Nitrous oxide (N_2O): Misuse by Young People and Potential Harms

Summary

Nitrous oxide, commonly known as laughing gas, has been used for many years in dental and medical practice – usually diluted with equal parts of oxygen - to provide sedation or pain relief: for example, in labour/childbirth, or for short procedures in children. Today nitrous oxide's main legitimate use is as a food additive. Recent widespread recreational misuse of nitrous oxide, particularly by children and young adults, has raised safety concerns; this is well summarised here. While significant harm is infrequent, misuse has been associated with severe neurological injury or even death. In 2023, non-legitimate possession of nitrous oxide was made an offence, under the Misuse of Drugs Act (1971). The impact of this recent UK legislative change is not yet evident. The environmental impact of nitrous oxide release on global warming is also a potential concern although emission from the uses described in this statement represent a very small percentage of the total.

Chemistry

Nitrous oxide is a colourless, sweet-smelling gas. It is heavier than air. Nitrous oxide consists of two nitrogen atoms bound to an oxygen atom and has the chemical formula N_2O.

Nitrous oxide is a recognised *"greenhouse gas"*. The bonds between the oxygen atom and the nitrogen atoms absorb energy from reflected sunlight and trap it in the Earth's atmosphere, contributing to global warming.

The release of nitrous oxide into the atmosphere has a high impact with a global warming potential of 298 compared to 1 for carbon dioxide. A molecule of nitrous oxide has been estimated to persist in the atmosphere for approximately 100 years, so the environmental impact from nitrous oxide release is considerable. However, the nitrous oxide emissions from the uses described in this statement are a tiny proportion of the total from other sources, principally agriculture (circa 80%).

History

Nitrous oxide was first synthesised by Joseph Priestly in 1772 and some of the effects in humans, including the mood-altering effects, were described by Humphrey Davy in 1800. The first use of nitrous oxide as a dental anaesthetic was reported in 1844.

Legitimate uses of nitrous oxide

Nitrous oxide has been used for many years in dental and medical practice to provide sedation or pain relief, such as in labour/childbirth, or for short procedures in children.

Medical nitrous oxide is diluted with oxygen, typically a gaseous mixture of 50% N_2O and 50% oxygen (Entonox) due to the risk of asphyxia (severe lack of oxygen) associated with inhaling concentrated nitrous oxide - see below.

The main legitimate non-medical use of nitrous oxide today is as a food additive (E942), principally as an aerating agent in the food industry in the production of whipped creams and in baking. Nitrous oxide is also used as an additive in high performance fuels.

Nitrous oxide used in the catering trade is undiluted and is therefore more potent than medical nitrous oxide mixtures, with concentrations typically tending towards 100%. Catering nitrous oxide is available in small, single use, 8 g cartridges (known as *whippits* or *nangs*) or in large canisters: 600 g to 2 kg.

Misuse of nitrous oxide

The UK Office for National Statistics (ONS) estimated that around 796,000 individuals misused nitrous oxide between March 2019 and March 2020. The ONS reported that 8.7% individuals in the 16 to 24 year age range had used nitrous oxide over the period 2017-2020, which is three times the proportion in the wider 16 to 59 year age range.

Widespread recreational misuse of nitrous oxide, particularly by children and young adults, has raised safety concerns in the UK and across Europe. Discarded small canisters in parks (figure) or back streets are a telltale sign of a gathering place for misuse of nitrous oxide and, of course, degrade the local environment.

Non-legitimate supply of nitrous oxide was controlled under the UK Psychoactive Substances Act (2016). Non-legitimate possession of nitrous oxide was made an offence under the UK Misuse of Drugs Act (1971), when nitrous oxide was entered into Schedule C of the Act in 2023. It is too early to say what impact this recent change in the UK legislative framework will have.

Short-term effects of nitrous oxide on humans

The short-term effects of nitrous oxide are proportional to the concentration of the gas in inhaled air. Inhalation of nitrous oxide at concentration of 6% to 25% typically produces a sensation of euphoria and relaxation. At higher concentrations, 26% to 45%, individuals experience sedation and loss of coordination. Nitrous oxide has to be delivered above atmospheric pressure to reach the minimal alveolar concentration,

that is the lowest concentration in the air sacs of the lung, to achieve anaesthesia. There is, however, considerable variation in the individual response to nitrous oxide.

Nitrous oxide gas is volatile and poorly soluble in the blood. The onset of the effects of the gas are rapid but of short duration and typically resolve within minutes of discontinuing to inhale the gas. Nitrous oxide does not usually accumulate within the body with repeated exposures over a 12-hour period, however, the sedative effects are expected to increase due to fatigue and would also be increased if an individual was also exposed to other central nervous system depressants, such as alcohol.

Nitrous oxide is released from a pressurised container at a temperature of -45 to -50°C. Inhaling nitrous oxide directly from cartridges or cylinders poses a high risk of severe burns and lung injury.

Long-term effects of nitrous oxide on humans

Vitamin B12 is essential for good health. It is a key molecule in the production of blood cells and the normal function of the nervous system, especially the sensory nervous system. Long-term exposure to nitrous oxide is associated with neurological injury due to the inactivation of vitamin B12. Vitamin B12 has a central cobalt ion. Nitrous oxide, oxidizes the cobalt ion required for normal B12 function, rendering it inactive. The injury can range from comparatively minor and reversible changes such as abnormal feeling (tingling, pins and needles) to degenerative injury to the spinal cord, which could be potentially disabling if not promptly treated.

The dose required to cause this effect is uncertain but appears to be associated with the regular use of nitrous oxide at doses exceeding 400 g/day. A case series of patients with nitrous oxide at doses exceeding 400 g/day identified 119 cases, who presented to NHS Teaching Hospitals in London, Manchester and Birmingham, between 2014 and 2022. The majority of the patients were male, with ages ranging from 14 to 39 years and an average age of 22 years.

Nitrous oxide related deaths

Nitrous oxide use is associated with death. Between 2001 and 2020, the ONS reported 56 deaths involving nitrous oxide exposure in England and Wales. Deaths associated with nitrous oxide exposure occur from secondary effects rather than the direct toxicity of the gas.

The principle mechanism of death is likely to be asphyxiation/suffocation, due to a reduction in the amount of oxygen circulating in the blood stream resulting in low levels of oxygen (hypoxia) in tissues that are critical to sustain life. When an individual ceases to inhale nitrous oxide, the gas is released from the blood into the air sacs of the lungs. This may dilute oxygen present in the air sacs to the extent that hypoxia results. The risk of this is increased if the gas is used in a confined space, such as a car, or if the gas is administered by a face mask or by rebreathing air in a plastic bag over the head. It has been suggested that deaths associated with nitrous oxide use may also occur through an increased risk of accidents, including occupational related trauma or road traffic accidents.

BTS v.1.0 February 2024