics and some details of the case were changed to protect patient anonymity and confidentiality.

## Takeaway Points

- Nitrous oxide misuse is increasingly prevalent among young adults and can cause significant neurological harm despite its perception as a "low-risk" recreational drug.
- Functional vitamin $B_{12}$ deficiency is the key pathological mechanism, leading to peripheral neuropathy, myelopathy, or a mixed myeloneuropathy.
- Early symptoms may be subtle, including distal paresthesia, sensory change triggered by cold, or mild gait disturbance.
- GBS remains an important diagnosis in the differential, particularly in patients presenting with progressive sensory symptoms and areflexia.
- Urgent care clinicians play a key role in early identification and appropriate escalation of care for suspected nitrous oxide–associated neurotoxicity. ■

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