tect hemoglobin Köln primarily as if it were a mixture of COHb and HHb, somewhat more of the former.

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An Unexpected Finding with Pulse Oximetry in a Patient with Hemoglobin Köln

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THE hemoglobinopathies characterized by an unstable hemoglobin, an array of more than 100 similar disorders caused by mutations of the hemoglobin molecule, are inherited in an autosomal dominant pattern and produce hemoglobins that denature spontaneously.[1] Clinically, these patients present with hemolytic anemia, which can be exacerbated by oxidants or infection.[1,2] However, their clinical course usually is benign.[1,2] An important feature of these disorders is variation in the affinity of the abnormal hemoglobin for oxygen.[1–6] An unexpected finding during the care of a patient with hemoglobin Köln, one of the hemoglobinopathies characterized by an unstable hemoglobin, was artifactually low hemoglobin oxygen saturation (Sp_{O_2}) recorded by pulse oximetry. It was hypothesized that methemoglobinemia produced by autoxidation of the unstable hemoglobin was responsible for the falsely decreased Sp_{O_2} observed.

Case Report

A 42-yr-old man presented for a unilateral Caldwell-Luc procedure for chronic sinusitis. At 26 yr of age, spherocytosis and splenomegaly had been found. Although asymptomatic, he underwent a splenectomy under an uneventful general anesthetic. Three years later, the patient's father had a myocardial infarction and was hospitalized. Routine complete blood count revealed polycythemia with a paradoxically elevated reticulocyte count of 5% in the father. A hematology consultant found the father's blood to have an increased oxygen affinity. Hemoglobin electrophoresis subsequently revealed an abnormal band characteristic of hemoglobin Köln, and additional questioning revealed that the patient's father was born in Germany. Subsequently, the hematology consultant performed hemoglobin electrophoresis on the father's immediate family, and the patient was found to have 30% hemoglobin Köln. Since the time of the patient's initial diagnosis, a daughter was born and found to have hemoglobin Köln.

The patient was otherwise healthy. He did not smoke cigarettes, specifically denied dyspnea on exertion or other pulmonary symptoms, and played tennis regularly. At the time of the Caldwell-Luc procedure, he had not seen a hematologist for more than 10 yr. He took no medications and denied any allergies. On physical examination, he was 196 cm tall and weighed 83 kg. Blood pressure was

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110/80 mmHg, heart rate was 60 beats/min, respiratory rate was 16 breaths/min, and body temperature was normal.

The preoperative laboratory examination was notable for normal electrolytes, creatinine, glucose, and coagulation indices. The hemoglobin concentration was 13.7 g/100 ml with a hematocrit of 45%, the leukocyte count was 9,500/μl, and the platelet count was 312,000/μl. The mean corpuscular volume was 100 fL (normal 80–100), the mean corpuscular hemoglobin was 30 pg (normal 27–33), and the mean corpuscular hemoglobin concentration was 30% (normal 31–36). An arterial blood gas, drawn the evening before surgery with the patient breathing room air, disclosed: *p*H 7.44, Pa_{CO_2} 41 mmHg, and Pa_{O_2} 103 mmHg. Co-oximetry was not performed on the arterial blood sample. The chest x-ray and the electrocardiogram results were unremarkable.

Before the induction of general anesthesia, the patient was found by pulse oximetry (Nellcor N-100, Hayward, CA) to have an Sp_{O_2} of 89% on room air. Spontaneous breathing of 100% O_2 *via* the anesthesia mask and circuit increased the Sp_{O_2} to 92%. (Using the same pulse oximeter, the anesthesiologist, while breathing room air, was found to have an Sp_{O_2} of 97%.) Because the symptom-free cardiopulmonary state of the patient had not changed since the previous evening when the arterial blood gas was obtained, the anomalous Sp_{O_2} was attributed to the patient's hemoglobinopathy, and the decision was made to proceed with general anesthesia and surgery without additional studies. After preoxygenation, anesthesia was induced with thiopental and succinylcholine; after tracheal intubation, anesthesia was maintained with isoflurane in nitrous oxide and oxygen, fentanyl (2 μg/kg), and vecuronium. Intraoperatively, with ventilation controlled to an end-tidal carbon dioxide of 36 mmHg and with a fraction of inspired oxygen ($F_{I_{O_2}}$) of 33%, the pulse oximeter read 90%. After an uneventful operative course and emergence, while in the recovery room, a different pulse oximeter (Nellcor N-100) indicated an Sp_{O_2} of 91% while the patient was breathing humidified gas with $F_{I_{O_2}}$ = 40% *via* a face tent.

An arterial sample of blood was obtained from the patient several years after his sinus surgery. At that time, the Sp_{O_2} was 89% while breathing room air and 91% while breathing 100% O_2 through a mask. A representative arterial blood gas while breathing room air exhibited: *p*H 7.39, Pa_{CO_2} 46 mmHg, and Pa_{O_2} 101 mmHg. Co-oximetry with a seven-wavelength co-oximeter (Corning 2500, Ciba-Corning, Medfield, MA) indicated Sp_{O_2} of 84.9%, a carboxyhemoglobin level of 6.6%, and a methemoglobin level of 3.7%.

