

Nitrous oxide: increasing misuse associated with serious neurological consequences

Although nitrous oxide has long been misused due to the fact that it is freely available via cartridges for whipped cream dispensers, the number of such misuses has increased sharply since 2019. French poison control centres had issued an alert regarding the increase in the number of calls between 2017 and 2019 and the serious neurological symptoms observed in some people. An analysis of the cases from 2020 confirmed this increase as well as the occurrence of persistent neurological consequences, especially in users who regularly inhale large amounts. It also showed the growing use of (larger capacity) cylinders instead of cartridges. A legislative framework has now been established in France, with an act designed to prevent this misuse being adopted on 1 June 2021. At the same time, consumers and healthcare professionals need to be better informed of the risks involved.



Tank of nitrous oxide. Photo credit : C. Greillet

An alert already issued in 2019

The inhalation of nitrous oxide is a "recreational" practice that has been known to the vigilance networks for about a decade, due to the availability of cartridges for whipped cream dispensers in shops and on the internet. Indeed, as a food additive under Regulation (EC) No 1333/2008, nitrous oxide is freely available for sale to consumers [1].

Several alerts regarding the misuse of this food gas have recently been issued by the health authorities: in late 2019, the French Interministerial Mission for the Fight against Drugs and Addictive Behaviour (Mildeca) published a press release confirming an increase in serious cases reported to the centres for evaluation and information on drug dependence and addiction monitoring (CEIP-A) [2]; in June 2020, messages targeting young consumers and their families and friends were posted by Mildeca on social media [3]; in July 2020, ANSES and the French Health Products Safety Agency (ANSM) simultaneously published two reports on cases reported to Poison Control Centres (PCCs) [4] and to the CEIP-A [5] between 2017 and 2019.

Data from poison control centres, presented in Issue 11 of Vigil'Anses [6], showed an increase in cases of recreational inhalation of nitrous oxide from whipped cream cartridges in 2019 (46 cases compared to 20 between 2017 and 2018). The consumers, mostly young adult men, inhaled this gas at evening social events (festivals and student parties, for example) but also at private parties. Consumption was mainly from cartridges, with several hundred sometimes being consumed in a day. In this study, only two out of 66 people had consumed nitrous oxide from a cylinder (containing the equivalent of about 100 cartridges). The mildest symptoms reported were nausea and headaches, while the most severe were neurological disorders including peripheral neuropathy¹.

Worrying results that justified further monitoring during 2020

Because of these worrying results, the decision was taken to continue identifying cases reported to poison control centres in 2020. Indeed, it was thought that the pandemic context and the successive periods of lockdown and curfew could favour the inhalation of nitrous oxide at home.

1. Peripheral nerve damage, most frequently resulting in paraesthesia and hypoaesthesia of the lower limbs, night-time pain and muscle weakness.

Compared to the previous report, the number of calls to poison control centres concerning recreational nitrous oxide use more than doubled in 2020. Between 1 January and 31 December 2020, a total of 134 people called poison control centres concerning a case of nitrous oxide exposure (canisters for whipped cream dispensers or any other packaging containing nitrous oxide), compared to 20 cases between 2017 and 2018, and 46 cases in 2019.

Of these 134 cases, 126 were symptomatic. With 83 men and 51 women, the sex ratio of 1.6 confirmed the male preponderance that had already been noted in the previous study. Users were young, ranging from 13 to 42 years old, with a median age of 20.

Ile-de-France was the most commonly affected region with a quarter of the cases for only 18% of the French population, followed by Hauts-de-France. These two regions were already the most represented in 2017-2019.

Furthermore, the 2020 data confirmed the occurrence of serious neurological disorders, especially among regular consumers. At least one neurological and/or neuromuscular symptom was reported in 76.2% of cases. Of these cases, three quarters had at least one motor and/or sensory sign such as paraesthesia², hypoaesthesia³, motor deficit, tremor of the extremities or muscle pain.

Four cases of subacute combined degeneration of the spinal cord⁴ were confirmed by MRI. In addition, three cases of myelitis⁵ and peripheral neuropathy were diagnosed.

In this report, 61.1% of cases were of low severity, 26.2% of moderate severity and 12.7% of high severity.

In 19.4% of cases, nitrous oxide consumption occurred alongside the use of psychoactive substances (compared to 30.3% in the previous study). Alcohol was involved in 10.4% of cases, cannabis, amphetamines or "poppers" in 10.4% of cases, and medicines in 3.0% of cases, with some users having consumed several psychoactive substances at the same time.

Lastly, in 76.1% of cases, the nitrous oxide was inhaled in the home of the exposed person or their family or friends (compared with 47% between 2017 and 2019).

2. Tingling, numbness, prickling.

3. Decreased sensitivity.

4. Simultaneous damage to two areas of white matter in the spinal cord (posterior column carrying sensation and lateral column carrying motor function). It causes sensory disorders associated with involuntary muscle contractions, especially in the lower limbs.

5. Inflammation of the spinal cord causing motor and sensory impairment. Symptoms set in within a few hours to a few days, initially affecting the legs. Partial or complete loss of strength in the limbs, numbness and bladder-sphincter problems are observed.

These trends in the number of cases and practices most certainly reflect an increase in the number of young people inhaling nitrous oxide during this unusual year, but above all, an intensification of practices among certain consumers who have been using nitrous oxide sometimes for more than two years.

The 2020 study showed a higher proportion of calls involving regular consumption for over a year, of several dozen or even hundreds of cartridges per day, with this chronic consumption increasing the occurrence of severe neurological damage over time.

