

## Blue Treatment for Blue Patient

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### Abstract

Cyanosis is a clinical sign indicates lack of tissue oxygenation due to various causes. Methemoglobinemia is one of those causes due to oxidation of iron moiety of haem in haemoglobin, making it a lesser oxygen carrier to tissue. Various drugs, gases and substances can produce oxidative stress upon a genetically predisposed or a normal individual, converting haemoglobin to methaemoglobin and cause varying degree of cyanosis. Prompt identification and proper antidote can save patient's life and decreases need for unnecessary invasive ventilatory support and complications.

**Keywords:** Cyanosis; Methemoglobinemia; Methylene blue

### Introduction

Methaemoglobin is an abnormal form of haemoglobin where iron moiety present in a "Haem" is oxidized [Ferrous ( $Fe^{2+}$ ) to Ferric ( $Fe^{3+}$ ) iron] and oxygen carrying capacity is reduced several times than the normal one. In our body there is constant transformation of methaemoglobin to haemoglobin by enzyme NADH cytochrome b5 reductase [1]. Individuals who are genetically deficient of NADH cytochrome b5 reductase or sometimes toxic exposure to substances like aniline, nitrobenzene, nitrite pesticides in normal individual can cause methemoglobinemia [2]. Clinical signs and symptoms vary due to level of exposure genetic susceptibility and level of methemoglobinemia. The common presenting sign is cyanosis and symptom is breathlessness with varying degree of altered sensorium, which indicates marked tissue hypoxia [1]. Antidote available for methemoglobinemia is Methylene blue, which makes reversal of methaemoglobin to normal haemoglobin and recovery from clinical manifestations [3]. Presenting a case of such scenario, where patient was successfully treated and discharged after full recovery due to early suspicion, detection and proper antidote administration in the emergency department.

### Case Report

A 27-year-old male was brought to Emergency Department with altered sensorium, cyanosis and 2 episodes of vomiting. His relatives gave a history of unknown substance intake few hours back. He was found lying on the floor in his room and vomit by the side. He was immediately shifted to the hospital.

On examination, his airway was patent, respiratory rate was 18/min, oxygen saturation of 74% (on room air) with clear chest on auscultation, pulse rate 122/min, and BP 98/52 mm of Hg. His Glasgow coma scale was E3V4M5. Pupils were normal sized, reacting to light. The blood sugar was 130 mg/dl and cyanosis was seen over tip of tongue and lips (Figure 1).



**Figure 1:** Cyanosis was seen over tip of tongue and lips.



**Figure 2:** Blood drawn for investigation was chocolate brown in colour.

He was started on high flow 100% oxygen via non-rebreather mask but patient's oxygen saturation didn't improve. His oxygen saturation

continued to fall. Decision for endotracheal intubation and mechanical ventilatory support were made. In the meantime, two wide bore intravenous cannula were put and 1 liter of normal saline bolus given. His blood drawn for investigation was chocolate brown in colour (Figure 2). Bedside chest X-ray and ECG were done, chest X-ray was normal (Figure 3) and ECG showed sinus tachycardia (Figure 4).

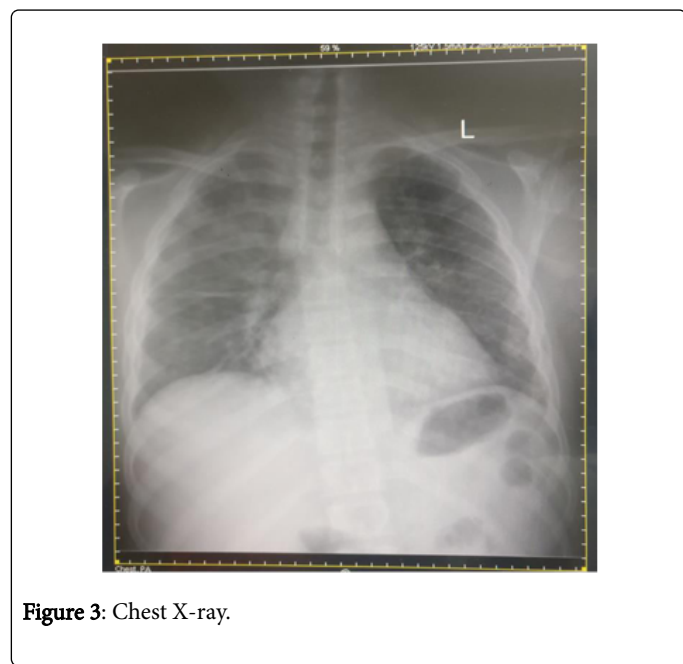


Figure 3: Chest X-ray.

