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Case Report

A Case-Based Review of Nitrous Oxide Toxicity: Multisystem Pathology, Fragmented Care, and Self-Guided Harm Reduction

Priya Choudhary[1, *], Jessica Cho[1], Aneeqa Ahmed[2], Andy Ngo[2], Mujeeb Shad[2]

[1]Touro University Nevada College of Osteopathic Medicine, Henderson, Nevada, the United States
[2]Psychiatry Department, Valley Health System, Las Vegas, United States of America

Abstract

Although recreational inhalation of nitrous oxide (N_2O) often causes acute, severe symptoms–most notably spinal cord degeneration due to functional vitamin B_{12} inactivation–diagnosis remains challenging. It is frequently missed by frontline providers because multi-system involvement complicates the differential diagnosis, which is further obscured by internet-guided harm reduction. This diagnostic trap results in significant management delays, increased emergency department (ED) visits, and fragmented care. Illustrating this, 24-year-old male with untreated Major Depressive Disorder and Attention Deficit/Hyperactivity Disorder presented to the ED three separate times over a period of five days exhibiting progressively severe multisystem manifestations of toxicity. The patient had a history of polysubstance use, including methamphetamine, heroin, and cocaine, reportedly in remission; however, he transitioned to heavy inhalation of N_2O canisters obtained from retail suppliers, a shift motivated by the gas's unique ability to evade standard hospital urine drug screenings. His initial presentation involved acute chest pressure and tachycardia, which was shortened by Against Medical Advice (AMA) elopement. Upon return to a different ED facility the following day, he presented with abdominal pain, early motor weakness, and enteritis. The patient again departed AMA due to auditory paranoia. By his third presentation, he exhibited profound bilateral paresthesias, generalized weakness, and active N_2O -induced psychosis. Notably, the patient spontaneously rationalized a simple B_{12} deficiency as the cause, reflecting the dangerous trend of superficial internet-driven self-diagnosis that can easily misdirect unwary clinicians. Ultimately, collateral history from his father confirmed massive N_2O exposure, evidenced by five empty culinary canisters, alongside vivid visual hallucinations, which proved instrumental in securing the correct toxicological diagnosis. The patient later acknowledged this, albeit with persistent symptom minimization. This case exemplifies the profound dangers of fragmented care in substance use disorders. The rapid escalation from cardiopulmonary to gastrointestinal to severe neuropsychiatric symptoms due to B_{12} inactivation illustrates multisystem chemical toxicity. Because N_2O evades routine toxicology, it is increasingly abused by patients seeking to avoid the stigma and consequences of traditional substance use. The patient's rationalizations of B_{12} depletion underscore a growing trend of internet-driven harm reduction that can be misdiagnosed in such cases. Consequently, frontline clinicians must maintain a high index of suspicion for functional B_{12} deficiency in all suspected users, particularly those demonstrating symptom minimization or threatening elopements. Gaining collateral information and synthesizing these fragmented clinical narratives are essential for accurate diagnosis and comprehensive management of severe N_2O use disorder, thereby preventing long-term neurological damage and associated comorbidities.

*Correspondence: Priya Choudhary (pchoudha@student.touro.edu)

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1. Introduction

Nitrous oxide (N_2O), commonly known as “laughing gas”, is a colorless gas with a slightly sweet odor used clinically in dentistry and procedural medicine for its analgesic and sedative properties [2]. It is also widely used as a propellant in whipped cream canisters and commercial food dispensers [3]. In recent years, increased recreational use has raised growing public health concern among adolescents and young adults, often seeking euphoric and dissociative experiences [4]. Large-scale survey data indicate that N_2O is among the most commonly used psychoactive substances worldwide with high prevalence in nightlife and festival settings [5].

