



THE MEDICAL HISTORY OF NITROUS OXIDE

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THANK YOU FOR THE
OPPORTUNITY TO SPEAK!

EVOLUTION OF NITROUS OXIDE OVER TIME

- Joseph Priestley isolates nitrous oxide (1772)
- Humphry Davy discovers the biological effects of the gas (1800)
- Horace Wells discovers anaesthesia with nitrous oxide (1844)
- Rogerson investigates the potential use of nitrous oxide in psychotherapy (1944)
- A look at nitrous oxide and its role in society today

JOSEPH PRIESTLY

- English scientist and clergyman
- Isolated many gases (flogisticated theory of air).
- E.g mice and the mint plant.
- Isolated Nitrous oxide in 1772.



WHAT IS NITROUS OXIDE?

- Colourless gas (N_2O)
- Inert gas at room temperature, supports combustion of oxygen.
- Biological mechanism unclear. Acts on a variety of receptors (AMPA, GABA, glycine, NMDA-R, opiod...)
- **Uses:** dental, medical, frothing gas for whipped cream, and oxidizer for propellants such as rocket and motor racing fuel.



SIR HUMPHRY DAVY (1778-1829)

- Born in Cornwall
- Apprenticed a surgeon, and went to study chemistry in Bristol.
- Well known for isolating elements using electrolysis in 1807.



SIR HUMPHRY DAVY (1778-1829)

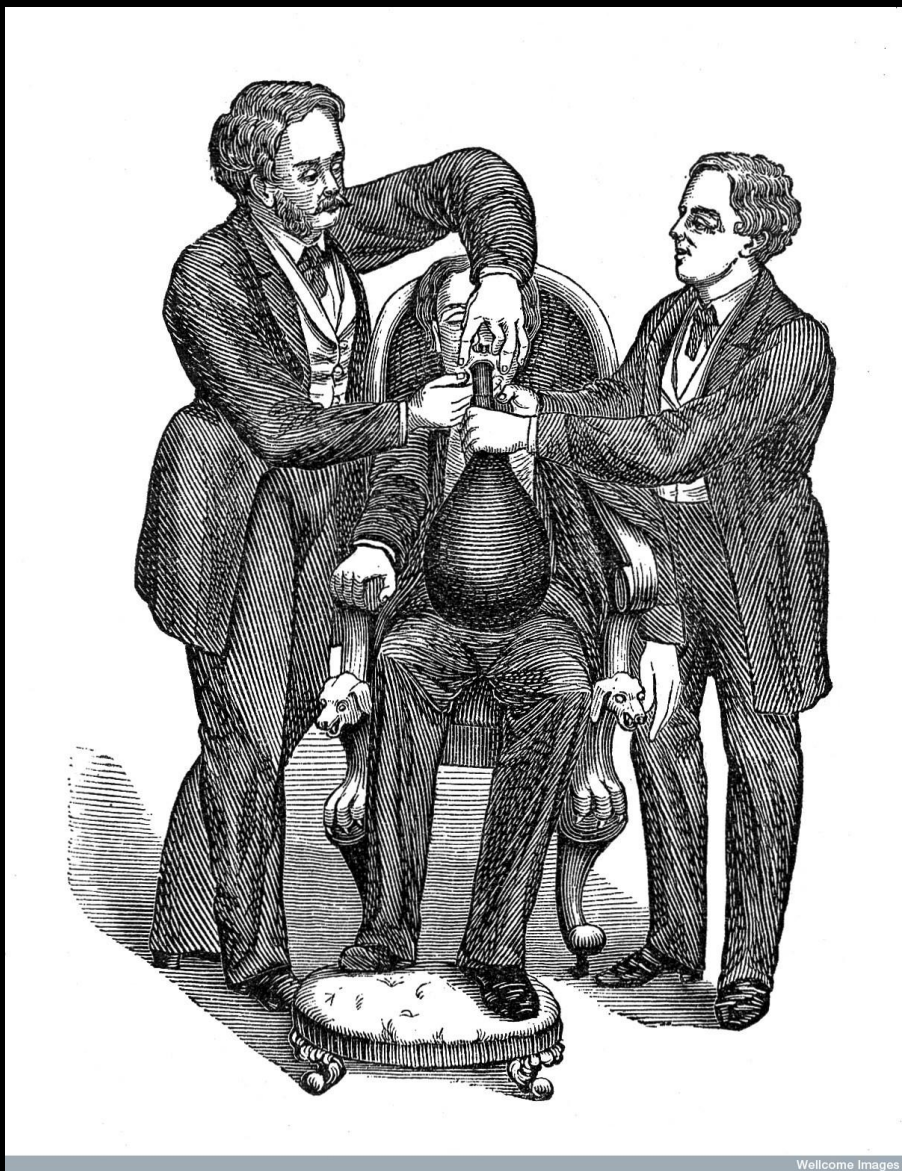
- Met Thomas Beddoes (scientific writer and physician).
- Hired him as the medical superintendent at the “Pneumatic institute” in Bristol (age the of 19...).