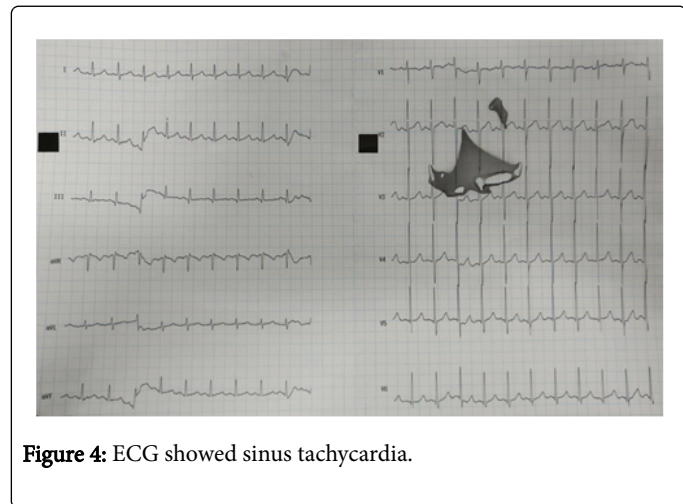


Figure 4: ECG showed sinus tachycardia.

On clinical ground, we suspected methemoglobinemia and venous blood gas analysis showed high methaemoglobin level of 48% and increased lactate level (7.9 mmol/L), confirmed our diagnosis. So, we deferred endotracheal intubation and he was treated with intravenous methylene blue (1%) at 1 mg/kg and dextrose containing intravenous fluid. Over one hour the condition of patient improved significantly (heart rate 110/min, BP 110/68 mm of Hg, GCS E4V5M6). The oxygen saturation improved to 90% and cyanosis disappeared. Subsequent blood gas analysis showed decrease in methaemoglobin level to 4%. He was admitted and later on discharged with non-traceable methaemoglobin level on blood gas analysis.

Though we couldn't identify the culprit substance as it could not be recovered but early suspicion and timely management with proper antidote saved the patient's life.

## Discussion

Normal methaemoglobin concentration in blood is 0% to 2%, different concentration in body leads to various clinical features [4] (Table 1).

Clinical features	
10-15%	Cyanosis
20-40%	Headache, dyspnoea, chest pain, tachypnoea, tachycardia
Above 40%	Confusion, lethargy, metabolic acidosis, coma, seizures, dysrhythmia and hypertension
Above 50%	Fatal and leads to death

Table 1: Clinical features in varying concentration of methaemoglobin in blood.

Clues for diagnosis are a history of ingestion of compound, central cyanosis with no apparent respiratory distress, and low pulse oximeter (observed) oxygen saturation with normal ABG (calculated) oxygen saturation and persisting cyanosis on oxygen therapy, without cardiopulmonary disease. Recurrent methemoglobinemia is defined by persistence of significant levels up to 72-96 hours. Bedside detection can be made by observing for colour change after placing few drops of blood on white filter paper where deoxyhaemoglobin brighten and methaemoglobin holds colour [5]. Methemoglobinemia leads to decrease cutaneous pulse oximetry estimation of oxygen saturation. All the patients with symptomatic methemoglobinemia require careful observation and monitoring until symptoms subside or level falls below 15% [6]. The antidote for the methemoglobinemia is Methylene blue, which is an exogenous cofactor that donates electron which rapidly reduces methaemoglobin to ferrous state through NADPH dependent methaemoglobin reductase system. 1-2 mg/kg (up to 50 mg) Intravenous as a 1% solution over 5 minutes is the desired doses, which can be repeated in 1 hour, if necessary. Mostly the response is seen within 1 hour of administration. It reduces the elimination half-life of methemoglobinemia to 45-90 minutes. Bluish green colored urine is seen after methylene blue administration which is leucomethylene blue, excreted primarily in the urine (Figure 5), sometimes they are excreted unchanged in the urine [7]. Repeat methaemoglobin levels should be checked after 1 hour and if required repeat dose may be given. Methylene blue is known to cause erroneous SpO<sub>2</sub> levels and the antidote is toxic at doses more than 7 mg/kg. It is contraindicated in G6PD deficiency patients. Ascorbic acid is an antioxidant, free radical scavenger that may be administered at doses of 0.5-1 gm 8th hourly. Dextrose should be administered as it's the major source of NADH in the erythrocyte. Exchange transfusion and hyperbaric oxygen therapy are usually reserved for refractory cases [4]. This case had many manifestations of methemoglobinemia like central cyanosis, altered mentation, persisting cyanosis on oxygen therapy. Diagnosis was confirmed by raised methaemoglobin level. His methaemoglobin level was 48% and he had complications. Early recognition, availability of methylene blue and quick administration lead to uncomplicated outcome.



**Figure 5:** Bluish green colored urine is seen after methylene blue administration which is leucomethylene blue, excreted primarily in the urine.

exposure to culprit agents sometimes easily clenches the diagnosis. But where history is unknown, clinicians should make a suspicion of methemoglobinemia and subsequent blood tests and prompt diagnosis with treatment by proper antidote can reduce chances of complications and unnecessary use of mechanical ventilatory support.

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### Conclusion

Methemoglobinemia is not an uncommon presentation in emergency, clinical features and positive correlation with history of