depression of cardiac output and, therefore, further deterioration of systemic oxygenation.

Changes in A-aD\text{O}_2 following therapeutic interventions or clinical occurrences that could alter any of the other variables affecting A-aD\text{O}_2 should not be attributed to intrapulmonary shunting unless all of the other variables have been measured. Investigations that equate changes in arterial oxygenation with improvement or deterioration of pulmonary function must be interpreted with caution and in context with other factors that may modify these values.

The authors thank the nurses and technicians of the Surgical Intensive Care Unit for their cooperation, Robert Fuchs for statistical consultation, Ms. Diana Kosman for editorial assistance, and Jerome H. Modell, M.D., for his suggestions.

REFERENCES


Sulfhemoglobinemia and Methemoglobinemia—Uncommon Causes of Cyanosis

C. R. SCHMITTER, JR., M.D.*

Cyanosis has long been stressed as a sign of inadequate oxygenation. The alert anesthetist observing cyanosis immediately makes diligent efforts to determine and correct the cause of the hypoxia. Occasionally cyanosis is produced by causes other than hypoxia, as the following case report illustrates.

REPORT OF A CASE

A 56-year-old white man was admitted for an esophagogastrectomy for carcinoma of the distal esophagus. Physical examination revealed "bronzed"
skin, emaciation from a 60-pound weight loss, and slight hemiparesis on the right from a cerebrovascular accident. The patient had been taking Norgesic (orphenadrine, aspirin, phenacetin and caffeine) and Fiorinal (butalbital, aspirin, phenacetin, and caffeine) for pain prior to admission, and was given Empirin #3 (codeine, aspirin, phenacetin and caffeine) in the hospital. Laboratory studies, chest x-ray and EKG disclosed no abnormality. Hemoglobin was 15.5 g/100 ml.

Following premedication with Innovar and atropine, anesthesia was induced with thiopental after oxygenation with 5 l/min O₂. Endotracheal intubation was accomplished with ease with succinylcholine, iv. Anesthesia was maintained with 1–1.5 per cent halothane, 3 l/min N₂O–2 l/min O₂, and d-tubocurarine. Blood pressure, pulse and electrocardiogram were monitored and were normal throughout the course of the anesthesia. When the abdominal incision was made, the blood from the subcutaneous tissues was very dark. N₂O was discontinued and anesthesia was maintained with 0.5 per cent halothane and 5 l/min O₂. Auscultation of the chest was performed to rule out endobronchial intubation. Breath sounds were present bilaterally. A radial-artery catheter was inserted and arterial blood gases obtained. The sample was described as appearing venous, but PaO₂ was 331 torr, PaCO₂ 28 torr, pH 7.49, saturation greater than 98.8 per cent, HCO₃⁻ 21 mEq/l, and total CO₂ 21.5 mEq/l. When a blood sample shaken in a syringe with 100 per cent O₂ failed to turn pink, methemoglobinemia was suspected and a sample of blood was sent for confirmation of the diagnosis. Methylene blue, 100 mg, was administered empirically iv, with no effect on the cyanosis. The laboratory reported that no methemoglobin was present, but that 7 per cent of the patient's hemoglobin was in the form of sulfolhemoglobin.

The remainder of the intraoperative and postoperative course was uneventful, and the patient was discharged—still cyanotic—2 weeks after operation. He was lost to follow-up.

**DISCUSSION**

While 5 g/100 ml of reduced hemoglobin must be present for cyanosis to be evident, only 1.5 g/100 ml of methemoglobin or 0.5 g/100 ml of sulfolhemoglobin suffice to produce cyanosis.¹ In the case described, approximately 1.1 g/100 ml of the patient's hemoglobin was sulfolhemoglobin, leaving 14.4 g/100 ml of normal hemoglobin for oxygen transport.

Methemoglobin results from oxidation of the iron of the hemoglobin molecule to the ferric state.¹,³ Methemoglobin is converted to hemoglobin by reducing enzymes associated with the hexose-monophosphate shunt in the erythrocytes.² This process can be enhanced by reducing agents such as ascorbic acid, glutathione, or methylene blue, the latter in doses of 1–2 mg/kg, which accelerate the normal erythrocyte reconversion mechanism.²,³ The structure of sulfolhemoglobin is unknown.¹,² Sulphohemoglobin can not be reconverted to hemoglobin; the only means of removal is erythrocyte destruction.¹,²

Neither methemoglobin or sulfolhemoglobin can effectively transport oxygen. These conditions produce symptoms when present to such an extent that the oxygen-carrying capacity of the blood is significantly impaired, usually at a level of 20 per cent of the total hemoglobin. Patients begin to complain of fatigue at this level.¹

While rare cases of congenital methemoglobinemia due to an enzymatic defect have been reported, most cases of methemoglobinemia and sulfolhemoglobinemia are related to medication.¹,³ Nitrites and nitrates commonly produce methemoglobinemia, while such drugs as sulfonamides, phenacetin, acetyl salicylic acid, and aniline may produce methemoglobinemia, sulfolhemoglobinemia or both.¹,³ Phenacetin appears to have been the cause of sulfolhemoglobinemia in the case reported.

The author thanks Robert Johnson, Ph.D., who performed the methemoglobin and sulfolhemoglobin determinations for the patient described.

**REFERENCES**