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Nitrous Oxide Use and Misuse

Jolene J. Bierly, MSFS, D-ABFT-FT

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Learning Objectives

1. Nitrous oxide misuse is a growing public health concern worldwide.
2. Nitrous oxide misuse produces significant impairment.
3. Nitrous oxide is eliminated from the body in minutes.
4. Blood collected in airtight containers with limited headspace is preferred for toxicology testing.
5. Nitrous oxide misuse produces significant driving impairment.

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Disclosures

- I am a paid employee of NMS Labs, a commercial provider of toxicology and other forensic testing services.
- Any brand names mentioned are for educational and display purposes only.

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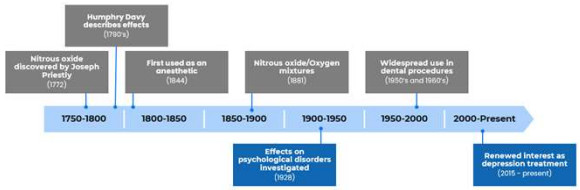
History of Nitrous Oxide (N_2O)



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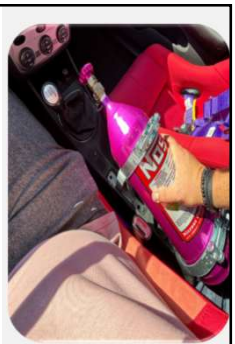
Legal Use

- Rocket fuel additive
  - Non-toxic alternative
- Automotive enhancement
  - Increases horsepower
- Culinary
  - Whipped cream dispensers
  - Aerate creams, beverages, desserts



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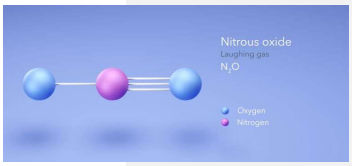
Chemistry

- Chemical Formula = N_2O
- Colorless, odorless, tasteless
- Molecular weight = 44.013 g/mol
- Boiling point = -88 °C
  - Room Temperature = 37 °C
- Blood/Gas Partition Coefficient = 0.47
  - Isoflurane = 1.4
- Elimination half-life = 5 minutes



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N_2O Misuse

Availability
- Legal in most jurisdictions
- Sold in retail stores and online
- Low cost

Rapid Effects
- Immediate effects
- Euphoric and dissociative high
- Lasts minutes

Difficult Detection
- Not included in routine toxicology
- Eliminated from the blood in minutes

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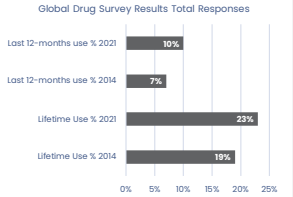
Global Trends

International

- N_2O misuse **increasing** globally
- Use varied by country in 2014
  - 39% United Kingdom
  - 29% USA
  - 11% Germany
- Ranked among **top 15 drugs** used in the last 12 months worldwide in global drug survey 2021

United States

- N_2O misuse **increasing** in USA
- **Emergency room visits** increased more than 6x between 2000 and 2019
- **N_2O fatal poisonings** increased 6-7x since 2010
- 103% increase in **intentional exposure** to N_2O between 2020 and 2023



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Patterns of Use

Clinical

- Anesthetic and analgesic in medical procedures
- Frequently combined with oxygen at 50-70% N_2O

Recreational

- 100% N_2O
- Inhaled from latex balloons or directly from containers
- Direct inhalation may cause frostbite
- Doses may range from 100g – 16,000g

Tank
x 400-600 N_2O

Canister
x 80-100 N_2O

Cartridge
~ 8 g N_2O

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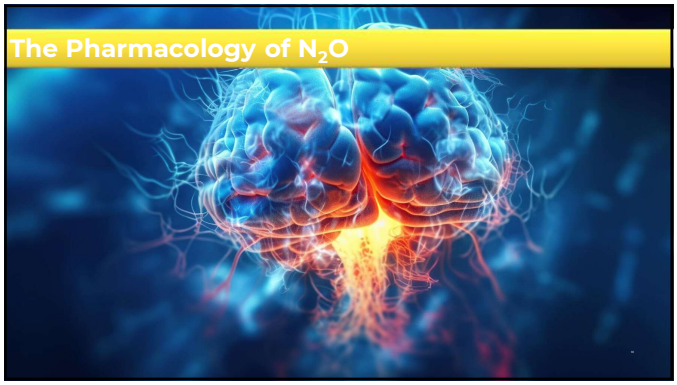
The Pharmacology of N_2O



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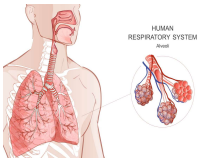
Pharmacokinetics

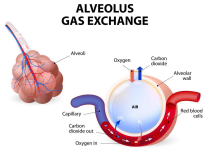
Absorption

- Absorbed in the respiratory tract
- Gas exchanged between alveoli and blood
- Uptake altered by pulmonary disease



Distribution

- Limited blood and tissue solubility
- Equilibrates quickly
- Diffusion hypoxia
  - N_2O fills alveolus
  - Limits oxygen