Recreational N_2O is typically inhaled via balloons filled from small steel pressurized cartridges (“whippits”) intended for culinary use [6]. Use is common in social environments such as festivals and nightclubs due to its rapid onset, short duration, and euphoric effects [5]. Its legal status, low cost, and widespread availability through retail and online sources further contribute to accessibility [4]. Additionally, its short-lived effects and lack of detection on routine urine drug screens increase its appeal [7].

Despite its perceived safety, chronic or high-dose exposure can result in significant neurologic and hematologic toxicity. N_2O irreversibly oxidizes the cobalt ion in vitamin B_{12}, inactivating methionine synthase. This impairs DNA synthesis, myelin maintenance, and creates a state of functional vitamin B_{12} deficiency [8]. This functional deficiency is particularly insidious because patients can present with severe peripheral neuropathy, ataxia, and spinal cord degeneration despite normal, or even elevated, serum B_{12} levels—a critical diagnostic pitfall for unwary clinicians [8, 9]. Furthermore, these symptoms may even progress to severe functional impairment if untreated, underscoring the importance of diagnosing in a timely manner, particularly given the absence of routine screening tests [9].

This case highlights the multisystem effects of nitrous oxide misuse, emphasizing its rising prevalence and the need for early recognition and diagnostic evaluation to prevent missed diagnoses and fragmented care. This challenge is further compounded by increasing reliance on online self-diagnosis and self-treatment, especially among young individuals, which may delay presentation and mask key clinical and laboratory findings.

2. Case Presentation

2.1. Patient Background

A 24-year-old male with a significant psychiatric history presented to the emergency department three times over five days. His past medical history included untreated attention-deficit/hyperactivity disorder (ADHD), untreated major depressive disorder, anxiety disorder, and a history of remote polysubstance use involving methamphetamine, heroin, cocaine, and alcohol (reportedly ceased). The patient is employed and close with family, who subsequently became a critical source of collateral information.

2.2. Visit 1 (Day 1): The Thoracic Presentation—Hypercoagulability Unmasked

The patient initially presented to the emergency department complaining of acute onset of chest pressure and right arm tingling that worsened while eating. He appeared acutely anxious and highly distressed. Initial vital signs revealed sinus tachycardia at 103 bpm and hypertension at 169/93 mmHg. A 12-lead electrocardiogram demonstrated sinus tachycardia with mild QTc prolongation, measuring 455 milliseconds. Laboratory investigations revealed mild anemia (hemoglobin 12.2 g/dL) and elevated creatinine (1.68 mg/dL), concerning for acute kidney injury or dehydration. High-sensitivity troponin, D-dimer, and creatine kinase were all within normal limits.

While awaiting repeat troponin and chest radiography, the patient abruptly announced he "had somewhere else to go," refused further evaluation, and eloped against medical advice before the workup could be completed. Notably, at the time of this first presentation, no collateral history was available regarding N_2O use, and the patient did not volunteer this information.

2.3. Visit 2 (Day 2): The Gastrointestinal and Early Neurologic Presentation—Escalating Toxicity

The following day, the patient presented to a different emergency facility complaining of crampy lower abdominal pain, bilateral arm numbness, and right leg swelling with numbness. Emergency Medical Services personnel noted that the patient

had used N_2O immediately prior to arrival. Computed tomography of the abdomen and pelvis revealed findings suggestive of acute enteritis with distal stomach wall thickening—a gastrointestinal manifestation of N_2O toxicity.

Neurologic examination now revealed objective deficits: 4 out of 5 strength in the left lower extremity, word-finding difficulty, and a notably unsteady gait suggesting early ataxia. The treating physician emphasized the critical need for inpatient admission and magnetic resonance imaging of the brain and spinal cord to investigate the new-onset neurologic deficits. However, despite this urgent recommendation, the patient again eloped AMA for a second time. In retrospect, this second AMA elopement was later understood to have been driven by auditory hallucinations of "loud music and partying"—manifestations of N_2O-induced psychosis that the patient had not initially disclosed.

