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Brunei International Medical Journal
2026;22:31-34

Brunei International Medical Journal

Case Report

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Acquired Methaemoglobinaemia Following Inhalation of Alkyl Nitrites ("Super Rush")

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Abstract

Methaemoglobinaemia is a rare but potentially life-threatening cause of hypoxemia that may be overlooked in emergency settings. We report a case of acquired methaemoglobinaemia in a 36-year-old man following inhalation of an alkyl nitrite–containing recreational product ("Super Rush"). The patient presented with cyanosis and hypoxemia on pulse oximetry despite minimal symptoms and preserved arterial oxygen tension. Diagnosis was confirmed by co-oximetry demonstrating elevated methaemoglobin levels. Prompt treatment with intravenous methylene blue led to rapid clinical and biochemical improvement. This case highlights the importance of suspecting and recognising recreational inhalants as a cause of methaemoglobinaemia and the utility of co-oximetry in patients with unexplained cyanosis and a saturation gap.

Keywords: Methaemoglobinaemia; Alkyl nitrites; Poppers; Recreational drug toxicity; Cyanosis; Methylene blue

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INTRODUCTION

Methaemoglobinaemia is caused by oxidation of haemoglobin iron from the ferrous (Fe^{2+}) to ferric (Fe^{3+}) state, impairing oxygen delivery to tissues.[1] While congenital forms exist, most cases encountered in the emergency settings are acquired, resulting from exposure to oxidizing agents such as nitrates, nitrites, topical anaesthetics, and certain antibiotics. Recreational inhalation of alkyl nitrites ("poppers") is a well-recognised but underreported cause. We present a case of mild-to-moderate acquired methaemoglobinaemia due to inhalation of an alkyl nitrite product, with prompt reversal following methylene blue administration.

CASE REPORT

A 36-year-old man presented to the emergency department with bluish discolouration of his lips and fingertips noticed approximately 90 minutes earlier. He denied chest pain, shortness of breath, dizziness, palpitations, abdominal pain, nausea, vomiting, or weakness. Concerned after searching his symptoms online, he sought medical attention. He has no significant past medical history.

On further questioning, he disclosed recent inhalation of "Super Rush," a recreational product containing alkyl nitrites, used as an aphrodisiac. He had also ingested a small amount of a coffee supplement ("Candy B" containing Tadalfil which is a phosphodiesterase 5 (PDE5) inhibitor. He reported previous use of "Super Rush" resulting in discolouration of the fingers which had resolved spontaneously within few minutes and so he had never sought medical advice.

On examination, the patient was alert and speaking in full sentences, with mild perioral cyanosis. Finger discolouration had improved. He was not in respiratory distress. Vital signs were as follows: heart rate 128 beats/min (regular), blood pressure 143/85 mmHg, oxygen saturation of 87% on room air.

The arterial blood shown in **Figure 1** appeared dark brown in colour. Arterial blood gas (ABG) analysis (**Table I)** revealed methaemoglobinaemia.

A diagnosis of acquired methemoglobinemia was made. The patient was treated with intravenous 100 mg dose of methylene blue infused over 10 minutes (Methylthioninium chloride, Proveblue ®- 5mg/ml, PROVEPHARM).

Following treatment, his urine became bluish-green, consistent with expected methylene blue excretion (**Figure 2**).

Thirty minutes post-treatment, venous blood gas analysis showed reduction in methaemoglobin levels (**Table II**). Clinically, cyanosis resolved, and the oxygen saturation improved. VBG was done only to show that the methaemoglobin levels had decreased. Doing an ABG can be painful, time consuming and can have complications and therefore was not done.

The patient was observed for six hours. Repeat vital signs demonstrated heart rate 90 beats/min, blood pressure 130/85 mmHg, and oxygen saturation 97% on room air. He remained asymptomatic and was discharged with counselling to avoid recreational inhalants and oxidizing substances.

Figure 1: Dark brown arterial blood.

Table I : Arterial blood gas (ABG) showing increased levels of methaemoglobin.

ABG (Room air)	Values	Normal range
pH	7.41	7.35-7.45
PaCO2	43 mmHg	35-48 mmHg
PaO2	76.7 mmHg	75-100 mmHg
HCO3	26 mmol/l	22-28 mmol/l
Base excess	-2.4	-3.2-1.8
MethHB	> 6%	-
lactate	1.6	0.5-1.8 mmol/L
Glucose	7.7 mmol/L	4-6 mmol/L
SpO2	93%	96-100%

Figure 2: Bluish green urine post administration of methylene blue.

DISCUSSION

Methaemoglobinaemia is a rare disorder. Acquired forms are more common, mainly due to the exposure to substances that cause oxidation of the Hb both directly or indirectly. Inherited forms are due either to autosomal recessive variants in the CYB5R3 gene or to autosomal dominant variants in the globin genes, collectively known as HbM disease. [1,2]

Table II : Venous blood gas (VBG) analysis at 30 mins. After methylene blue administration.