Discussion

Hemoglobin Köln is an unstable hemoglobin produced by a mutation whereby a valine is substituted for methionine at the 98th position of the β chain.[1] Like the other hemoglobinopathies associated with an unstable hemoglobin, hemoglobin Köln is inherited in an autosomal dominant pattern. However, the instability of the other hemoglobin molecules can be due to replacements, deletions, or insertions in either the α or the β chain.[1] The unstable hemoglobins generally are associated with some degree of hemolysis and a shifted hemoglobin dissociation curve due to either increased or decreased oxygen affinity.[1–6] Alterations in the cooperativity of the components of the hemoglobin tetramer also are described.[5] Sometimes methemoglobinemia can develop.[1] For the unstable hemoglobins with an increased oxygen affinity, such as hemoglobin Köln, the ongoing hemolysis is generally relatively well compensated, and a paradoxical reticulocytosis is observed.[3,5] Heinz bodies may be observed in a peripheral smear, particularly after splenectomy.[1] In general, the clinical course of patients with unstable hemoglobins is benign.[1] However, the association of gallstones with hemolytic disease makes this group of patients more likely to present for cholecystectomy.[1] Additionally, hemolysis can be increased by either oxidative drugs such as the sulfonamides or infection, and death has been reported following a common cold.[7] It may be that the presence of an unstable hemoglobin can contribute to perioperative morbidity given that several patients have died of thromboembolic complications following splenectomy.[6] The likely mechanism for these fatal thromboembolic events is the increased erythrocytosis and thrombocytosis that can accompany the removal of the spleen.

Using a pulse oximeter, we observed an unexpectedly low Sp_{O_2} in a patient with hemoglobin Köln who was without obvious pulmonary disease and who had a normal arterial oxygen tension. Hemoglobin Köln is one of the unstable hemoglobins with an increased oxygen affinity, and measured partial pressure at half saturation ranges from 17.6 to 23.0 mmHg.[3,5] This feature would lead to a prediction of an unexpectedly *elevated* Sp_{O_2} for a given arterial oxygen tension. However, the opposite was observed. Additionally, even with $F_{I_{O_2}}$ = 1.0, the pulse oximeter did not indicate an Sp_{O_2} greater than 92%. Consequently, some additional feature of hemoglobin Köln must be responsible for our observations.

Methemoglobinemia can confound pulse oximetry, producing both falsely increased and falsely decreased estimates of the true Sp_{O_2}.[8] Methemoglobinemia sometimes accompanies the hemoglobinopathies with unstable hemoglobin.[1] Hemoglobin Köln has shown a methemoglobin production rate that exceeds that of normal hemoglobin and other unstable hemoglobins.[9] Pulse oximeter readings obtained from dogs breathing 100% O_2 while methemoglobin levels were increased would indicate that this patient had a methemoglobin level of approximately 10% on the day of operation, if the pulse oximeter reading of 92% is to be accounted for on the basis of methemoglobinemia.[8] Therefore, the co-oximetry results are confounding and do not

support the hypothesis that methemoglobinemia is the etiology of this patient's unexpectedly low observed Sp_{O_2} with pulse oximetry. The pulse oximetry data[8] from dogs breathing 100% O_2 while methemoglobin levels were increased would predict a pulse oximeter reading in excess of 95% for a patient breathing 100% O_2 who has a methemoglobin level of 3.7%. Additionally, the carboxyhemoglobin level is excessive for a patient who does not smoke or have other features of his history compatible with carbon monoxide exposure. However, carboxyhemoglobin levels can be elevated in hemolytic disease, but reported carboxyhemoglobin levels are less than 3%.[10] Regardless of its source, carboxyhemoglobin would be expected to contribute to the Sp_{O_2} reading on the pulse oximeter almost to the same extent as oxyhemoglobin.[11] Therefore, the observation in this patient with hemoglobin Köln of an unexpectedly decreased Sp_{O_2} is probably the result of a difference in the absorption spectra of the mutated hemoglobin molecule when compared to that of normal hemoglobin. However, no data are available on the absorption spectra of hemoglobin Köln or the other unstable hemoglobins.

The inaccuracy of pulse oximetry for assessing Sp_{O_2} in patients with hemoglobin Köln is in contrast to the reported accuracy of pulse oximetry in patients with hemoglobin SS and SC.[12-13] Our explanation for this inaccuracy makes it difficult to anticipate the results from pulse oximetry in patients with other variants of the unstable hemoglobinopathies because a mutation involving a single amino acid has the capacity to affect the structure of deoxyhemoglobin, the hemoglobin oxygen dissociation curve, the stability of the hemoglobin molecule, and the absorption spectra of oxyhemoglobin.

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