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Pharmacokinetics

Metabolism
- No metabolism
- Eliminated unchanged

Elimination
- Lungs as breath
  - Detected for hours
- Kidneys as urine
  - Detected for days
  - Produced by gram negative bacteria

Elimination Studies Summary
- N_2O breath concentrations dropped from 66-70% to 6-9% at 5 min and 2-4% at 30 min
- Elimination rate the same across ages
- Detected in breath over 2 hours after 5 min of 50% N_2O

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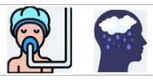
Mechanism of Action and Clinical Effects

Inhibits NMDA Receptor
- Anesthetic
- Antidepressant



Activates Opioid Receptors
- Analgesic

Activates GABA System
- Anti-anxiety

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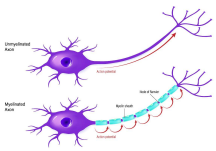
Pharmacodynamics

Recreational Effects
- Euphoria and dissociation
- Ataxia
- Impaired attention
- Hypoxia
- Loss of consciousness

Chronic Effects
- Paresthesia
- Muscle weakness
- Paralysis
- Gait unsteadiness
- Bladder and bowel disturbances



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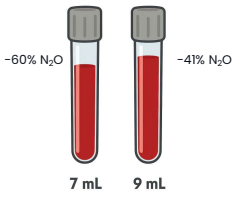
Sample Collection

Blood
- **Anticoagulant** preferred
  - Gray or lavender topped tubes
- Collect and submit **promptly**
- **Airtight**, glass containers preferred
- Designate one tube for testing
- **Limit headspace**

Alternative matrices
- Antemortem
  - Urine
  - Breath
- Postmortem
  - Lung
  - Liver
  - Brain



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Stability

Storage
- **Refrigerate** during short-term storage (<7 days)
- Ship cold
- **Freeze** during long-term storage

Repeat Testing
- **Not recommended** even when stored frozen
- **Significant decreases** in N_2O concentrations observed
- May be reported **qualitatively**

Case	Concentration (mcg/mL)	Days Elapsed Between Tests	Percent Change
1	58	3	-62%
	36		
2	25	19	-56%
	14		
3	53	3	-45%
	24		

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Testing

HS GC/MS

- Headspace gas chromatography/mass spectrometry
- Pure N_2O gas injected into headspace vials for controls
- Air injected onto the GC column
- GC separates the drugs present
- MS identifies each one

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N_2O and Traffic Safety

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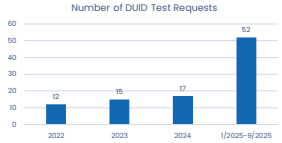
Traffic Safety

Trends

- Drug Recognition Expert (DRE) **inhalant opinions** increased between 2023 and 2024
- Toxicology **test requests** for N_2O are increasing
- N_2O **DUID reports** are increasing in the Netherlands and United Kingdom

Legal Status

- Most states prohibit **driving** while intoxicated by inhalants
- Several states have banned N_2O **misuse**
- Some states have also banned **possession**



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Controlled Studies

Psychomotor Impairment

- Memory
- Reaction time
- Processing speed
- Attention

Driving Impairment

- More driving errors following N_2O
- Turning
- Emergency braking

Highlights

- N_2O produces significant driving impairment
- Psychomotor impairment lasts approximately 5 minutes post-inhalation
- Driving impairment was detected up to 30 minutes post-inhalation

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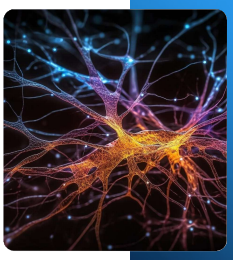
DRE Category

Inhalant
1,1-Difluoroethane (DFE), 1,1,1,2-Tetrafluoroethane (TFE)

Eye Exam
Horizontal gaze nystagmus (HGN), vertical gaze nystagmus (VGN), lack of convergence (LOC), normal pupil size, slow reaction to light

Physiology
Elevated body temperature, pulse, and blood pressure; normal or flaccid muscle tone

General
Confusion, disorientation, lack of muscle control, slurred speech, slow responses



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DUID Toxicology Testing

Basic DUID Panel
- Immunoassay screen

Compound	Reporting Limit	Compound	Reporting Limit
Amphetamines	20 ng/mL	Fentanyl/Acetyl Fentanyl	0.50 ng/mL
Benzodiazepines	20 ng/mL	Methamphetamine/MDMA	20 ng/mL
Buprenorphine/Metabolite	0.50 ng/mL	Opiates	20 ng/mL
Cannabinoids	10 ng/mL	Oxycodone/Oxymorphone	10 ng/mL
Carisoprodol/Metabolite	500 ng/mL	Phencyclidine	10 ng/mL
Cocaine/Metabolites	20 ng/mL	Tramadol/Metabolite	50 ng/mL
Zolpidem	5.0 ng/mL	Methadone/Metabolite	25 ng/mL