HUMPHRY DAVY BEGAN TO EXPERIMENT WITH NITROUS OXIDE...

- Joseph Priestly had discovered “deflogisticated nitrous air” and Davy was curious about the potential biological effects of this gas (?healing).
- Davy wanted to disprove the thinking that nitrous oxide was dangerous and could cause contagion.
- Nitrous oxide appeared to have no effect on meat, plants or open wounds, so tried it on himself...



HUMPHRY DAVY
CONTINUES
EXPERIMENTING...

MORE AND MORE...

- April 11th 1799 -> confirms gas can be breathed “safely”.
- Then tried 3 quarts of gas...
- Then tried 4 quarts of gas...
- Then tried 10 quarts of gas...this effect lasted 10-12 hours.

HUMPRY DAVYS PUBLISHES WORK ON NITROUS OXIDE

- Davy published a book almost 500 pages long describing his findings of nitrous oxide including his descriptions of experimentations on himself and others.
- Poor reception to his work, some people could not reproduce the effects and others felt his reputation was tainted due to Thomas Beddoes.



all into my lungs. While the respiration was continued, my sensations became more pleasant. On taking the bag from my mouth, I staggered a little, but felt no other effect.

On the second time of making the experiment, I took nearly four quarts, but still found it difficult to continue breathing long, though the air which was left in the bag was far from being impure.

The effects however, in this case, were more striking than in the former. Increased muscular action was accompanied by very pleasurable feelings, and a strong desire to continue the inspiration. On removing the bag from my mouth, I laughed, staggered, and attempted to speak, but stammered exceedingly, and was utterly unable to pronounce some words. My usual state of mind, however, soon returned.

SELF EXPERIMENTATION



On the 18th, I breathed nearly six quarts of the pure nitrous oxide. It is not easy to describe my sensations; they were superior to any thing I ever before experienced. My step was firm, and all my muscular powers increased. My senses were more alive to every surrounding impression; I threw myself into several theatrical attitudes, and traversed the laboratory with a quick step; my mind was elevated to a most sublime height. It is giving but a faint idea of the feelings to say, that they resembled those produced by a representation of an heroic scene on the stage, or by reading a sublime passage in poetry when circumstances contribute to awaken the finest sympathies of the soul. In a few minutes the usual state of mind returned. I continued in good spirits for the rest of the day, and slept soundly.

Since the 18th of May, I have very often breathed nitrous oxide. In the first experiments when pure, its effects were generally similar to those just described.

