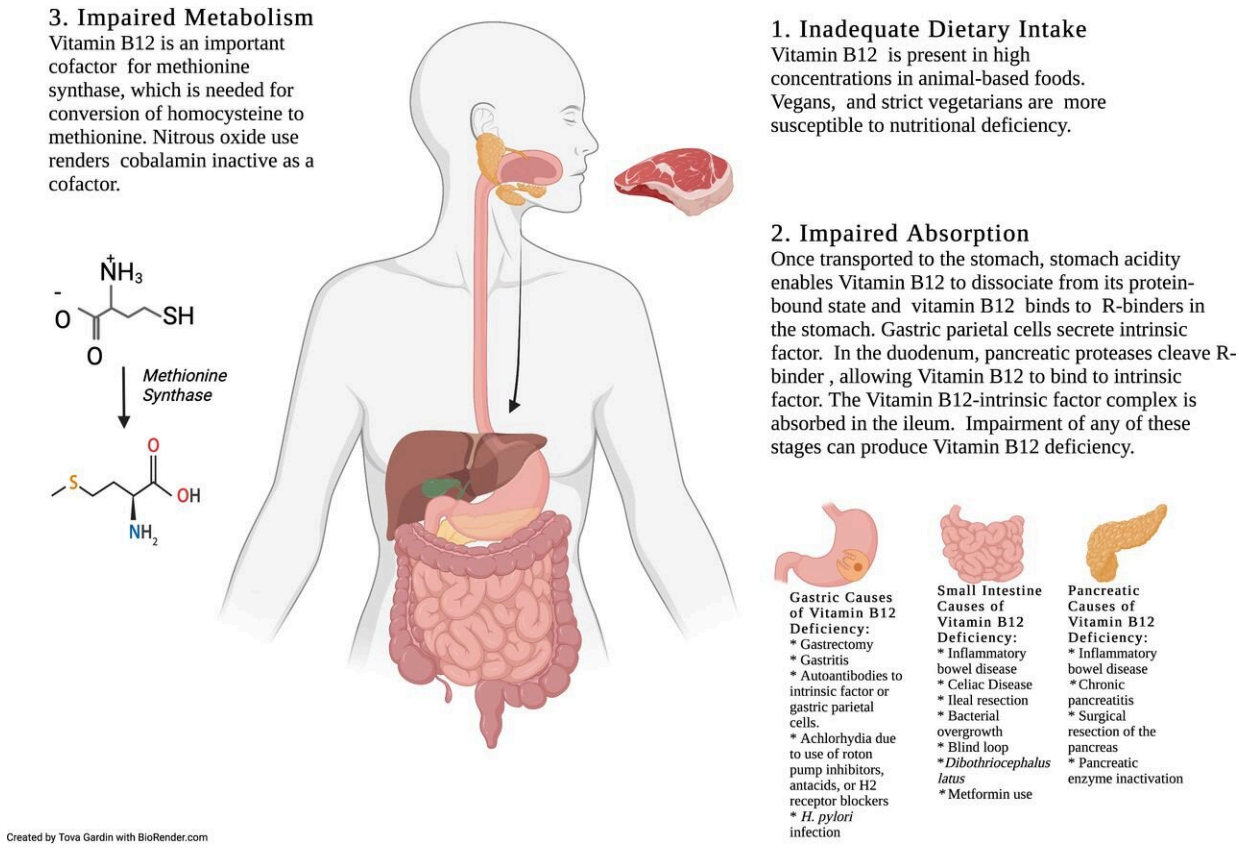
Nitrous oxide effects are reversible with early treatment: Case study

January 9 2024, by Isabella Backman



Vitamin B12 intake, absorption and metabolism, and the etiologies of vitamin B12 deficiency (image created by Tova Gardin using Biorender.com). Credit: *BMJ Case Reports* (2023). DOI: 10.1136/bcr-2023-254727

Nitrous oxide is readily accessible to those who want to use it

recreationally for the high it can provide. With just a few clicks, it can easily be bought online. But despite its availability, using the drug—commonly referred to as "whippets" (or "whippits"), "laughing gas," or "hippie crack"—can have sobering consequences, including permanent, full, or partial paralysis.

The good news is that the damage can be reversed, but clinicians must be quick to diagnose and appropriately treat patients, Yale experts say.

In 2020, nitrous oxide was the second most commonly used recreational drug among 16- to 24-year-olds in the U.K., second only to cannabis, according to a British government report. In the United States, its use is now rising rapidly. A U.S. Substance Abuse and Mental Health Services Administration 2019 survey found that almost 13 million Americans aged 12 and older had misused nitrous oxide in their lifetime. Some experts fear that the COVID pandemic may have exacerbated its abuse.

When recreationally inhaled, nitrous oxide can impair the body's metabolism of vitamin B12. This is a dangerous effect because vitamin B12 is essential for maintaining the body's myelin sheath, which insulates and protects nerves in the brain and spinal cord. Nitrous oxide's long-term use can lead to range of neurological, hematologic [related to blood], and psychiatric complications, including nerve damage and psychosis.