2.4. Visit 3 (Day 5): The Severe Neurologic and Psychiatric Presentation—Full System Failure

Three days after his second elopement, the patient was brought to the emergency department by his father, who noted a profound deterioration in the patient's mental status and physical function. The patient presented with generalized weakness and severe, ongoing bilateral upper and lower extremity paresthesias. Most notably, his father revealed that the night before arrival, the patient had experienced vivid visual hallucinations, explicitly describing seeing "strippers in the room grinding on police officers." Furthermore, the father conducted a search of the patient's residence and discovered five empty culinary N_2O canisters—objective evidence of massive, recent exposure.

A formal psychiatric consultation dramatically reframed the clinical picture. The patient disclosed that he had actually been inhaling N_2O daily for four months to manage work-related stress. His previous AMA elopement from the second hospital, initially unexplained, was now understood to have been triggered by auditory hallucinations. During this third evaluation, the patient spontaneously suggested that his physical symptoms could be explained by a B_{12} deficiency—a dangerous example of incomplete self-diagnosis based on internet research.

Neurology consultation revealed profound gait instability with bilateral paresthesias highly suspicious for subacute combined degeneration of the spinal cord. Magnetic resonance imaging of the neuraxis and high-dose intramuscular vitamin B_{12} therapy were initiated. Psychiatry began pharmacologic management with aripiprazole and trazodone for mood stabilization and treatment of psychotic symptoms.

3. Discussion

3.1. The Pathophysiology of Multisystem N_2O Toxicity

This case exemplifies the remarkably broad range of acute and subacute complications arising from N_2O toxicity. The mechanism by which N_2O induces functional B_{12} deficiency is biochemically well-established: the gas irreversibly oxidizes the cobalt center of cobalamin, inactivating the enzyme methionine synthase (Figure 1, [10]). This inactivation interrupts two critical biochemical pathways: the conversion of homocysteine to methionine (required for DNA synthesis and myelin formation) and the conversion of methylmalonyl-CoA to succinyl-CoA (required for myelin maintenance). The result is a state of profound functional B_{12} deficiency despite potentially normal circulating B_{12} levels—a critical diagnostic distinction that must be recognized by frontline clinicians.

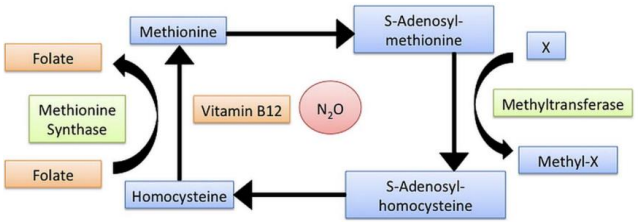

Figure 1. *Schematic representation of the role of vitamin B_{12} in homocysteine metabolism and the point at which nitrous oxide exerts its effect [10].*

The resulting hyperhomocysteinemia creates a severe hypercoagulable state that predisposes patients to acute thrombotic and cardiovascular events [10], explaining this patient's initial presentation with chest pressure and tachycardia. The cardiopulmonary manifestations of N_2O toxicity are increasingly recognized as acute medical emergencies requiring rapid rule-out of myocardial infarction and pulmonary embolism.

The gastrointestinal manifestations, evidenced in this patient by acute enteritis with stomach wall thickening, represent a less commonly discussed but equally important complication of N_2O toxicity. The mechanism underlying this presentation is not fully elucidated but may relate to direct toxic effects on rapidly dividing epithelial cells or vascular insufficiency secondary to hypercoagulability [11].

3.2. Fragmented Care and the AMA Elopement Cascade

This patient's clinical course is a tragic illustration of how fragmented emergency care in the setting of substance use disorders can delay life-saving diagnosis and treatment. The patient presented three times over five days to emergency care

systems, yet the progression from cardiopulmonary to gastrointestinal to severe neuropsychiatric pathology was not synthesized into a cohesive clinical picture. Not until the third visit at least, when collateral history from his father provided critical context.