Lately I have seldom experienced vivid sen-

SELF EXPERIMENTATION

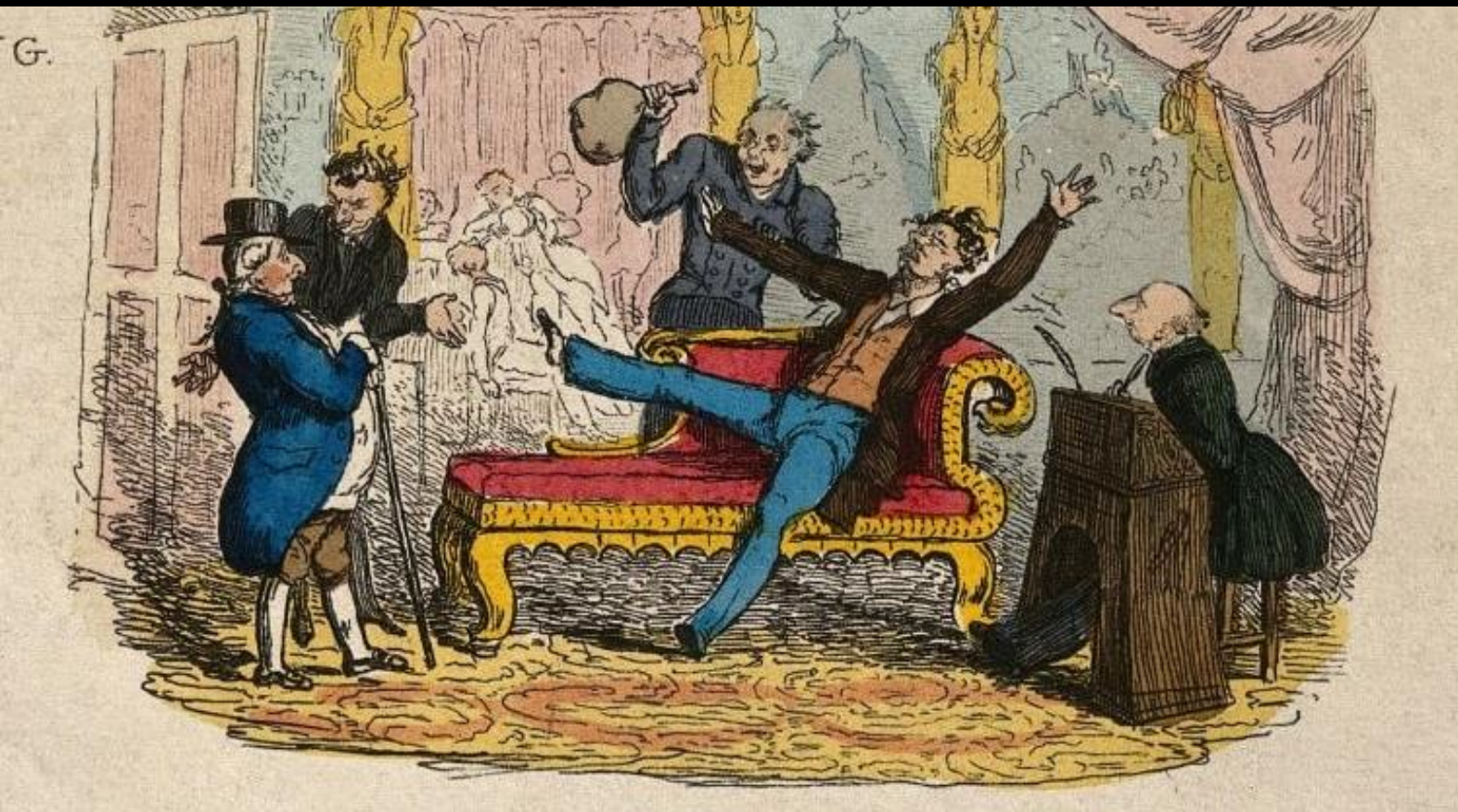
An abstract graphic at the bottom of the page featuring flowing, wavy lines in shades of blue and teal, set against a dark background.



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LAUGHING GAS PARTIES IN THE 1820'S



NOT MUCH HAPPENED FOR THE NEXT FEW DECADES...

- Recreational nitrous oxide became a fad.
- Humphrys would walk through town with a silk bag filled with gas and inhale it as he composed poetry.

HORACE WELLS (1815-1848)

- Dentist in Hartford Connecticut
- December 10th 1844 – attended a demonstration on the effects of nitrous oxide by Quincy Colton and Samuel Cooley.
- The next day tried it on himself to extract a tooth – successful.
- Then went to Boston to demonstrate it but the gas was improperly administered...



HORACE WALLS (1815-1848)

- He eventually was able to perform procedures with anaesthetic.
- He had issues with his mental health, and closed his practice multiple times.
- He eventually committed suicide in 1848 while in jail.



HORACE WALLS (1815-1848)

- Posthumously honoured for discovering modern anaesthesia.
- 12 days before his death, unknown to him the Parisian medical society voted him as the first to perform surgical operations without pain.
- He had a different approach to pain.



MOVING INTO THE 20TH CENTURY

- Stanislaw Klikovich (Polish physician in Greater Russia) publishes his thesis on mixing nitrous oxide with oxygen to avoid hypoxia or unconsciousness (1944).
- Julius Zador publishes work on the effect of nitrous oxide gas for 2-3 minutes on patients with mental health illness (e.g major depressive disorder, catatonia and schizophrenia) (1928).

DENTISTRY UPTAKE

- By the 1950's and even today it is used primarily as an anxiolytic.
- They utilize it in mixtures with 30-40% oxygen.



WHAT ABOUT IN PSYCHIATRY?

- Earlier studies (e.g Rogerson in 1928) focused on using >50% concentrations of nitrous oxide for unconsciousness.
- Later evidence focused on lower doses titrated gradually or PAN (psychotropic analgesic nitrous oxide).
- 1970 - report of 50:50 nitrous oxide/oxygen to relax patients in conjunction with verbal psychotherapy.
- In 1972 there is a case report of a 41yo woman with substance abuse of pentazocine (opiod) which was successfully weaned using 202 days of daily nitrous oxide.

WHAT ABOUT IN PSYCHIATRY?

