

Its time to 'Whippit' into shape: the importance of developing treatment guidelines for Nitrous Oxide

Dr Elizabeth Hawke¹, Dr Mary Thornton¹, Dr Mike Kelleher¹, Dr Emily Finch¹
¹South London and Maudsley NHS Foundation Trust

Background

Nitrous oxide (N₂O) use is increasing. Its recreational use is a growing public health concern, with a recent call for evidence by the Advisory Council on the Misuse of Drugs regarding associated health and social harms. (N₂O), is known to have wide ranging mental, physical and social impacts. Despite this there are no national treatment guidelines. We present a complex case highlighting these harms, the need for a multidisciplinary approach and the development of local and national guidelines.



What is nitrous oxide and what are its effects?

- Nitrous oxide (N₂O), colloquially known as ‘laughing gas’, balloons or whippits. It's legally used in the catering industry and anaesthetics. In 16–24 year olds it is the 2nd most prevalent substance (1).
- N₂O acts on the gamma-aminobutyric acid (GABA), N-methyl-D-aspartate (NMDA) and endogenous opioid receptor systems (2).
- It has dissociative, analgesic, and euphoric effects (2).
- It inactivates vitamin B12, leading to functional B12 deficiency. Long-term use of N₂O can lead to loss of sensation, co-ordination problems and paralysis (3).
- Fatalities have occurred due to asphyxiation (4) and cardiac arrhythmias (5).
- Psychiatric manifestations include psychotic symptoms, cognitive impairment, anxiety and affective instability (5).

Case report

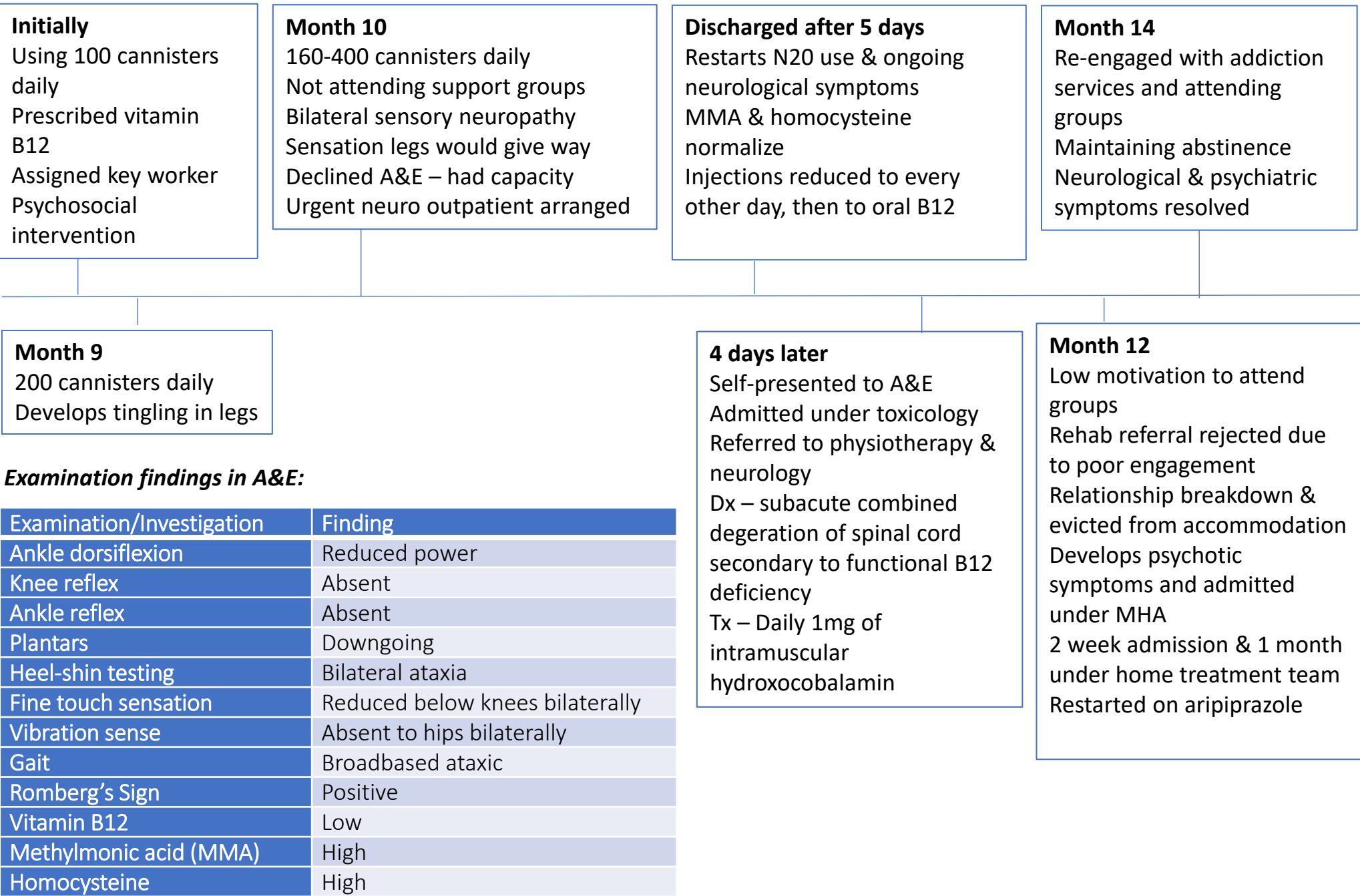
Presenting complaint:

