



TOXTALKS

A BULLETIN FOR HEALTHCARE PROFESSIONALS WHO MANAGE POISONED PATIENTS

Blue Ridge Poison Center

University of Virginia Health

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NITROUS OXIDE ABUSE

Background

Nitrous oxide (N₂O) is a gaseous substance traditionally used in medicine as an inhalational anesthetic. It is also used as a food additive and aerosol spray propellant particularly for whipped cream and cooking spray canisters. Nitrous oxide is commonly referred to as *laughing gas* because of the euphoria and dissociation it can cause when abused. The most common source of nitrous oxide for abuse is from the nitrous oxide chargers found in whipped cream canisters which are also known as whippets/whippits/whip-its. Users usually dispense the nitrous oxide from the canisters into a balloon and inhale it from there as inhaling directly from the canister may cause frostbite. These nitrous oxide containing products can be purchased easily online or in grocery stores.

Mechanism of action

Nitrous oxide exerts its therapeutic effects through multiple different mechanisms. It is a noncompetitive NMDA receptor antagonist, a GABA-A agonist and a partial opioid receptor agonist giving it anesthetic, anxiolytic and analgesic properties. It produces additional analgesia by stimulating the release of endogenous opioids.

Mechanism of toxicity

Nitrous oxide also has multiple mechanisms that lead to toxicity especially with use. It causes a displacement of oxygen from air filled spaces including the alveoli which can lead to syncope, hypoxic spells and chronic anoxic brain injury. Additionally, nitrous oxide causes a functional vitamin B12 deficiency which is thought to be due to the inactivation of the cobalt contained in B12. Chronic use eventually leads to a conversion of B12 into other analogues that are more likely to be excreted which causes an absolute B12 deficiency. Because B12 is an important coenzyme in multiple reactions in the body as seen in Figure 1, a B12 deficiency leads to multiple neurologic symptoms as well as anemia.

Symptoms with abuse

Acute symptoms of inhaling nitrous oxide include euphoria, syncope, hypoxia, tympanic membrane rupture, spontaneous pneumothorax and gastrointestinal distention. With chronic use, symptoms include peripheral neuropathy, ataxia, distal > proximal extremity weakness, bowel and bladder dysfunction, Lhermitte's sign and cognitive/memory deficits. Chronic symptoms may or may not be reversible depending on the structural damage done to the nervous system.

Lab and imaging findings

Megaloblastic anemia and B12 deficiency are seen in chronic nitrous oxide abusers similar to that seen in patients with pernicious anemia. Lab work can show decreased hemoglobin, decreased B12 and elevated methylmalonic acid. Thrombocytopenia and leukopenia have also been reported. Subacute combined

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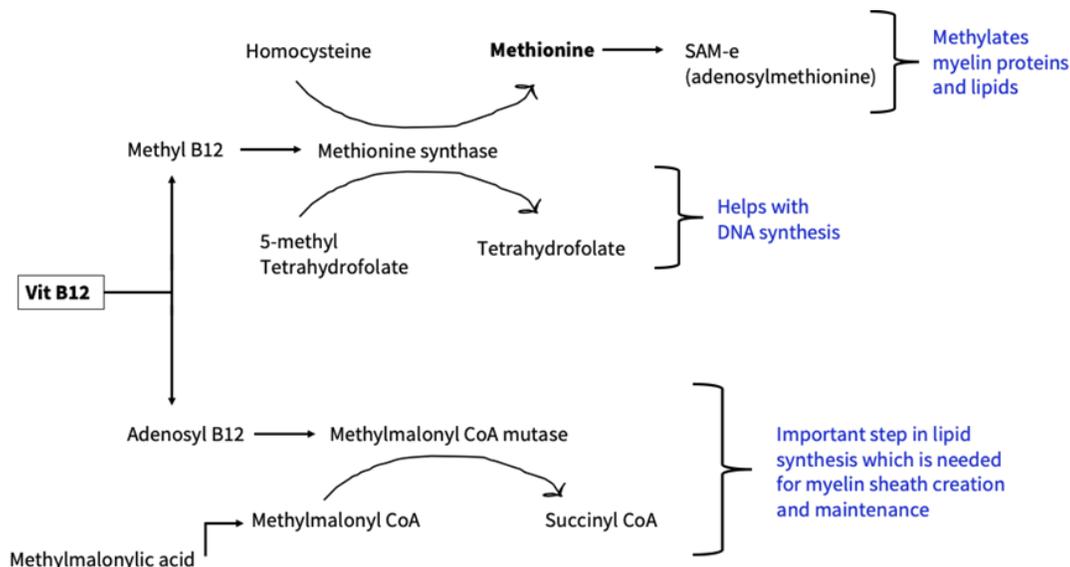
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degeneration of the spinal cord may be seen on MRI in about 68% of patients but does not have to be present for diagnosis. Changes associated with anoxic brain injury may also be seen on head imaging.

Figure 1. Reactions requiring vitamin B12 as a coenzyme.



Treatment

Treatment of symptoms is with cessation of nitrous oxide use and supplemental vitamin B12. Methionine is a potential supplemental treatment but due to a paucity of research it is unclear if it has clinical benefit. Symptomatic treatment for neuropathies and physical therapy for weakness is also recommended. Symptoms such as the weakness and neuropathies can improve with treatment but memory loss and ataxia from spinal column and brain damage may be permanent. It is important to encourage patients to stop using nitrous oxide even if they are on supplemental B12 as the nitrous oxide can still cause functional B12 deficiency and anoxic brain injury.

The Blue Ridge Poison Center at UVA Health is happy to assist: call 1-800-222-1222, or call the dedicated health care professional hotline at 1-800-451-1428.

The Blue Ridge Poison Center receives funding from University of Virginia Health, the Virginia Department of Health, and the U.S. Health Resources Services Administration (HRSA). We are accredited by the American Association of Poison Control Centers. We've been proudly serving the Commonwealth since 1978.