- Newer studies (1994, 2004) show that nitrous oxide can be used for alcohol withdrawal.

(NB Humphry Davy reported this too as he used it to cure his hangover!)

- 2015 double-blind randomised controlled trial concluded that one hour of nitrous oxide therapy (50/50 mixture) showed an improvement on 21-HDRS and QIDS-SR scales at 24 hours.



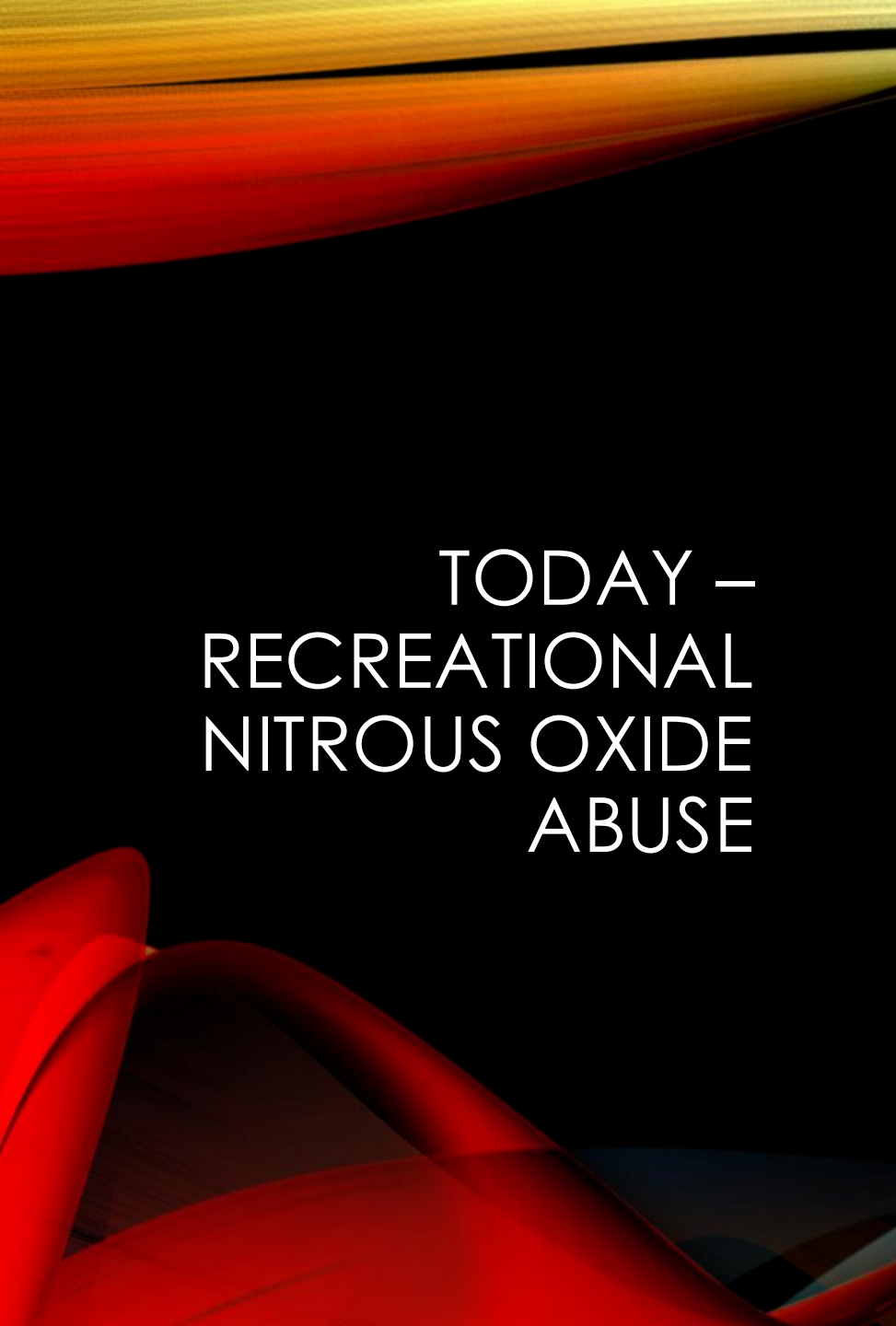
OBSTETRICS

- They have continued using nitrous oxide consistently since Klikovich's work in 1944.
- Used as 50:50 mixture of oxygen and nitrous oxide ("Entonox"). Good safety evidence.
- One study found of 483 woman taking Entonox during labour, 31% continued and 69% switched to another form of pain relief.