The serial AMA elopements—driven by the patient's psychiatric refusal or simple non-compliance—were actually manifestations of N_2O -induced psychosis. This represents a particularly dangerous situation: the substance's toxicological effects actively impaired the patient's capacity to remain in medical care and undergo the diagnostic workup required to prevent life-altering neurologic damage. When the patient fled the second hospital due to auditory hallucinations, he was simultaneously fleeing from the evaluation that might have detected his progressive myelopathy.

Furthermore, when patients elope AMA from one facility and present to a geographically different facility, subsequent providers inherit incomplete clinical datasets. Without integration across hospital systems, each treating team risks operating with only a snapshot of the information, leading to duplicative or missed diagnostic evaluation [12]. In this case, the second emergency department team did not have access to the first team's findings of chest pressure and tachycardia, nor did the third team have integrated imaging or laboratory results from the second facility. This fragmentation is particularly dangerous in substance use presentations, where complex polypharmacy, psychiatric comorbidity, and quickly evolving toxidromes demand synthesis of clinical data.

3.3. Accessibility in Grocery Stores

A fundamental barrier to effective harm prevention is the widespread legal availability of N_2O in culinary applications. N_2O canisters marketed as "whipped cream dispensers" or "whippets" are readily accessible in mainstream retail environments, including grocery stores. Personal observations from clinicians in Australia document that "a grocery store in metropolitan Sydney with trays of canisters in full view of patrons next to the cash register" exemplifies how casually this substance is displayed [13]. Unlike controlled pharmaceutical products or illicit drugs, N_2O occupies a regulatory gray zone: it is not a prohibited substance in most jurisdictions, making restriction difficult despite recognized abuse potential. This accessibility is particularly problematic for young, economically disadvantaged, or vulnerable populations. One documented case reported a 19-year-old international student who "had been able to afford and access $750 worth of N_2O charging canisters per night for seven consecutive nights," demonstrating both the affordability and ease of acquiring massive quantities [13]. The misconception that N_2O is harmless, reinforced by its "culinary legitimacy," may enable escalating use without triggering the same alarm bells as overtly illicit substances.

3.4. Why Do Urine Drug Screens Miss N_2O

A critical diagnostic vulnerability lies in the inability of standard urine drug screens to detect N_2O. Unlike opioids, benzodiazepines, amphetamines, and other substances of abuse that are routinely screened for in emergency and clinical settings, N_2O is not included in standard immunoassay panels or routine toxicology screens [14]. While modern high-resolution mass spectrometry methods (LC-MS/MS and GC-MS) can detect a far broader range of substances than traditional immunoassay-based screening, these confirmatory tests are typically ordered only when clinical suspicion is high or when initial immunoassay results are positive or discordant with clinical presentation [15]. In the case of N_2O, the absence of a positive screen may paradoxically create false reassurance: a clinician relying on negative urine toxicology may incorrectly conclude that illicit drug use has been excluded, thereby missing the diagnosis of N_2O-induced toxicity altogether.

3.5. New Biomarkers for Detecting N_2O Abuse

The biochemical gold standard for assessing N_2O-related B_{12} toxicity is measurement of methylmalonic acid (MMA) and homocysteine levels [16]. N_2O inactivates methionine synthase, the enzyme responsible for clearing both of these metabolic products (refer to Figure 1). As a result, both MMA and homocysteine become markedly elevated—sometimes to dramatic levels—even when serum B_{12} appears normal or even elevated [17]. These specialized assays directly reflect functional B_{12} status and should be obtained urgently in any patient with a compatible clinical presentation and history of N_2O exposure.