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DUID Toxicology Testing

Expanded DUID Panel

- Liquid Chromatography/Time of Flight-Mass Spectrometry (LC/TOF-MS)
- Prescription, Over-the-Counter (OTC), and illicit drugs

Included Drug Classes
Anticonvulsants
Carbamazepine, Gabapentin, Topiramate
Antidepressants
Bupropion, Citalopram/Escitalopram, Doxepin, Fluoxetine
OTC/Antihistamines
Chlorpheniramine, Dextro/Levo Methorphan, Hydroxyzine
Hallucinogens
LSD, Psilocin, Mescaline
Novel Psychoactive Substances
Etizolam, Flualprazolam, Carfentanil, Xylazine

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Driving Investigation 1

History	Toxicology
Background ❖ 25 years old ❖ Driver crashed into a parked car ❖ Witnesses stated: ➢ Driver was "unsteady on his feet and slurring his words" Observations ❖ Driver appeared dazed and confused ❖ Ignored officer instructions ❖ Hundreds of small chargers in vehicle ❖ Completed SFSTs with minimal infractions	❖ Blood was collected for testing approximately 80 mins after law enforcement (LE) arrived ❖ Comprehensive toxicology testing performed ➢ Basic and expanded panel ➢ N_2O = 16 mcg/mL

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Driving Investigation 2

History	Toxicology
Background ❖ 29 years old Observations ❖ Driver observed huffing N_2O in a parking lot ❖ Driver refused SFSTs	❖ Blood was collected for testing approximately 37 mins after LE arrived ❖ Comprehensive toxicology testing performed ➢ Basic panel ➢ N_2O = 6.0 mcg/mL

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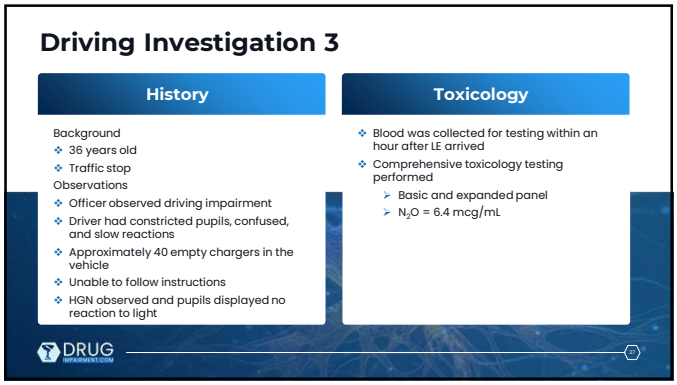
Driving Investigation 3
History
Background
36 years old
Traffic stop
Observations
Officer observed driving impairment
Driver had constricted pupils, confused, and slow reactions
Approximately 40 empty chargers in the vehicle
Unable to follow instructions
HGN observed and pupils displayed no reaction to light
Toxicology
Blood was collected for testing within an hour after LE arrived
Comprehensive toxicology testing performed
Basic and expanded panel
N_2O = 6.4 mcg/mL
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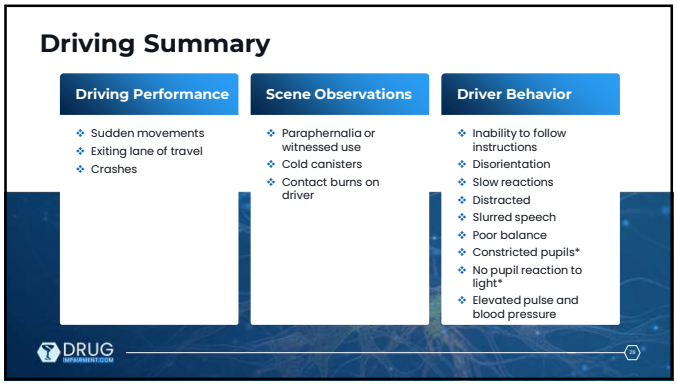
Driving Summary
Driving Performance
Sudden movements
Exiting lane of travel
Crashes
Scene Observations
Paraphernalia or witnessed use
Cold canisters
Contact burns on driver
Driver Behavior
Inability to follow instructions
Disorientation
Slow reactions
Distracted
Slurred speech
Poor balance
Constricted pupils*
No pupil reaction to light*
Elevated pulse and blood pressure
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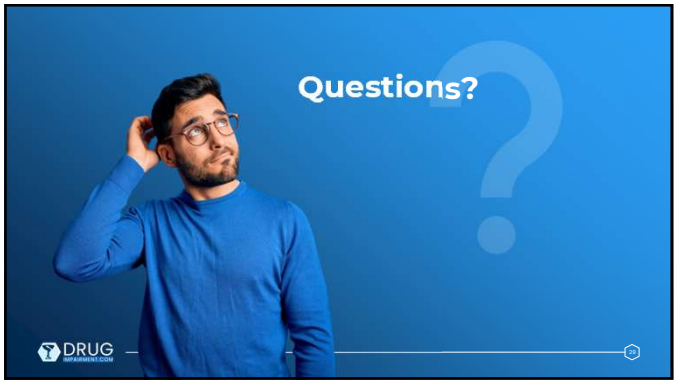
Questions?
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