

NITROUS OXIDE ABUSE PRESENTING AS FUNCTIONAL VITAMIN B12 DEFICIENCY

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BACKGROUND

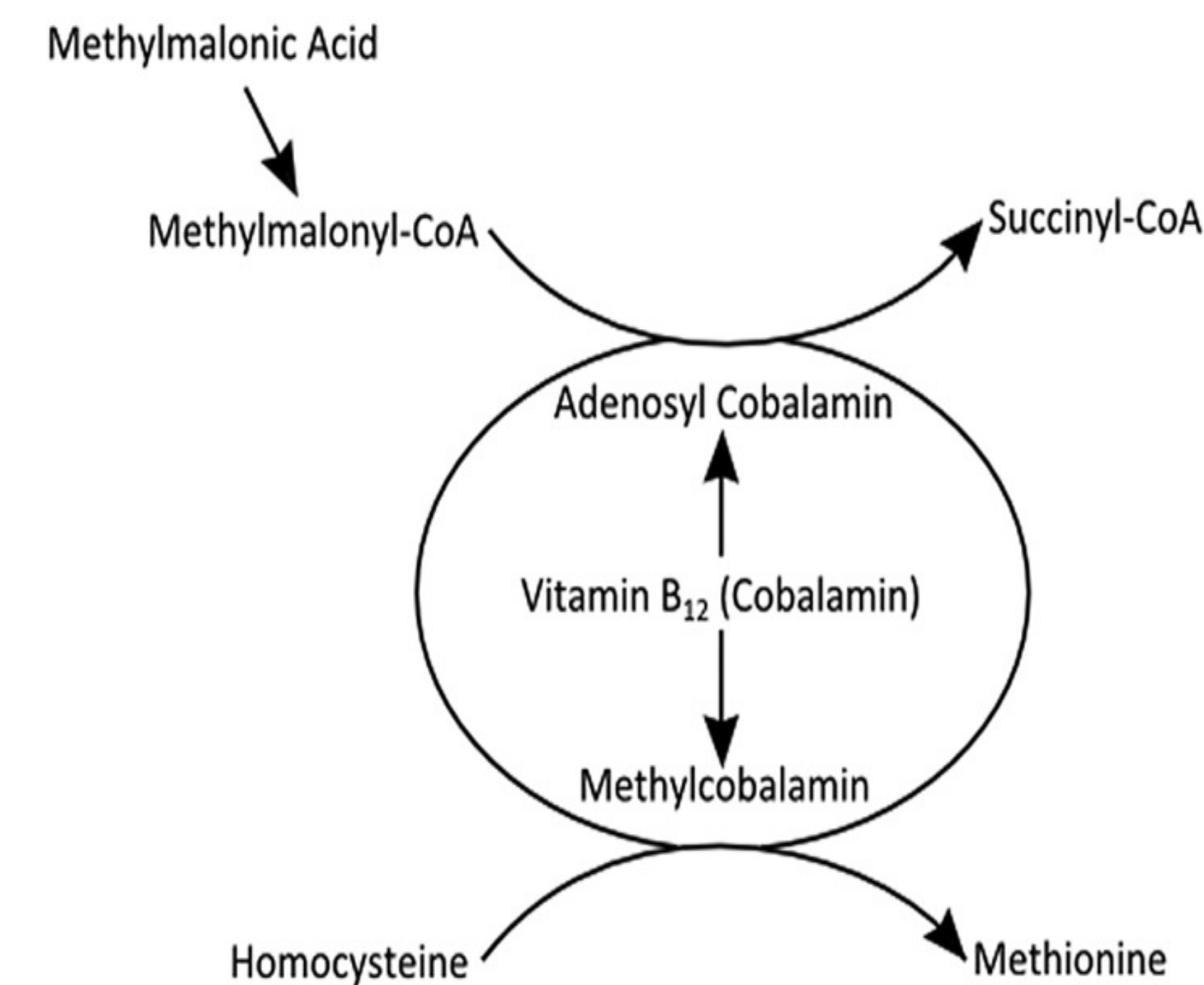
- Nitrous oxide (N₂O) is used in anesthesia, dentistry, and whipped cream dispensers
- The gas is also inhaled recreationally because of its ability to induce euphoria and reduce anxiety
- There have been several reports of disabling neurological consequences due to prolonged nitrous oxide use, resulting in functional inactivation of vitamin B12
- Common neurological presentations of nitrous oxide toxicity include paresthesias and gait disturbance
- Vitamin B12 deficiency may cause weakness, fatigue, paresthesias, poor balance, and neurocognitive issues
- Demyelinating myeloneuropathy affecting the dorsal columns tends to be the most common neurologic presentation of nitrous oxide toxicity
- Effects of nitrous oxide last for minutes; release of endogenous opiates, GABA activation, and inhibition of NMDA pathways are thought to be potential mechanisms of action of N₂O

CASE PRESENTATION

A 24-year-old female presented with 4 days of ascending lower extremity weakness and paresthesias in a stocking-glove distribution. Symptoms began in bilateral feet and progressed to the trunk, and she sustained a fall at home secondary to gait instability as well as leg weakness. Patient reported huffing nitrous oxide from “whippet” canisters every other weekend during the previous 9 months. On physical exam she was noted to have instability in gait, symmetrical loss of flexor and extensor strength in lower extremities, absent ankle reflexes and absent proprioception in the toes.

CT head was negative and labs were mostly unremarkable except for WBC count 11.9 K/mcL (4.2-11) and magnesium level 1.6 md/dL (1.7-2.4). Neurology recommended high dose methylprednisolone for suspicion of transverse myelitis. MRI of brain and cervical/thoracic spine showed no abnormalities and patient underwent lumbar puncture with negative CSF culture, cell count, MS panel, and meningitis/encephalitis panel.

Subsequent lab studies were notable for negative ANA, serum vitamin D 21.2 ng/mL (30-100), vitamin B12 242 pg/mL (211-911), and methylmalonic acid 25,626 nmol/L (79-376). Treatment with high dose intramuscular cyanocobalamin injections was initiated, and her ambulation gradually improved over the next several days.



The substrates MMA and homocysteine can be elevated in functional B12 deficiency, despite normal vitamin B12 levels in the serum.



No pathological enhancement was seen on MRI of cervicothoracic spine.

DISCUSSION

- Patients with nitrous oxide-induced neurological dysfunction may have normal vitamin B12 levels. In these situations, a functional deficiency can be diagnosed by measuring levels of methylmalonic acid and homocysteine, which are substrates of reactions catalyzed by vitamin B12
- Nitrous oxide is believed to inhibit the enzyme methionine synthase, which is a vitamin B12-dependent enzyme
- Coenzyme forms of cobalamin are inactivated by N₂O when the fully reduced cobalamin (I) is oxidized to cobalamin (II)
- The resulting clinical syndrome is indistinguishable from vitamin B12 deficiency
- Prolonged use of nitrous oxide can lead to disabling consequences within the peripheral and/or central nervous system
- High dose B12 replacement has been shown to improve neurological symptoms

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