

# Nitrous Oxide Induced B12 Deficiency with Suspected Subacute Combined Degeneration and Concurrent Psychiatric Symptoms: A Case Report

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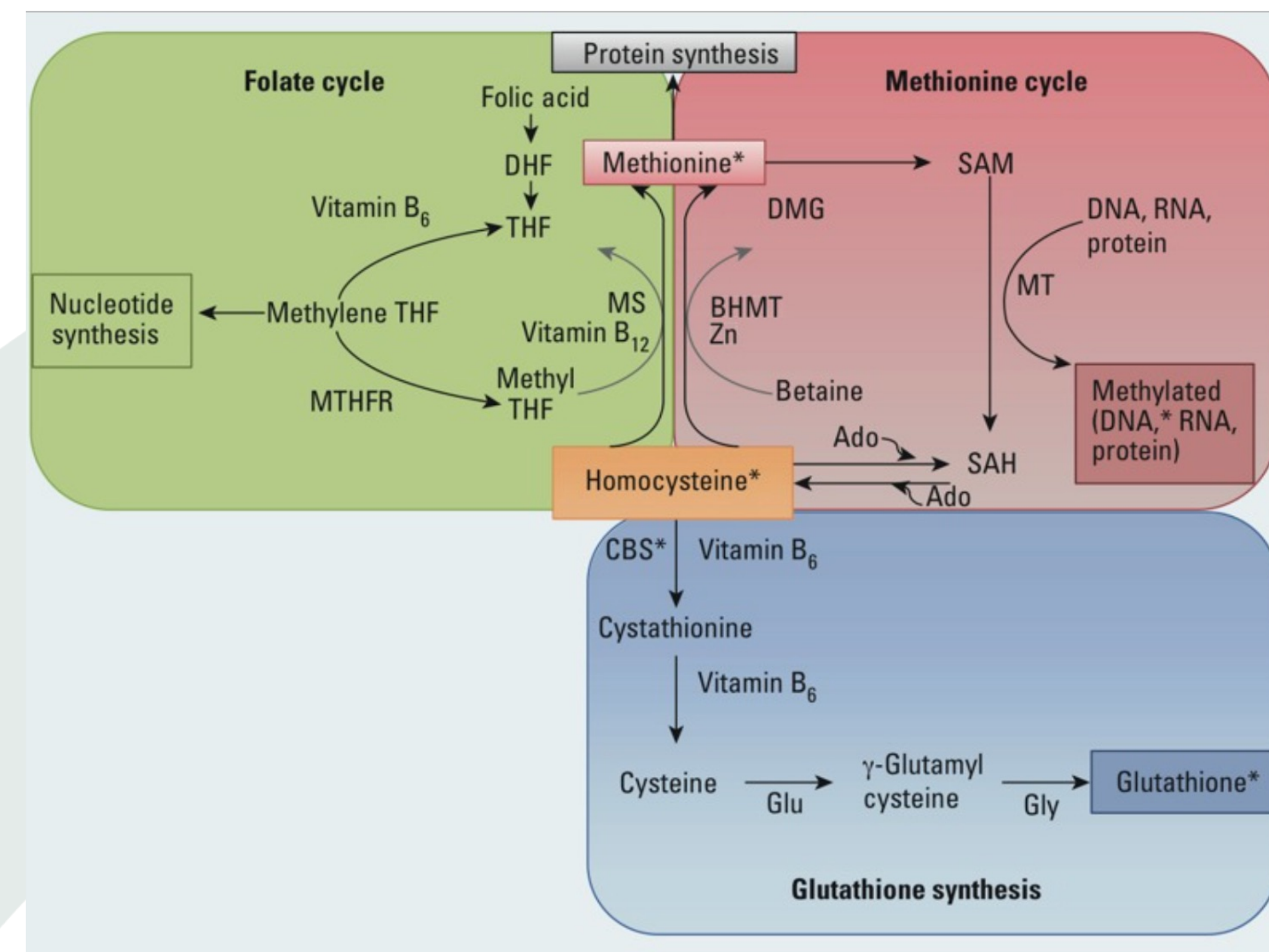
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## Introduction

