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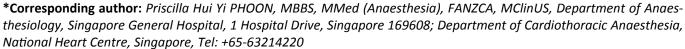


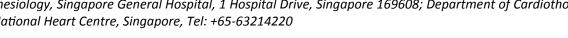
**CASE REPORT** 

# Low Saturation Readings in a Patient with Congenital Methemoglobinemia Exposed to Patent Blue Dye: A Case Report

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#### **Abstract**

Pulse oximetry is widely used perioperatively to detect respiratory events. Abnormal haemoglobins such as methemoglobin can result in inaccurate readings. Here we present the clinical challenges of managing a patient with congenital methemoglobinemia who went for surgery involving injection of patent blue dye and subsequently had a prolonged duration of poor saturation readings post-operatively. Differentials include desaturation due to respiratory causes. worsening of methemoglobinemia and delayed excretion of patent blue dye.

## Introduction

Pulse oximetry monitoring is standard of care in the peri-operative period to detect respiratory failure. Here we present a case of a patient with congenital methemoglobinemia who underwent bilateral mastectomy with sentinel lymph node sampling involving injection of patent blue dye and subsequently developed low saturation readings for over 48 hours. The patient has provided written informed consent for this case report to be published.

## Description

A 46-year-old female (height 165 cm, weight 62 kg, body mass index 22.8 kg/m<sup>2</sup>) presented for bilateral skin-sparing mastectomy, sentinel lymph node biopsy and breast tissue expander reconstruction after being diagnosed with bilateral invasive lobular breast carcinoma. She had a history of congenital methemoglobinemia with a resting peripheral blood oxygen saturation level (SpO<sub>2</sub>) of 92-93% on room air. Baseline methemoglobin levels were not available. Aside from a greyish hue appearance, she was otherwise asymptomatic with good exercise tolerance. Preoperative hemoglobin level was 14.7 g/dL.

General anesthesia was induced with intravenous propofol 100 mg, rocuronium 30 mg, dexamethasone 8 mg and target controlled infusion (TCI) of remifentanil at an effect-site concentration (Ce) of 3 ng/ml. Following endotracheal intubation, anesthesia was maintained with desflurane and TCI remifertanil at a Ce of 1-2 ng/ ml. Intravenous cefazolin 2 g was given prior to surgical incision for antibiotic prophylaxis with repeated 1 g dosing every 4 hours. An intra-arterial line was inserted to facilitate hemodynamic monitoring and repeated arterial blood gas (ABG) analysis. Baseline methemoglobin level sent off at the start of surgery was 21.7% (normal range: 0-1.5%). Due to the chronicity and asymptomatic nature of the underlying condition, it was elected not to treat the methemoglobinemia with methylene blue.

The patient tolerated induction of anesthesia well with stable hemodynamics and a SpO, of 94-96% on a fraction of inspired oxygen (FiO<sub>2</sub>) of 50%. However, 10 minutes after 2.5% patent blue V dye (Guerbet, B.P. 57400, Roissy, France) 1.5 ml had been injected subareolarly and subdermally on each side for sentinel lymph



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node mapping, there was a gradual fall in SpO<sub>2</sub> to 90% with no concomitant changes in ventilator settings, hemodynamics or disconnection and leaks from the ventilator circuitry. A corresponding ABG analysis was essentially normal (pH 7.44, PaO<sub>2</sub> 298 mmHg, PaCO<sub>2</sub> 35.4 mmHg, base excess 0 mmol/L, hemoglobin 12.9 g/dL). An hour later, greenish blue urine was noted in the urinary catheter with gradual improvement of SpO<sub>2</sub> to 93-95%. A bluish discoloration of the patient's face was noted at the end of the 7-hour surgical procedure. She was extubated successfully and maintained a SpO<sub>2</sub> of 92-95% on supplemental 2-liters of oxygen per min (L/min) via nasal cannula. Subsequently she was sent to the high dependency ward for overnight monitoring.

Two hours after completion of surgery, there was a drop in the patient's SpO<sub>3</sub> to 87% on supplemental oxygen of 2 L/min, which triggered emergency consults with both the critical care and hematology teams. Upon review, the patient was otherwise asymptomatic, alert and not in any respiratory or hemodynamic distress. An ABG analysis done when the patient was placed on a non-rebreather mask showed the following: pH 7.39, PaO, 312 mmHg, PaCO, 34.3 mmHg, base excess -3.6 mmol/L, hemoglobin 13.9 g/dL. A lung examination and chest radiograph were otherwise unremarkable. Despite the escalation in oxygen therapy with a corresponding increase in PaO, levels, there were no changes in the patient's SpO<sub>2</sub> values. A methemoglobin level done during this period was 20.1%. In addition, she was screened for and found not to be glucose-6-phosphate dehydrogenase (G6PD) deficient. Since the difference in methemoglobin levels was not significant, the cause of the patient's falsely decreased SpO<sub>2</sub> values was attributed to the intraoperative use of patent blue dye. Methylene blue was not given.