VBG (Room air)	Values	Normal values
pH	7.39	7.35-7.45
PaCO2	51 mmHg	35-48 mmHg
Pa02	32 mmHg	75-100 mmHg
HCO3	27 mmol/l	22-28 mmol/L
Base excess	-5.7	-3.2-1.8
MethHB	0.9%	-
Lactate	1.8 mmol/L	0.5-2 mmol/L
Glucose	7.7 mmol/L	4-6 mmol/l
SpO2	59%	65 – 75%

This case illustrates a classic presentation of acquired methaemoglobinaemia caused by recreational inhalation of alkyl nitrites. Alkyl nitrites are potent oxidizing agents that convert haemoglobin iron into the ferric state, reducing oxygen delivery and producing cyanosis. Patients may appear less clinically distressed than expected for the degree of hypoxemia seen on pulse oximetry.

"Super rush" can be ingested or inhaled. Commonly referred to as "Poppers", manufacturers are packaging and labeling these products in a way that can mislead lead for recreational use, including sexual experience enhancement. Some common names are Rush, Super Rush, Jungle Juice, Locker Room, Sub-Zero and Iron Horse.

Poppers are often packaged in small bottles similar to energy shot beverage products and commonly sold online or in adult novelty stores, and are marketed as air fresheners, liquid incense, deodorizers, leather cleaners, cosmetics, solvents or nail polish removers.

Other medications or drugs that can cause acquired methaemoglobinaemia are summarised in **Table III**.[3-10]

A key diagnostic clue in methaemoglobinaemia is the "saturation gap": low oxygen saturation on pulse oximetry despite relatively preserved PaO_2 on arterial blood gas analysis. Pulse oximetry is unreliable in the presence of dyshaemoglobinemias. The characteristic chocolate-brown discoloration of blood further supports the diagnosis.

Treatment is indicated in symptomatic patients or when methaemoglobin levels exceed 20–30%, or at lower levels in those with cardiopulmonary disease.[11] Methylene blue acts as an artificial electron carrier, accelerating the reduction of methaemoglobin back to functional haemoglobin via the NADPH-dependent pathway.[12] Expected side effects include blue-green discolouration of urine and transient interference with pulse oximetry readings. Methylene blue is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency due to the risk of haemolysis.

Table III: Medications reported to cause methaemoglobinaemia.[3-10]

Drugs	Notes
Acetaminophen[3]	Acetaminophen overdose can cause MetHb.
Benzocaine[4]	Benzocaine is one of the most common causes of significant MetHb. Most serious cases involve use of topical sprays.
Dapsone[5]	Because of the long half-life of Dapsone, prolonged or repeated antidote treatment or exchange transfusion may be required.
Nitrites and nitrates[6] (amyl nitrite, silver nitrate, nitroglycerin, nitroprusside)	Environmental and industrial nitrites and nitrates are common inducers of MetHb; therapeutic nitrates can cause MetHb as well.
Phenazopyridine[5]	Common cause of MetHb in both children and adults. The resemblance to candy and sugar coating makes Phenazopyridine tablets attractive to children.
Prilocaine[7]	Prilocaine is the next most common local anaesthetic reported to cause MetHb (after benzocaine).
Primaquine[8]	Primaquine causes mild MetHb when used as an antimalarial but levels >30% can be occasionally seen.
Sulphonamides[9] (sulfadiazine, sulphanilamide, sulphapyridine, sulfasalazine)	Topical silver sulfadiazine dressings have been reported to cause MetHb. The sulphapyridine portion is responsible for MetHb seen with sulfasalazine.
Zopiclone[10]	Levels ranging from 10.4% to 23.8% have been reported following large overdoses of zopiclone.

Intravenous vitamin C, riboflavin, exchange transfusion, and hyperbaric oxygen treatment are second-line options for patients with severe methemoglobinemia whose condition does not respond to methylene blue or who cannot be treated with methylene blue such as those with glucose-6-phosphate dehydrogenase (G6PD) deficiency.[11,12]

This case also highlights the importance of taking a detailed exposure history, including recreational substances marketed as room deodorizers, leather cleaners, or aphrodisiacs. Public awareness of the potential toxicity of alkyl nitrites remains limited, and patients may not initially disclose their use unless specifically asked.

CONCLUSION

Acquired methaemoglobinaemia should be suspected in patients presenting with unexplained cyanosis and hypoxemia with preserved arterial oxygen tension. Recreational alkyl nitrite inhalation is an important and potentially overlooked cause. Prompt recognition and treatment with methylene blue result in rapid clinical improvement and favourable outcomes. Public should be made aware of the risks of "Super rush" and other similar products.

Take Home Message

- Methaemoglobinaemia is a rare but potentially life-threatening cause of hypoxemia, and can be missed.
- In most cases, it is acquired and associated with many medicinal products.
- Treatment is with methylene blue.
- It is important to be aware and consider methaemoglobinaemia in patient presenting with cyanosis and hypoxia..

Abbreviations

PDE	Phosphodiesterase 5
ABG	Arterial blood gas
VBG	Venous blood gas
PaO2	Partial arterial oxygen
NADPH	Nicotinamide adenine dinucleotide phosphate

Declarations

All the authors declared no competing interests.

Patient Consent

Written consent was obtained from all patients for publications of the clinical details and accompanying images.

Acknowledgement

We would to acknowledge the assistance provided by Dr Biju Benjamin with guidance and preparation of the manuscript.

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