CASE REPORT / PRIKAZ SLUČAJA

# WHEN OXYGEN LIES: A CASE OF HIDDEN METHEMOGLOBINEMIA

## KADA KISIK ZAVARAVA: PRIKAZ SLUČAJA SKRIVENE METHEMOGLOBINEMIJE

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## Abstract

Acquired methemoglobinemia is a potentially life-threatening condition in which haemoglobin is oxidised into a form incapable of transporting oxygen. Recreational use of alkyl nitrites ("*poppers*") represents an under-recognised cause, particularly among young individuals without underlying comorbidities. We report a 30-year-old male who ingested 3,4-methylenedioxymethamphetamine (MDMA) and inhaled poppers, subsequently developing mild cyanosis, headache, and persistently reduced oxygen saturation unresponsive to supplemental oxygen. Co-oximetry demonstrated a methemoglobin level of 17.4 %. The patient remained circulatory stable, with headache as the sole symptom. Supportive management consisting of oxygen at 2 L/min and intravenous crystalloids was initiated, methylene blue was withheld. Serial measurements showed spontaneous improvement to 9.0 % at two hours and complete normalisation (1.2 %) at six hours. This case underscores the importance of targeted exposure history and early co-oximetry in patients with unexplained cyanosis or an oxygen saturation gap. It demonstrates that supportive therapy may be adequate in moderate methemoglobinemia.


**Key words:** 3,4-methylenedioxymethamphetamine (MDMA); alkyl nitrites; cyanosis; emergency medicine; methemoglobinemia; methylene blue


## Sažetak

Stečena methemoglobinemija potencijalno je životno ugrožavajuće stanje u kojem je željezo u hemoglobinu oksidirano u feri ($Fe^{3+}$) oblik, čime se narušava sposobnost vezanja kisika. Rekreativna uporaba alkil-nitrita ("*poppers*") predstavlja često zanemareni uzrok intoksikacije kod mladih i inače zdravih odraslih osoba. Prikazujemo slučaj 30-godišnjeg muškarca koji je nakon unosa 3,4-metilenedioksi-metamfetamina (MDMA-e) i inhalacije *poppers-a* razvio simptome blage cijanoze usana i nokatnih ploča i glavobolju te perzistentno nisku saturaciju unatoč oksigenoterapiji. Ko-oksimetrijom je utvrđena razina methemoglobina od 17.4 %. Bolesnik je bio hemodinamski stabilan, bez značajnih simptoma osim blage glavobolje. Primijenjena je isključivo potporna terapija, nadoknada kisika 2 L/min i intravenska infuzija kristaloida, a antidot (metilensko modrilo) nije bio primijenjen. Serijskim mjerenjem ko-oksimetrije zabilježeno je spontano smanjenje razine methemoglobina na 9,0 % unutar dva sata i normalizacija na 1,2 % nakon šest sati. Ovaj slučaj ističe važnost usmjerene anamneze izloženosti i ko-oksimetrije kod pacijenata s neobjašnjenom cijanozom, niskom saturacijom kisikom ($SaO_2$) te značajnim zjapom saturacije kisikom (engl. *oxygen saturation gap*), te pokazuje da potporna terapija može biti dovoljna u umjerenim oblicima methemoglobinemije.


**Ključne riječi:** 3,4-metilendioksimetamfetamin (MDMA); alkil-nitriti; cijanoza; hitna medicinska služba; methemoglobinemija; metilensko modrilo

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## Introduction

Methemoglobinemia occurs when haemoglobin is oxidised from its reduced state to a form incapable of transporting oxygen efficiently. This process also increases haemoglobin's affinity for oxygen, limiting its release to peripheral tissues (1). Acquired methemoglobinemia is most commonly associated with exposure to oxidising substances, including nitrites, nitrates, certain local anaesthetics, and select antimicrobial agents (1–6).

Recreational alkyl nitrites are inhaled compounds that produce brief vasodilatory and psychoactive effects due to rapid pulmonary uptake. High nitrite concentrations may exceed endogenous reductive capacity, leading to methemoglobin accumulation (2). Clinical manifestations range from minimal symptoms and mucocutaneous discolouration to significant impairment of oxygen delivery Although 3,4-methylenedioxymethamphetamine (MDMA) has rarely been associated with methemoglobinemia, alkyl nitrites are the primary causative agent in most reported cases (7).

Standard pulse oximeters frequently yield artefactual low oxygen saturation readings because methemoglobin alters light absorption. Consequently, pulse oximetry alone cannot reliably identify the condition. Co-oximetry, which quantifies individual haemoglobin species, remains the diagnostic gold standard (8).

**Standard pulse oximeters often show falsely low oxygen saturation in methemoglobinemia because methemoglobin changes light absorption, making pulse oximetry alone unreliable for diagnosis.**

Current haematology and toxicology guidelines recommend early measurement of methemoglobin levels in patients presenting with unexplained cyanosis or a saturation gap. Supportive care is usually sufficient for mild to moderate elevations, while methylene blue is reserved for symptomatic patients or those with substantially higher levels (1). American Heart Association recommendations follow similar principles but emphasise caution in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, in which methylene blue may induce haemolysis (3).

## Case presentation

A 30-year-old man with no known medical history presented to the emergency department with head pressure and bluish discolouration of the lips and nail beds. He denied chest pain, dyspnea, dizziness, palpitations, or syncope. He reported ingesting two MDMA tablets approximately twelve hours before presentation and intermittently inhaling poppers throughout the evening, including immediately before symptom onset.

