VOLUME
38
December
2025

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GERMAN SOCIETY OF
TOXICOLOGY

Poison of the month

Laughing gas

The proposal to select laughing gas as "Poison of the Month" comes from the Tox Wiki Working Group...

as, by doing so, the group highlights an everyday chemical compound that, for decades has had safe applications in food preparation and in medicine, yet attracted little attention until, fuelled by social-media posts and videos, it developed into a dangerous party drug that ultimately requires more public information and stricter regulation.

Nitrous oxide – chemical and historical background

Dinitrogen monoxide (N_2O) is a small inorganic molecule from the family of nitrogen oxides. It has a linear structure and at room temperature it is a colourless gas. Historically, N_2O was first described and prepared in 1772 by Joseph Priestley, among other methods by heating ammonium nitrate and subsequently purifying the resulting gas. Nitrous oxide gained its decisive boost in popularity at the end of the 18th century when Humphry Davy, from 1799 onward at the "Pneumatic Institution of Bristol", conducted extensive experiments with nitrous oxide, including many self-experiments. He described the effects systematically and helped shape the image of "laughing gas". As an anaesthetic, N_2O later became particularly established in dentistry and obstetrics, where it has been used since the 19th century.

Laughing gas – the dangerous short high

Laughing gas, chemically dinitrogen monoxide (N_2O), an inorganic nitrogen oxide, has long been established as a colourless gas for technical and medical use. As early as the 1790s it was demonstrated in Europe and North America because of its rapid-onset, short-lived central nervous effects and used for entertainment at fairs and other leisure events. In parallel, its controlled medical use developed as an analgesic and anaesthetic, for example in dentistry or obstetrics. A prerequisite for an effective and safe treatment is controlled administration in a mixture with oxygen under continuous monitoring.

At the same time, nitrous oxide is currently being misused as a party drug, particularly by adolescents and young adults. Signals from poison information centres suggest that use is increasing. Typically, the gas is taken from cartridges that are actually sold as a propellant for whipped-cream siphons, transferred into balloons and inhaled from there. What is often underestimated is that in such settings neither oxygen supply nor dose, purity or duration of exposure can be reliably controlled—creating situations that may become life-threatening.

From a toxicological perspective, two interacting mechanisms are central in misuse. First, N_2O acts on the central nervous system and can quickly lead to intoxication, disinhibition and altered perception. Second, when inhaled it displaces oxygen, which can pose an acute risk (diffusion hypoxia). The effect begins rapidly: after inhalation, a euphoric state may occur within about ten seconds and typically lasts only a few minutes. If inhalation is repeated or occurs under unfavourable circumstances (e.g., sitting/lying down, without fresh air, under the influence of alcohol or other drugs), hypoxia may develop, ranging from dizziness, drowsiness and coordination problems to loss of consciousness. Additional physical hazards arise because the gas leaving cartridges is strongly cooled, so cold burns on the lips or skin can occur. After direct inhalation from

Deutsche Gesellschaft für Toxikologie

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Nitrous oxide in the environment

N_2O is not only a gas used in technology and medicine, it is also a natural component of the nitrogen cycle. In the environment it is formed mainly by microorganisms in soils. During nitrification (aerobic oxidation of ammonium) and denitrification (anaerobic reduction of nitrate), N_2O occurs as a by-product or intermediate and can escape from the soil into the atmosphere. The oceans also contribute to natural N_2O emissions through microbial processes.

N_2O becomes problematic because human activities greatly intensify these natural emissions. Particularly important are agricultural nitrogen inputs (fertilisation, slurry/manure management), which "feed" microbial conversions in soils and thus increase N_2O emissions. Further contributions come, among other sources, from industrial processes and various combustion processes. Accordingly, measurement series show that atmospheric N_2O concentrations are rising.

From a climate perspective, nitrous oxide is relevant because it is a long-lived, potent greenhouse gas and can additionally affect the ozone layer.

This climate relevance and its long residence time in the atmosphere contribute to the fact that its use, including in medicine, is increasingly being critically reassessed, and active efforts are being made to reduce emissions wherever feasible.

pressurised containers, airway injuries have also been described, caused by the rapid expansion of the gas.

Chronic risks arise mainly through the functional inactivation of vitamin B_{12} (cobalamin): nitrous oxide can irreversibly oxidise the cobalt in the active centre of vitamin B_{12}. The vitamin is then altered in a way that vitamin B_{12}–dependent enzyme reactions proceed less efficiently, affecting metabolic pathways that are important for nerve function and blood formation. With repeated, high-frequency use, a functional vitamin B_{12} deficiency may develop gradually. Symptoms may include tingling and numbness and later unsteady gait and incoordination (peripheral neuropathy) and, in more severe cases, may be accompanied by signs of spinal cord involvement. These changes can lead to long-lasting and, in an unfavourable course, even permanent neurological damage. Changes in blood formation can also occur and may present as anaemia (megaloblastic anaemia). With repeated use, tolerance may develop so that more nitrous oxide is required to produce the desired effects, resulting in psychological—but not physical—dependence.

Stricter regulation of nitrous oxide is currently being discussed in Germany to curb misuse, particularly among minors, without unnecessarily hindering legitimate medical and technical applications. One option under consideration is classification under the New Psychoactive Substances Act (NpSG) with the aim of restricting purchase and supply. If the legislative process continues to progress swiftly, the law could enter into force in Germany by the end of April 2026.

By Ute Haßmann

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