

Learning Objectives

- Nitrous Oxide (N₂O) is a widely used inhaled anesthetic in medical settings.
- As a recreational drug, it is described as a rare cause of vitamin B12 deficiency.

Case Presentation

A 27-year-old male with history of polysubstance abuse, (including inhalant N₂O, benzodiazepines, and heroin), and questionable history of renal cancer, presented to the hospital with six months history of progressive bilateral lower extremity weakness, numbness, and paresthesia. Two weeks prior to admission, he developed ataxia and gait instability, prompting medical evaluation. He denied dysphagia, blurred vision, shortness of breath, dysuria, or changes in bowel habits.

Physical examination:

- Intact cranial nerves, decreased motor strength (4/5) in the lower extremities, associated with diminished sensation to light touch, vibration, and proprioception in the same distribution. Romberg's test was positive
- Rest unremarkable

Differential diagnosis:

- Spinal/epidural abscess
- Paraneoplastic/malignant etiology
- Syphilis
- Transverse myelitis, Guillain Barre Syndrome
- Subacute combined degeneration secondary to B12 deficiency

Clinical features:

• **Laboratory analysis:** macrocytic anemia with a hemoglobin of 12 mg/L and an MCV of 96 fL. Syphilis and HIV negative. Folate normal. TSH normal. Low vitamin B12 levels (167 pg/mL; normal > 300)

• **Magnetic resonance of the brain and complete spine with and without contrast:** unremarkable

• **Electromyography and nerve conduction studies of the lower extremities:** severe sensorimotor polyneuropathy with axonal loss consistent with vitamin B12 deficiency.

Case Continued

Management and clinical evolution:

- Patient was initiated on high-dose intramuscular vitamin B12 supplementation.
- The patient was eventually discharged to acute inpatient rehabilitation on continued vitamin B12 supplementation..

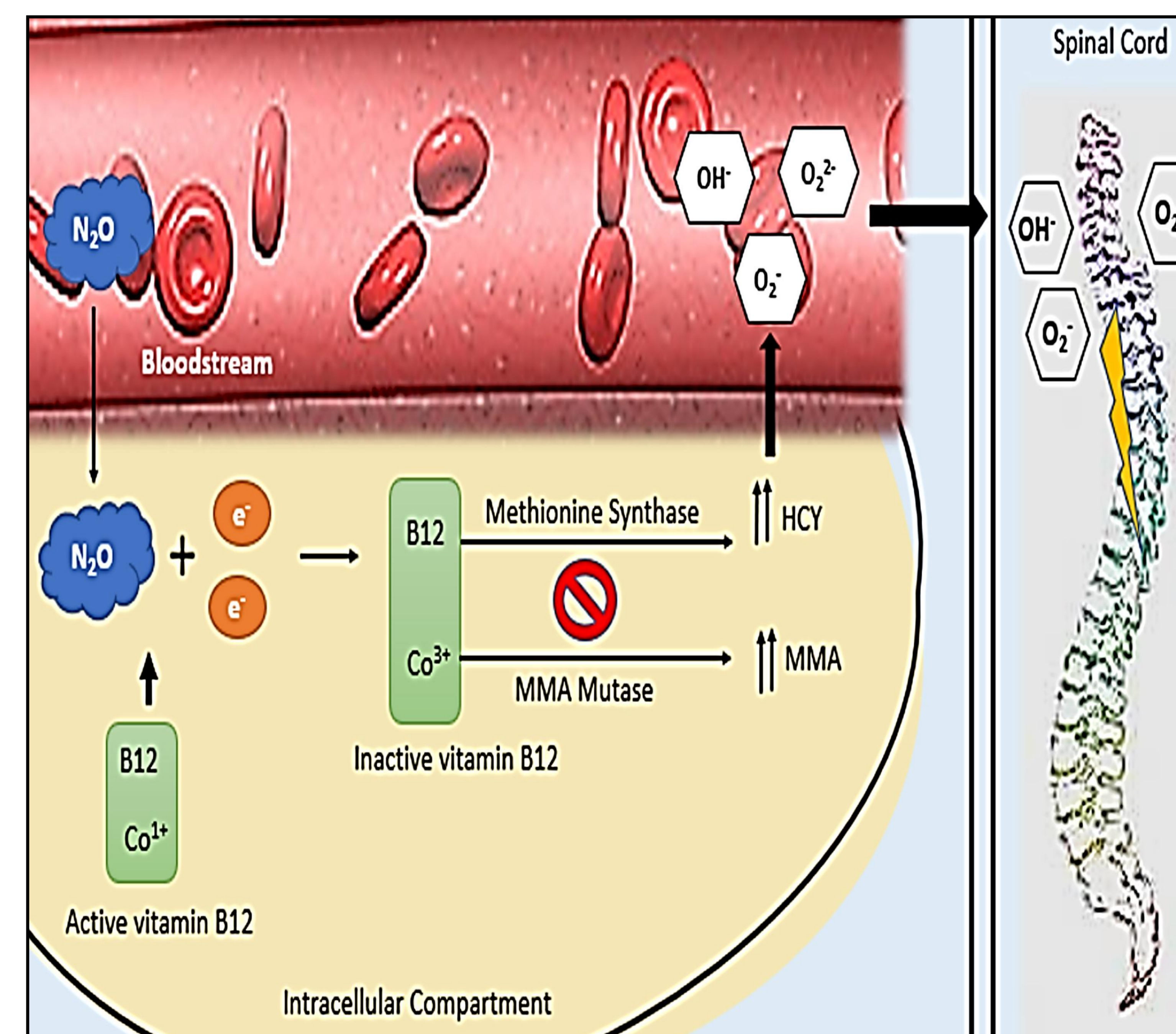


Figure 1. Mechanism of N₂O-induced vitamin B12 depletion and subsequent myelopathy. N₂O oxidizes the active cobalt atom (1+) of vitamin B12 to inactive cobalt form (3+), producing inactive methylcobalamin (a cofactor of methionine synthase and the active form of intracellular vitamin B12). Eventually, this process inhibits the methionine synthase enzyme-induced conversion of homocysteine to methionine and methyltetrahydrofolate to tetrahydrofolate. The proposed mechanism for myelopathy is glial cell dysfunction secondary to B12 depletion, with subsequent demyelination of the posterior columns and corticospinal tracts.

HCY, homocysteine; MMA, methylmalonic acid; N₂O, nitrous oxide.

Discussion

- Neurological effects of N₂O are due to inactivation of methylcobalamin, a critical form of vitamin B12, via oxidation of the cobalt ion (See Figure 1).
- Early diagnosis and treatment are critical to prevent disease progression and irreversible neurologic damage.
- While about 86% of patients experience clinical improvement with vitamin B12 supplementation, only 14% achieve complete resolution of neurologic symptoms.
- The prognosis is mainly driven by the duration of symptoms rather than serum vitamin B12 levels.
- Despite recent increased recognition of N₂O abuse, it remains significantly underreported.
- In conclusion, clinicians must be aware of N₂O abuse and its potentially lethal consequences mediated by vitamin B12 deficiency, as neurologic symptoms can be subtle and easily overlooked. Timely recognition and treatment increase the odds of neurologic recovery.

References

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