H107 No Laughing Matter: Deaths Associated With Chronic Nitrous Oxide (N_2O) Abuse

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Learning Overview: The goal of this presentation is to describe mechanisms by which chronic recreational N_2O use can contribute to death.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by raising awareness of the neurological and hematological sequalae of chronic N_2O abuse.

N_2O is an inhalant anesthetic, propellant in the food industry, and used recreationally by some inhalant abusers. A case series of three decedents with histories of chronic recreational N_2O abuse, and the associated neurological and hematological sequelae associated with N_2O use, is presented.

Case 1: The decedent was a 57-year-old male who was found deceased in bed. His medical history included daily inhalation of 20 to 50 canisters of N_2O, ethanol abuse, diabetes mellitus, macrocytic anemia, and lower extremity weakness with difficulty ambulating thought to represent Guillain-Barre syndrome. Autopsy findings included cardiomegaly, moderate coronary artery atherosclerosis, and steatosis of the liver. Microscopically, the spinal cord showed demyelination, presence of macrophages, and reactive astrocytes of the posterior and lateral columns. Postmortem (femoral) blood N_2O concentration was 34mcg/mL.

Case 2: The decedent was a 43-year-old male who was found deceased on his couch. He reportedly had been lying on the couch for several days prior to death inhaling canisters of N_2O almost continuously. He had a clinical history of difficulty ambulating, which was attributed to vitamin B12 deficiency associated with chronic N_2O inhalation. He was treated with vitamin B12 injections and over-the-counter supplements. Autopsy findings included consolidations of the lungs. Microscopically, the lungs had acute pneumonia, and the spinal cord showed mild demyelination, rare macrophage, and gliosis of the lateral columns. N_2O was not detected in postmortem blood.

Case 3: The decedent was a 21-year-old female found deceased on her couch. Reportedly weeks prior to death, she had sustained a right ankle strain, limiting her mobility and causing her to utilize a wheelchair. Numerous N_2O canisters were found throughout her residence. Autopsy demonstrated an obese female with pulmonary artery thromboembolism and deep venous thromboses of the lower extremities. Microscopically, the spinal cord showed demyelination, macrophages, and reactive astrocytes within the white matter tracts. N_2O was not detected in postmortem blood.

N_2O is a colorless and odorless non-flammable gas with various uses, including clinically as an anesthetic, as an aerosol propellant for food products, and auto racing. Inhalation of N_2O, also known as "laughing gas," reportedly causes euphoria, anxiolysis, hallucination, and has a narcotic effect. Common mechanisms of inhalation include balloons filled by medical or commercial N_2O tanks, and from whipped cream dispensers using N_2O chargers, commonly referred to as "whippits," easily purchased over the internet. Death from acute N_2O toxicity are rare, and deaths associated with N_2O use are often due to a local suffocating environment, such as a plastic bag over the head.

Chronic use of N_2O can have both neurologic and hematologic complications as seen with vitamin B12 (cobalamin) deficiency. In the body, cobalamin is converted to its active forms, methylcobalamin or adenosylcobalamin. N_2O inactivates methylcobalamin, a cofactor for methionine synthase, resulting in decreased methionine production. This results in impaired myelination of the spinal cord causing Subacute Combined Degeneration (SCD) of the spinal cord or impaired DNA synthesis leading to megaloblastic anemia. SCD is the degeneration of white matter in the posterior and lateral columns of the spinal cord, and clinical manifestations include numbness, paresthesia, polyneuropathy, or myelopathy. Other comorbid conditions such as malnutrition associated with chronic ethanolism (as in Case 1) or pernicious anemia could be a factor in an individual developing SCD or megaloblastic anemia. Vitamin B12 supplementation may also be a reason that in Case 2, the histological changes were subtle compared with Cases 1 and 3.

Though the decedents did not die from acute N_2O toxicity, all three displayed clinical or histological signs of SCD, which are associated with chronic N_2O abuse. Decreased mobility associated with chronic N_2O use in Cases 2 and 3 was a contributory condition for developing pneumonia and deep vein thrombosis respectively. In Case 1, the decedent also had history of megaloblastic anemia, which could be linked to N_2O use as well as chronic ethanolism. In summary, chronic N_2O use can have neurological as well as hematological sequelae potentially contributing to death.

Nitrous Oxide, Subacute Combined Degeneration, Inhalants

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