Now, in a case study published in October 2023 in *BMJ Case Reports*, Yale researchers have highlighted the urgent need for clinicians to thoroughly evaluate patients suffering symptoms of impaired B12 metabolism. With quick response, even severe consequences can be successfully treated, they say.

"Recreational nitrous oxide use is increasing," says Tova Gardin, MD, neuroimmunologist and psychiatrist at Yale School of Medicine and first

author of the study. "If we treat our patients early, we can reverse serious neurologic complications. So, it's important to know about nitrous use, and it's important to screen for it."

What is nitrous oxide and how long has it been used recreationally?

Nitrous oxide is a colorless gas that is used as a sedative for various dental and medical procedures. It is also available for purchase, intended to be used in dispensers to give whipped cream the fluffy consistency found in store-bought cans. When inhaled, nitrous oxide can produce short-lived feelings of euphoria or relaxation. But those who use it may also experience headaches, dizziness, anxiety, or loss of consciousness.

Recreational nitrous oxide use stems all the way back to the late 18th century, shortly after its invention in 1772 by English chemist Joseph Priestly. Another English chemist, Humphry Davey, soon became known for throwing parties in which surgeons and playwrights would inhale the gas from a green silk bag.

In fact, it was through these parties that Davey became one of the first to realize the drug's analgesic effects. By the mid-19th century, dentists and doctors began experimenting with the drug's numbing effect on patients undergoing various procedures. Now, it is the most frequently used anesthetic for partial sedation in dentistry. It is also commonly used in surgical procedures in combination with other anesthetics and even in childbirth.

Fueled by the fact that it is both legal and not difficult to get, recreational nitrous oxide use has skyrocketed in popularity. It is especially prevalent at underground raves and music festivals. And, dangerously, its misuse is especially prevalent among adolescents and

young adults.

Given the accessibility of nitrous oxide, few who use the substance recreationally are aware of how deeply dangerous it can be.

"It was shocking to me when I visited a popular retail website and typed in 'nitrous oxide,' the products algorithmically suggested to be bought together were those that would be used for substance use—not for whipped cream," says Gardin.

Treating nitrous oxide effects requires thorough evaluation

In her case study, Gardin reports that her team's recent research was inspired by a man in his 30s who developed numbness, weakness, and difficulty walking after chronic nitrous oxide use. He had no prior issues with mobility. After taking a thorough clinical history, the clinicians learned that he had been using nitrous oxide daily for four to five months.

The team's first step in trying to understand what was going on was to order a magnetic resonance imaging (MRI) scan, which revealed abnormalities in the man's dorsal column. The dorsal column is a central nervous system pathway associated with sensory function. They diagnosed him with subacute combined degeneration of the spinal cord, which was causing his symptoms.

Next, the team looked for any concomitant causes of vitamin B12 deficiency. They performed a blood test and found that the patient's level of B12 was in the normal range. However, further testing revealed he had elevated levels of two metabolites of vitamin B12—methylmalonic acid and homocysteine. "This gave us a clue that

the patient had some sort of difficulty with B12 metabolism," says Gardin.

From there, the clinicians ran tests looking for antibodies to intrinsic factor and gastric parietal cells. This would signal pernicious anemia, a rare autoimmune disorder that can also impair vitamin B12 absorption. They found this was the case in their patient.

Nitrous oxide effects reversed by vitamin B12 repletion

Treating impaired metabolism of vitamin B12 first required the complete cessation of nitrous oxide use. Then, the clinicians began the repletion process, treating the patient with a seven-day course of intramuscular vitamin B12. He then received weekly injections for one month and, going forward, will need lifelong monthly vitamin B12 repletion. Physical and occupational therapy are required as well. Importantly, mental health care services were also recommended to help with his substance use.

Following treatment, the patient regained sensation and the ability to walk. "Our patient wanted his story shared so that others would know that intervening early allows people to regain neurologic function," says Gardin. "It would have been easy for us to have chalked up his problems to nitrous oxide use and called it a day. But it's important to perform additional screening to look for issues with B12 metabolism and B12 deficiency, as well as to make sure such patients get the neurologic and psychiatric care they need."

What clinicians should know about nitrous oxide use

Gardin emphasized that nitrous oxide use is increasingly common and

more extensive than many realize, and that patients presenting with neurologic or psychiatric symptoms related to nitrous oxide use should be promptly screened for other vitamin B12 metabolism issues. Furthermore, treating the complications of chronic nitrous oxide use requires a multi-disciplinary approach addressing all underlying neurologic and psychiatric causes.

"The chronic use of nitrous oxide can be part of a reinforcing cycle in which use causes B12 impaired metabolism resulting in neurologic and psychiatric symptoms which can, in turn, reinforce nitrous oxide use. Ensuring comprehensive neurologic and psychiatric care is the best way to treat and prevent relapse for those who chronically use nitrous," says Gardin.

More information: Tova Michal Gardin et al, Subacute combined degeneration of the spinal cord in a patient with nitrous oxide use and autoimmune atrophic gastritis, *BMJ Case Reports* (2023). DOI: 10.1136/bcr-2023-254727

Provided by Yale University