3.6. The Harm Reduction Trap: Internet Literacy as a Diagnostic Decoy

The widespread availability of online medical information has created an unsettling paradox in clinical care. While intended to support harm reduction, it can very well function as a diagnostic decoy. In this case, the patient presented with knowledge of the link between his paresthesia and vitamin B_{12} deficiency (likely informed by internet sources), requesting vitamin B_{12} supplementation while in the emergency room unprompted. Recreational N_2O users increasingly have access to online communities and educational resources that explain, in superficial terms, the association between N_2O and B_{12} depletion. Users may attempt to self-monitor by taking B_{12} supplements or by educating themselves about expected symptoms. The pitfall, however, is the failure to recognize the nuances of the mechanism of functional B_{12} inactivation from nitrous oxide exposure. This partial self-diagnosis may delay presentation, minimize symptom severity, and contribute to premature disengagement from care as demonstrated by repeated medical elopements once symptoms subsided.

Additionally, self-directed interventions, such as unsupervised vitamin supplementation, may obscure key diagnostic findings. In nitrous oxide toxicity, serum B_{12} levels may appear normal despite profound functional deficiency as a result of self-directed vitamin supplementation and the underlying pathology of enzymatic inactivation rather than absolute depletion. A patient taking oral B_{12} supplements or one with a "normal" serum B_{12} level may feel falsely reassured that their symptoms are not serious—or worse, may convince a clinician to de-escalate evaluation based on a "normal" B_{12} assay. This is precisely what nearly happened in this case: a naive reliance on a standard serum B_{12} level could have delayed recognition of severe functional deficiency and progressive myelopathy.

Recognition of this harm reduction trap is essential. Clinicians must maintain a high index of suspicion and interpret laboratory data within the appropriate biochemical context, especially in a world where internet-informed self-diagnosis is the inescapable reality of modern day.

3.7. Critical Diagnostic Implications

This case underscores several critical diagnostic principles for emergency physicians evaluating patients with suspected N_2O toxicity:

1) Maintain a high index of suspicion for functional B_{12} deficiency in all patients with N_2O exposure, regardless of the presenting complaint. N_2O toxicity does not announce itself as a single constellation of symptoms; instead, it can present acutely as chest pain, abdominal pain, psychiatric crisis, or progressive neurologic deficit—or any combination thereof.
2) Do not rely solely on serum B_{12} levels. Standard serum B_{12} assays measure the quantity of circulating cobalamin, not its functional capacity. A "normal" or even "elevated" serum B_{12} does not rule out functional deficiency from N_2O inactivation.
3) Obtain methylmalonic acid and homocysteine assays in any patient with compatible presentation and N_2O exposure history. These metabolic markers directly reflect methionine synthase activity and functional B_{12} status. Markedly elevated levels confirm the diagnosis even when serum B_{12} is reassuring.
4) Recognize that repeated AMA elopements in the context of substance use disorder may reflect drug-induced psychiatric pathology rather than simple non-compliance. The neuropsychiatric effects of N_2O and other drugs can directly obstruct medical care by impairing the patient's ability to tolerate evaluation and hospitalization.
5) Implement systems-level approaches to integrate care across multiple presentations. When patients present to different facilities or over multiple days, mechanisms should exist to ensure that prior presentations are not overlooked and that progressive pathology is recognized.

Abbreviations

N_2O	Nitrous Oxide
MMA	Methylmalonic
ED	Emergency Department
AMA	Against Medical Advice
ADHDd	Attention-Deficit/Hyperactivity Disorder

Author Contributions

Priya Choudhary: Conceptualization, Investigation, Writing – original draft, review & editing

Jessica Cho: Investigation, Writing – original draft, review & editing

Aneeqa Ahmed: Supervision, Writing – original draft

Andy Ngo: Supervision, Writing – original draft

Mujeeb Shad: Supervision, Writing – original draft, review & editing

Conflicts of Interest

The authors declare no conflict of interest.