On room air, vital signs were as follows: blood pressure 125/78 mmHg, heart rate 88 beats/min, respiratory rate 16 breaths/min, temperature 36.8 °C, and oxygen saturation ($SaO_2$) 92 %. Physical examination revealed mild cyanosis without respiratory di stress. Cardiovascular, respiratory, and neurological examinations were unremarkable (Glasgow Coma Scale score of 15).

Arterial blood gas analysis with co-oximetry showed a $PaO_2$ of 95 mmHg and a methemoglobin level of 17.4 %. CT head showed no acute pathology; an incidental orbital mass adjacent to the medial rectus muscle was noted.

Given the moderate elevation in methemoglobin and the absence of significant symptoms, conservative management was pursued. At a methemoglobin level of 17.4 %, in the absence of cardiopulmonary or neurological compromise, current recommendations support observation and supportive care rather than methylene blue administration. The patient improved steadily with supportive care. After six hours, cyanosis had resolved, the headache had subsided, and room-air oxygen saturation had increased to 98 %. He was discharged with instructions for outpatient follow-up, including further evaluation of the orbital lesion and repeat laboratory testing.

## Discussion

Small quantities of methemoglobin are continuously produced under physiological conditions but are normally reconverted to functional haemoglobin through efficient enzymatic pathways (1). When exposure to oxidising agents overwhelms these mechanisms, clinically significant methemoglobinemia develops. Numerous reports in emergency medicine underscore the importance of early identification to prevent progression to severe hypoxic injury (4,5).

Methemoglobin interferes with the light-absorption principles used by pulse oximeters, resulting in persistently low saturation readings despite adequate arterial oxygen tension. When cyanosis persists and no respiratory disease is evident, co-oximetry should be performed to quantify haemoglobin derivatives directly (7).

As methemoglobin levels increase, symptoms typically intensify. Minor elevations may be asymptomatic, whereas progressive increases can lead to cardiopulmonary strain, neurological impairment, or respiratory compromise. Markedly elevated levels may result in life-threatening hypoxic injury (7).

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Methylene blue accelerates the NADPH-dependent reduction of methemoglobin to functional haemoglobin and is indicated in patients with significant symptoms or high methemoglobin concentrations. In individuals with G6PD deficiency, methylene blue may precipitate haemolysis, necessitating alternative therapies such as high-dose ascorbic acid or exchange transfusion (1,2).

Supportive care alone is often sufficient in clinically stable patients with moderate methemoglobinemia, as demonstrated in this case. Once the offending agent is eliminated, methemoglobin levels generally decline predictably. When appropriate, clinicians should also provide brief harm-reduction counselling to reduce the risk of recurrent exposure (5,6).

## Conclusion

Although medications such as dapsone and local anaesthetics are well-recognised causes of methemoglobinemia, recreational substances including MDMA and alkyl nitrites represent an increasingly relevant but frequently overlooked aetiology. MDMA metabolism may generate oxidative intermediates, while alkyl nitrites exert a direct oxidising effect on haemoglobin iron. Combined use may increase the likelihood of clinically significant methemoglobinemia in individuals without underlying comorbidities (9–11).

This case underscores the importance of a thorough exposure history, awareness of pulse oximetry limitations, and early use of co-oximetry in evaluating unexplained cyanosis. In clinically stable patients with modest elevations, supportive therapy alone may be sufficient to achieve full recovery. Continued recreational use of these substances underscores the need for ongoing clinician awareness.

## References


1. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med. 1999;34(5):646-56. doi: 10.1016/s0196-0644(99)70167-8.
2. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. Medicine (Baltimore). 2004;83(5):265-273. doi: 10.1097/01.md.0000141096.00377.3f.
3. Curry S. Methemoglobinemia. Ann Emerg Med. 1982;11(4):214-21. doi: 10.1016/s0196-0644(82)80502-7.
4. Sonck E, Bourmanne E, Bruteyn J, Dolip W. Methemoglobinemia due to use of poppers: a case report. J Med Case Rep. 2022;16(1):244. doi: 10.1186/s13256-022-03475-8.
5. Skold A, Cosco DL, Klein R. Methemoglobinemia: pathogenesis, diagnosis, and management. South Med J. 2011;104(11):757-61. doi: 10.1097/SMJ.0b013e318232139f.
6. Barker SJ, Tremper KK, Hyatt J. Effects of methemoglobinemia on pulse oximetry and mixed venous oximetry. Anesthesiology. 1989;70(1):112-7. doi: 10.1097/00000542-198901000-00021.
7. Verhaert LL. Methaemoglobinemia Induced by MDMA? Case Rep Pulmonol. 2011;2011:494328. doi: 10.1155/2011/494328.
8. Valenzuela M, Phan T, Samones E, Dukes WS. Do Not Drink Poppers: A Case Report of Near Fatal Methemoglobinemia After Ingestion of Alkyl Nitrite. Cureus. 2025;17(1):e77190. doi: 10.7759/cureus.77190.
9. Umbreit J. Methemoglobin--it's not just blue: a concise review. Am J Hematol. 2007;82(2):134-44. doi: 10.1002/ajh.20738.
10. Hunter L, Gordge L, Dargan PI, Wood DM. Methaemoglobinaemia associated with the use of cocaine and volatile nitrites as recreational drugs: a review. Br J Clin Pharmacol. 2011;72(1):18-26. doi: 10.1111/j.1365-2125.2011.03950.x.
11. Carvalho M, Carmo H, Costa VM, Capela JP, Pontes H, Remião F et al. Toxicity of amphetamines: an update. Arch Toxicol. 2012;86(8):1167-231. doi: 10.1007/s00204-012-0815-5.