Increased use of cylinders

While nitrous oxide was almost exclusively consumed from cartridges and inhaled via balloons, the study highlighted a much higher share of nitrous oxide consumption from cylinders. Twenty-six people had inhaled nitrous oxide via a cylinder, a much higher proportion than in previous years (19.4% versus 3.0% between 2017 and 2019).

These cylinders are only available via the internet as their sale is restricted to professionals (e.g. caterers). Nevertheless, they are freely available for sale on many websites, with the option of ordering large quantities or requesting rapid home delivery for a party. This makes it dangerously easy to consume nitrous oxide, since a "cracker" or bottle opener to empty the gas into a balloon is no longer necessary. These cylinders allow one user to consume considerable amounts of nitrous oxide over a short period of time.

Much awaited legislation adopted in 2021

Until very recently, only a few municipal by-laws had been passed to ban the consumption of nitrous oxide in public places or to restrict its sale in shops.

On 1 June 2021, the French Senate definitively adopted the Act on preventing dangerous uses of nitrous oxide [7].

This Act applies to adults as well as minors, and recommends a ban on the sale or offer of nitrous oxide to any person (minor or not) in licensed premises (drinking establishments and tobacconists).

The law provides for a fine of 15,000 euros for "causing a minor to misuse an everyday consumer product to obtain psychoactive effects". This offence is mainly intended for nitrous oxide but will be able to cover the misuse of everyday consumer products in other contexts. It prohibits "selling or offering nitrous oxide in any form to a minor". This will allow sellers to require proof of age from purchasers of nitrous oxide cartridges. Regarding online sales, websites will also have to mention this ban on sales to minors before allowing the purchase of nitrous oxide "in any form".

A "maximum quantity authorised for sale to private individuals" will be set by ministerial order.

Lastly, the Act "prohibits the sale and distribution of any product specifically designed to facilitate the extraction of nitrous oxide in order to achieve its psychoactive effects", i.e. "crackers" or any other device that may become available in the future.

With regard to information, a statement on the packaging indicating that "the misuse of nitrous oxide is dangerous to one's health" will be mandatory for sale.

This Act will be notified to the European Commission in the coming months to ensure its compliance with European law, in particular Regulation (EC) No 1907/2006 (REACH), which defines restrictions on the use and sale of chemicals [8].

Targeting young people with the appropriate tools

This awaited legislative development and its forthcoming notification at European level come at a time when young people are continuing to misuse nitrous oxide. Poison control centres are receiving increasing numbers of calls: in the first five months of 2021, the number of calls equalled that of the whole of 2020, with the use of cylinders and massive consumption practices being confirmed.

It is therefore still essential to provide consumers and their families with more information on the risks associated with this practice, which is still too often considered to be a harmless use of "laughing gas". The 2020 case report indicated

that severe and long-lasting neurological damage appears to be associated with heavy or chronic consumption of nitrous oxide. This damage requires prolonged medical monitoring in a neurology department, or even functional re-education with the complete interruption of work, ongoing training or studies. The data currently available provide no assurance that patients will fully recover after ceasing consumption of nitrous oxide or that the lesions will not worsen if use resumes. These patients are often reluctant to seek medical care, which implies regular multidisciplinary follow-up to assess the progression of the neurological damage. The risks continue to be underestimated by these users, in terms of both short-term problems such as asphyxiation and longer-term disorders such as neurological deficit complicated by gait and balance disorders. Media targeting young people, particularly social networks, and risk prevention associations working in universities, secondary schools and at student parties are the best channels for relaying public health messages.

The other driver for action already mentioned in the first toxicovigilance study remains information to healthcare professionals: general practitioners, hospital emergency workers, neurologists, paediatricians, and school doctors and nurses. For example, in April 2021, the CEIP-A in Lyon, France published a checklist informing healthcare professionals about the very real risks of massive or long-term consumption of nitrous oxide [9]. This checklist describes the symptoms observed in the event of neurological or haematological damage, as well as the biological and radiological examinations recommended for establishing a diagnosis. It also insists on multidisciplinary care between hospital emergency workers, general practitioners and neurologists, as well as addictologists, to help the patient stop using nitrous oxide.

Jean-Marc SAPORI (Nord-Ouest Hospital, Villefranche sur Saône), Chloé GREILLET (ANSES), Cécilia SOLAL (ANSES)

In case of unusual symptoms after use, contact a Poison Control Centres. In case of emergency, call the emergency services (15 or 112).

If you have difficulty controlling and stopping your consumption, consult a doctor or a structure specializing in the treatment of addictions, such as a young consumers' consultation, which offers a free and confidential service to receive, listen to, advise and, if necessary, provide guidance (www.drogues-info-service.fr).

TO FIND OUT MORE :

[Rapport d'étude de toxicovigilance. Proxymide d'azote. Bilan des cas rapportés aux Centres antipoison en 2020](#)

References

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- [5] French Health Products Safety Agency <https://ansm.sante.fr/actualites/de-nouveaux-chiffres-sur-lusage-detourne-de-protoxyde-dazote-gaz-hilarant-pour-eclairer-les-autorites-sanitaires-communique>
- [6] Vigil'Anses. 2020. https://www.anses.fr/fr/system/files/VigilAnsesN11_Juin2020_VPC_Proto.pdf
- [7] Act No. 2021-695 of 1 June 2021 on preventing dangerous uses of nitrous oxide <https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000043575111>
- [8] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1907-20140410&from=EN>
- [9] Centre for evaluation and information on drug dependence and addiction monitoring (CEIP-A Lyon). 2021. Usage détourné de protoxyde d'azote (N₂O): mémo sur l'atteinte neurologique et hématologique [Misuse of nitrous oxide (N₂O): memo on neurological and haematological damage]. Addict'o'News No. 4. <https://www.addictolyon.fr/post/addict-o-news-protoxyde-d-azote>