Nitrous Oxide (NO) is a widely used gaseous substance, commonly used in surgical and dental procedures (“laughing gas”), as well as in aerosol cans. Recently, it is being used as a street drug, via inhalation from cans of whipped cream, also called “whippets.”<sup>(1)</sup> Inhalation gives a sense of euphoria and dissociation, while chronic inhalation of nitrous oxide can have deleterious effects including a functional cobalamin (vitamin B12) deficiency, as presented in this case report. Pathophysiology is thought to arise from NO oxidation of the B12 contained cobalt ion, which irreversibly converts B12 from its active, monovalent form into an inactive, bivalent form.<sup>(1,7)</sup> Other adverse effects of NO inhalation include hypoxia, cardiac arrhythmias, and metabolic acidosis. Recent literature has also identified a connection between heavy nitrous oxide use and psychiatric symptoms, albeit these disturbances have been provided less attention.<sup>(3)</sup> This case report details the presentation of a 31-year-old female with no past medical history who presented with a functional B12 deficiency with suspected subacute combined degeneration and concurrent new onset psychiatric symptoms, secondary to heavy nitrous oxide use.

## Case Summary

- **HPI:** 31-year-old female presented with ascending bilateral lower extremity weakness, paresthesias, saddle anesthesia, urinary incontinence and worsening gait for 3.5 weeks. History of NO inhalation for ~6 months, approximately 10-60x/day.
- **Physical Exam:** Significant for truncal ataxia, visible tremors, positive Romberg sign. Sensory exam significant for impaired light touch in all extremities, and loss of vibratory sense noted in the lower extremities. Motor exam demonstrated 3/5 strength in the bilateral extremities.
- **Labs:** B12 level of 95 pg/mL (normal > 200), homocysteine of 69 umol/L (normal 5-15), methylmalonic acid level of 3.65 nmol/L (normal 70-270). CBC demonstrated a normocytic anemia (Hgb 10, HCT 29.8, MCV 93).
- **Neurology recommendations:** 1000 mcg Cyanocobalamin IM daily for 1 week, followed by weekly for 4-9 weeks, then monthly until symptoms resolve as well as MRI thoracic and lumbar spine.  
**Disposition:** During her hospital stay patient became acutely agitated and combative with all staff members, refusing further workup despite no previous history of psychiatric issues. Psychiatry was consulted however patient refused any psychiatric evaluation or intervention, appearing suspicious, guarded, and demonstrating poor insight into care management.
- Patient eventually discharged herself against recommendations, refusing to stay for IM B12 supplements or MRI studies.



**Figure 2:** Environmental Health Perspectives. (2014). *One carbon metabolism pathway*. EHP Publishing. Retrieved May 12, 2024, from <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1306931>.



**Figure 1:** *Subacute combined degeneration of the cord*. Radiology at St. Vincent's University Hospital. (n.d.). <http://www.svuhradiology.ie/case-study/subacute-combined-degeneration-of-the-cord/>

## Discussion

Subacute combined degeneration has become a known complication of NO abuse, however psychiatric symptoms have been given less attention in the literature. Recent studies demonstrate they may be just as prevalent and may even arise prior to neurologic or hematologic manifestations.<sup>(3)</sup> The question remains whether our patient's new behavior changes were a manifestation of a primary psychiatric disorder unmasked by substance abuse, or secondary to NO abuse. It was difficult to ascertain whether true paranoia, delusions or hallucinations were present given the refusal for evaluation. However, conversations with family revealed no previous history of similar behavior or previous psychiatric evaluation. A literature review by Paulus et al (2021) attempted to determine the relationship between recreational NO use, psychiatric symptoms and B12 status.<sup>(7)</sup> The most common psychiatric complaints cited were hallucinations, delusions and paranoia.<sup>(3)</sup> Another study described a so called “megaloblastic madness” which may involve the above symptoms or more subtle personality changes, as observed in our patient.<sup>(8)</sup> One proposed hypothesis of NO induced psychiatric changes involves B12 deficiency leading to decreased activity of methionine synthase, an essential enzyme for the neuronal myelin sheath. This with accumulation of homocysteine may contribute to the development, although the exact mechanism still appears unclear.<sup>(7)</sup>

## Conclusion

This case report is limited by the absence of MRI thoracic and lumbar spine studies, secondary to poor follow-up and non-adherence to recommendations. Expected findings of demyelination within the posterior columns of the spinal cord is considered pathognomonic of subacute combined degeneration, an example seen in Figure 1. Toxicology recommended parenteral repletion of B12 as the ideal method, aligning with current literature recommendations. In conclusion, NO abuse must be considered on the differential when a patient presents with signs of cobalamin deficiency, or with psychosis or hallucinations. As NO inhalation increases, clinician recognition of these sequelae is imperative for immediate intervention to prevent long-term deficits.

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