- A 24-year old female presented to addictions services for help with a seven-year history of daily cannabis and N₂O use
- Previous use of LSD, psilocybin, alprazolam, codeine, and promethazine
- She reported using psychoactive substances to escape emotional difficulties and past trauma.
- She had a history of childhood abuse. She had attended university. At presentation she was unemployed and living with her partner.
- Her father had depression

Past psychiatric and medical history:

- Under early intervention psychosis team. One previous psychotic episode, requiring admission under the mental health act and antipsychotic treatment.
- Asthma and Polycystic ovarian syndrome

Timeline of events:



Examination findings in A&E:

Examination/Investigation	Finding
Ankle dorsiflexion	Reduced power
Knee reflex	Absent
Ankle reflex	Absent
Plantars	Downgoing
Heel-shin testing	Bilateral ataxia
Fine touch sensation	Reduced below knees bilaterally
Vibration sense	Absent to hips bilaterally
Gait	Broadbased ataxic
Romberg’s Sign	Positive
Vitamin B12	Low
Methylmonic acid (MMA)	High
Homocysteine	High

Discussion:

- N₂O is not commonly thought of as an addictive substance, however this case demonstrates N₂O dependence syndrome meeting the following ICD-10 criteria: compulsion, difficulty controlling use, increased tolerance, neglect of other interests, and persistent use, despite undesirable consequences.
- Patients are not commonly seen in addictions services – a local audit showed that in two years, 44 presented to acute hospital Vs 1 in addiction services
- A quarter (10/44) of these patients represented with neurological symptoms, highlighting a potentially missed opportunity for addictions intervention
- Currently there are no local or national guidelines. These should be developed using a multidisciplinary approach. It is paramount that treatment pathways include addiction services with a goal of harm reduction, relapse prevention and reduction of long-term morbidity.
- Greater education is needed among general psychiatrists on the management of N₂O induced psychosis. Addiction services need to understand more about people who use N₂O in order to develop tailored interventions. There is also a need for greater public awareness of the potential dangers of N₂O use.
- This case raises a question as to whether intramuscular hydroxocobalamin could be administered in the community addictions setting (much like pabrinex) for hard to engage patients using N₂O, under the guidance of medical colleagues.

References: 1. Office for national statistics, 2020, Drug misuse in England and Wales, Office for national statistics, accessed 20th February 2023, 2. Farmer J, Romain K, Ibrahim M, Kumar M, The neuropsychiatric effects of nitrous and low vitamin B12, BJ Psych Advances, 2022, 28(4):216-225 doi: 10.1192/bja.2021.55 3. Abderrahim Oussalah et al, Global Burden Related to N2O Exposure in Medical and Recreational Settings: A Systematic Review and Individual Patient Data Meta-Analysis, J Clin Med, 2019, 8(4): 551 doi:10.3390/jcm8040551 4. Office of national statistics, 2022, Deaths related to volatile substances, helium and nitrogen in England and Wales: 2001 to 2020, Office of national statistics, access 20th Feburary 2023, 5. Garakani A et al, Neurologic, psychiatric, and other medical manifestations of N2O abuse: a systematic review of the case literature, Am J Addict, 2016 Aug, 25(5):358–369 doi: 10.1111/ajad.12372