References

[1] Mohammed R, et al. The pathway for "found down" or unidentified patients: From field to identification and social reintegration. Saudi Journal of Medicine and Public Health. 2024. https://doi.org/10.64483/202412589

[2] Becker DE, Rosenberg M. Nitrous oxide and the inhalation anesthetics. Anesth Prog. 2008; 55(4): 124-131. https://doi.org/10.2344/0003-3006-55.4.124

[3] Kaar SJ, Ferris J, Waldron J, Devaney M, Ramsey J, Winstock AR. Up: the rise of nitrous oxide abuse. An international survey of contemporary nitrous oxide use. J Psychopharmacology. 2016; 30(4): 395-401. https://doi.org/10.1177/0269881116632375

[4] European Union Drugs Agency (EUDA). Recreational use of nitrous oxide: a growing concern. Published 2023. https://www.euda.europa.eu

[5] van Amsterdam J, Nabben T, van den Brink W. "Recreational Nitrous Oxide Use: Prevalence and Risks." Regulatory Toxicology and Pharmacology. 2015; 73(3): 790-796. https://doi.org/10.1016/j.yrtph.2015.10.017

[6] Garakani A, Jaffe RJ, Savla D, et al. Neurologic, psychiatric, and other medical manifestations of nitrous oxide abuse: a systematic review of the case literature. Am J Addict. 2016; 25(5): 358-369. https://doi.org/10.1111/ajad.12372

[7] Cousaert C, Heylens G, Audenaert K. Laughing gas abuse is no joke. An overview of the implications for psychiatric practice. Clin Neurol Neurosurg. 2013; 115(7): 859-862. https://doi.org/10.1016/j.clineuro.2013.04.004

[8] Oussalah A, Julien M, Levy J, et al. Global burden related to nitrous oxide exposure in medical and recreational settings: a systematic review and individual patient data meta-analysis. J Clin Med. 2019; 8(4): 551. https://doi.org/10.3390/jcm8040551

[9] Hathout L, El-Saden S. Nitrous oxide-induced B_{12} deficiency myelopathy: perspectives on the clinical biochemistry of vitamin B_{12}. J Neurol Sci. 2011; 301(1-2): 1-8. https://doi.org/10.1016/j.jns.2010.10.033

[10] Massey TH, Pickersgill TT, Peall KJ. Nitrous oxide misuse and vitamin B12 deficiency. BMJ Case Rep. 2016; 2016: bcr2016215728. https://doi.org/10.1136/bcr-2016-215728

[11] Weir DG, Scott JM. Homocysteine as a risk factor for cardiovascular and related disease: nutritional implications. Nutr Res Rev. 1998; 11(2): 311-338. https://doi.org/10.1079/NRR19980020

[12] Bolton DJ, Sabel JC, Baumgartner T, Kushner T, Karras B. Using health information exchange to improve use of prescription monitoring data. Online J Public Health Inform. 2017; 9(1): e074. https://doi.org/10.5210/ojphi.v9i1.7735

[13] Weastell S. Whipping up public policy discussion: Australia's problem with recreational nitrous oxide use. Intern Med J. 2022; 52(7): 1279-1281. https://doi.org/10.1111/imj.15779

[14] Stellpflug SJ, Cole J, Greller H. Urine drug screens in the emergency department: the best test may be no test at all. J Emerg Nurs. 2020; 46(6): 923-931. https://doi.org/10.1016/j.jen.2020.06.003

[15] Parekh A. B-309 Validation and application of a gas chromatography–mass spectrometry method in emergency drug testing. Clin Chem. 2025; 71(Suppl 1): hvaf086.696. https://doi.org/10.1093/clinchem/hvaf086.696

[16] Marsden P, Sharma A, Rotella J. Review article: Clinical manifestations and outcomes of chronic nitrous oxide misuse: a systematic review. Emerg Med Australas. 2022; 34(4): 492-503. https://doi.org/10.1111/1742-6723.13997

[17] Gyawali P, Suthaharen C, Chung J. B-285 Whippits, nangs, balloons, and crackers: functional inactivation of vitamin B12. Clin Chem. 2025; 71(Suppl 1): hvaf086.672. https://doi.org/10.1093/clinchem/hvaf086.672