EMERGENCY DEPARTMENT

- Also used regularly for analgesia and anxiolysis in acute settings by ED and paramedic staff.
- Infrequent case reports of frequent presenters leading to addiction or neuropathy.



TODAY – RECREATIONAL NITROUS OXIDE ABUSE

Age groups 16-24: 24% used nitrous oxide in 2021.

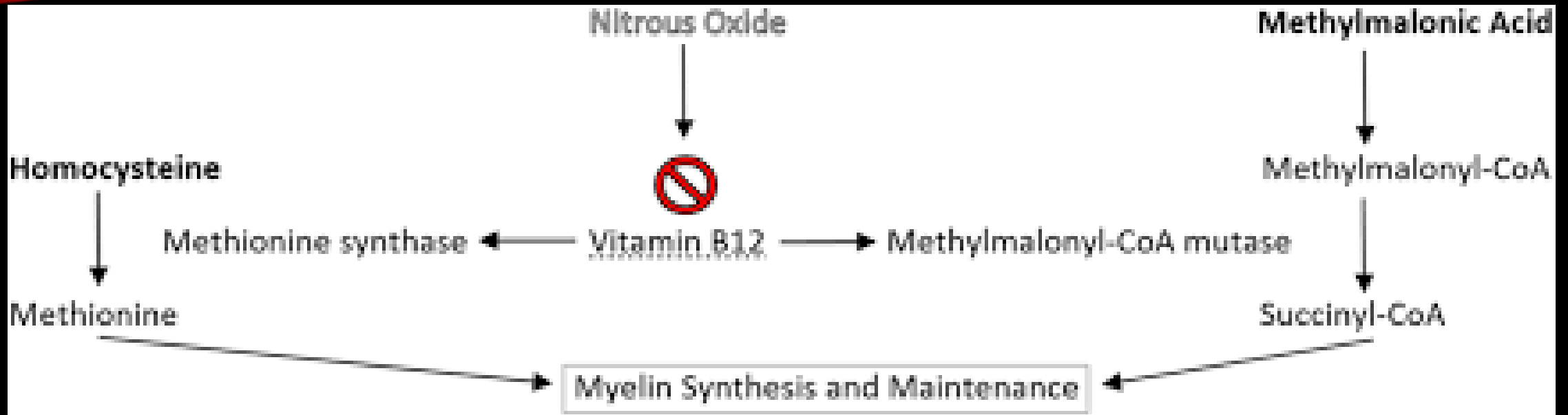
2015 - 2021, prevalence of nitrous oxide use globally increased from 10% to 24%

Prevalence of “low use” may be declining, while chronic and heavy use may be increasing.



WHAT ARE THE RISKS?

- Direct toxicity/harm – asphyxiation/"frostbite burn"/unconsciousness.
- **B12 deficiency and consequences of this*****



B12 DEFICIENCY AND NITROUS OXIDE

NITROUS OXIDE IN NEW ZEALAND

- 2003 prevalence study in NZ university students found that 3% of students used it monthly.
- A recent (2025) survey by The University of Otago found that only 6% of people who used nitrous oxide reported harm (e.g burns, confusion, injury, numbness).
- Overall most young people who use nitrous, use it infrequently and in small quantities.

Paddy Gower: It's time to get real about nangs

Patrick Gower

October 5, 2023 · 3:53pm

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Watch: Paddy Gower investigates nangs in the latest episode of Paddy Gower Has Issues.

HOSPITAL PRESENTATIONS ARE ON-GOING...

ARTICLE

49

Nitrous oxide myelopathy: a case series

Shilpan G Patel, Tony Zhang, Bernard Liem, Frederick Sundram, Richard H Roxburgh, P Alan Barber

ABSTRACT

AIMS: To describe the clinical features and outcomes of patients with myelopathy and neuropathy due to recreationally inhaled nitrous oxide.

METHODS: We identified patients presenting with nitrous oxide-associated myelopathy from an electronic database of all discharges in a large tertiary hospital between 2016 and 2023. Demographics, clinical features and the results of investigations were recorded. The primary outcome was modified Rankin Scale score (mRS) at least 3 months after hospital discharge where available.

RESULTS: There were 12 patients identified, six women, mean (SD) age 27.5 (5.1) years, range 19–47 years. The most common symptoms were numbness, weakness and mental state changes. Four patients used large amounts of inhaled nitrous oxide and also took over-the-counter vitamin B12 supplements. The median (range) hospital length of stay was 8.5 (2–56) days. Functional independence at last assessment (median [range] of 3 [1–34] months after discharge) was achieved in nine of the patients, with three requiring ongoing

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