The patient was monitored in the high dependency unit for another 2 days and weaned to supplemental oxygen of 2 L/min with normal PaO<sub>2</sub> levels though her SpO<sub>2</sub> values persisted between 80-87%. Her methemoglobin levels fell slightly to 19% on the first post-operative day. Over the next 4 days, her SpO<sub>2</sub> values gradually improved back to baseline and she was discharged well. She was admitted 2 months later for a latissimus dorsi flap surgery where she maintained saturations of 90-92% perioperatively. She did not receive any patent blue dye in this surgery and had an uneventful recovery.

### **Discussion**

Congenital methemoglobinemia is an uncommon condition, resulting from reduced enzymatic reduction of methemoglobin back to ferrohemoglobin. Methemoglobin is unable to reversibly bind oxygen and the oxygen affinity of the other ferrous hemes in the hemoglobin tetramer is increased. The most common cause of congenital methemoglobinemia is cytochrome b5 reductase deficiency, an autosomal recessive disorder which prevents transfer of electrons from reduced nic-

otinamide adenine dinucleotide (NADH) to cytochrome b5. Most of these patients have Type I disease where the defect is limited to red blood cells and patients are relatively asymptomatic [1]. In type II disease, the deficiency is present in all cells and patients have more serious sequelae such as severe developmental abnormalities and early mortality. The first-line treatment for methemoglobinemia is methylene blue and is usually considered when levels are above 20% with symptoms or above 30% without symptoms. Exchange transfusion can be considered in cases where methylene blue is ineffective or contraindicated e.g. in G6PD-deficiency where it causes hemolysis [2].

In our patient, we do not have a definitive etiology although given the family history and clinical presentation, it is likely that she had type I cytochrome b5 reductase deficiency. She was asymptomatic other than cyanosis noted at birth and has a younger sister with the same condition. She also had a previous uneventful pregnancy.

The principle of pulse oximetry is based on the absorption of light at wavelengths of 660 nm and 880 nm. Dyes such as methylene blue and patent blue absorb light at wavelengths similar to that of deoxyhemoglobin [3]. Patent blue dye absorbs light at wavelengths between 635 to 640 nm [4]. Hence, increased light absorption in this region by these dyes may be interpreted by the pulse oximeter as deoxyhemoglobin, which can result in a falsely low oxygen saturation level.

Patent blue dye is absorbed by lymphatic vessels after intradermal or intraparenchymal injection. It binds to albumin and is excreted in both the urine and bile [5]. The extent and duration of interference with peripheral pulse oximetry is largely determined by its dose and excretion rate from the systemic circulation [6]. Mammary parenchymal injection of patent blue dye has been found to decrease SpO<sub>2</sub> readings by up to 11% (average 5%) after 15 to 30 minutes [7].

To date, there has been conflicting data as to whether the use of patent blue dye results in methemoglobinemia [4]. False-positive results have been reported mainly due to the use of co-oximetry in various studies [8]. Co-oximetry measures methemoglobin at wavelengths near 635 nm, hence the presence of patent blue dye could lead to an overestimation of methemoglobin levels by up to 56% [9]. In this case, we did not find any significant increase in methemoglobin levels after administration of patent blue dye when the same blood gas analyzer (Cobas b221, Roche®) was used. Our patient did not receive any medications that are known triggers for methemoglobinemia.

We postulate that since the patient had received a large dose of patent blue dye for bilateral sentinel lymph node mapping, the combination of pre-existing methemoglobin together with patent blue dye, both of which absorbs light at wavelengths around 660 nm [10], contributed to excessively decrease her  $SpO_2$  levels for a prolonged period.

Studies have been published on the effects of patent blue dye on pulse oximetry readings [4-9] though there have been no reports on its use in patients with congenital methemoglobinemia. This case illustrates how patent blue dye can be a confounder for poor saturation readings in these patients and may also falsely depress readings for a prolonged period of time. Pulse co-oximetry technology is available and can help differentiate methemoglobinemia from true hypoxemia intraoperatively. Acute methemoglobinemia can then be treated with methylene blue. Unfortunately, it is likely that patent blue dye will also cause interference with pulse co-oximetry due to the similar wavelength absorption. Besides confirming arterial oxygen tension from an arterial blood gas sample, lactate levels may also be useful in identifying true tissue hypoxemia from severe methemoglobinemia.

## **Financial Disclosures**

None.

### **Conflicts of Interest**

None.

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