Case Report

An unusual explanation for low oxygen saturation

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Pulse oximeters are now commonplace in modern medical practice, but we still need to be aware of their limitations. We present here a case of a 62-yr-old gentleman who underwent general anaesthesia for a recurrent parietal meningioma. He had received multiple general anaesthetics in the past. Persistent low pulse oximetry readings in the perioperative period, without any suggestion of respiratory compromise, led us to investigate him further and to discover a new, but benign, haemoglobinopathy.

Keywords: blood, haemoglobin; complications, oxygen desaturation; equipment, pulse oximeters; measurement techniques, oximeters

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The first pulse oximeter became commercially available in 1975.1 Anaesthetists soon realized the advantages to be gained through the use of the pulse oximeter: primarily as a patient monitoring tool and an aid to improving patient safety. Their use is now considered essential in modern anaesthetic practice.2 We report here a case of a patient undergoing general anaesthesia whose pulse oximetry readings were persistently low without any evidence to suggest respiratory pathology.

Case report

A 62-yr-old man presented for elective surgery for excision of a recurrent right parietal meningioma. The diagnosis was made in 1997 and a primary excision was performed. However, he underwent three further operations as a result of surgical complications: a total of four general anaesthetics in a 15 month period. The patient reported no anaesthetic complications during these. He was an ex-smoker with a history of well-controlled, mild, seasonal asthma. He denied any symptoms on enquiry of cardiovascular and respiratory systems and clinical examination was completely unremarkable. He was not cyanosed. A chest radiograph was normal as were all laboratory investigations.

In the anaesthetic room, standard monitoring was applied. On room air, the $\text{SpO}_2$ recorded a value of 90%; this value increased to 93% when oxygen was administered at 6 litre min$^{-1}$ via an MC facemask. The plethysmograph trace was of good quality and the values did not improve with either alteration of the probe site or change of the probe itself. The pulse oximeter had worked satisfactorily on another patient before this case and recorded normal values from members of the anaesthetic team. At this point, we reviewed the patient’s case notes, incorporating previous anaesthetic charts. The records stated the same puzzling problem with these comments: ‘referral to a respiratory physician may be worthwhile’ and ‘needs CXR’. The general anaesthesia had nevertheless proceeded otherwise uneventfully on all previous occasions and without any suggestion of detriment to the patient.

The decision was made to proceed with the procedure: the dilemma and anaesthetic technique were fully explained to the patient. A 20 gauge radial arterial cannula was inserted preinduction. Arterial blood gases were measured before induction and revealed the $\text{PaO}_2$ to be 11.79 kPa (Table 1). The patient was induced i.v. with a remifentanil infusion and bolus doses of propofol and atracurium, after

<table>
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<th>$F_{\text{IO}_2}$</th>
<th>$\text{SpO}_2$ (%)</th>
<th>$\text{SaO}_2$ (%)</th>
<th>$\text{PaO}_2$ (kPa)</th>
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<td>98</td>
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<td>99.6</td>
<td>54.8</td>
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<tr>
<td>0.94</td>
<td>92</td>
<td>99.7</td>
<td>64.28</td>
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preoxygenation. The airway was secured with a size 9.0
cuffed reinforced oral endotracheal tube. Anaesthesia was
maintained with a sevoflurane/air/oxygen mixture via a
circle breathing system, in addition to the remifentanil infu-
sion. The lungs were ventilated with a Datex Ohmeda AS/5
anaesthetic machine in pressure control mode.

The operation progressed for 3 h in total. Arterial blood
samples were obtained throughout at varying fractional
inspired concentrations of oxygen (Table 1). The results
are tabulated with the corresponding pulse oximetry
readings.

As the case proceeded, we began to suspect an undiag-
nosed haemoglobinopathy and we discussed this with a
haematology specialist registrar. Methaemoglobin levels
peaked at 0.7% during anaesthesia, well within the normal
range of 0–1.5%. There was no laboratory evidence of
haemolysis. Following discussion with the patient and
informed consent, mass spectrometry was performed on
the preoperative blood sample. The operation was com-
pleted uneventfully and he was discharged home on the
third postoperative day before the results being made
available.

Results
Adult human haemoglobin A has a molecular weight of
64 585 Da. On a simplified level, it consists of two pairs
of polypeptide chains: two α and two β chains. Each com-
bines with one haem group. Mass spectrometry undertaken
at a regional haematology laboratory revealed that 7% of
our patient’s haemoglobin alpha chains were abnormal, as
illustrated in Figure 1.

The smaller peak at 15 098.21 Da (28 Da lighter than the
normal alpha chain) is the abnormal chain. Further analysis
involved repeated mass spectrometry of smaller peptide
units after further enzymatic digestions. These processes
identified that the amino acid valine at position 62 in a
normal alpha chain had been substituted with alanine in the
abnormal alpha chain. It was subsequently confirmed by the
regional haematology laboratory that this amino acid substi-
tution had not been previously described. This was poten-
tially a novel haemoglobinopathy. Unfortunately, we were
unable to confirm this: the patient changed his general prac-
titioner and we were unable to obtain further blood samples
for DNA analysis for the National Haemoglobinopathy
Reference Laboratory. In addition, an international data-
base of haemoglobin variants has also confirmed that this
amino acid substitution has not previously been described,
but that, again, further laboratory analysis would be required
to register this as a novel haemoglobin variant.

Discussion
The limitations of pulse oximetry as a result of low per-
fusion states, motion artifacts, skin pigmentation, and nail
polish are well documented. Pulse oximetry may be uti-
lized safely in patients with thalassaemias and sickle cell
disease in the majority of situations, but it may under-
estimate true arterial oxygen saturation in critically ill
sickle cell patients and those suffering a sickling crisis.5
The problems resulting from other haemoglobinopathies
are less well recognized. Hundreds of structural haemo-
globin variants have been described. The majority
are the result of a single amino acid substitution in one of
the globin chains. Structural changes may produce an
array of pathophysiological consequences: haemolysis due
to instability of the molecule; polycythaemia due to
increased oxygen affinity; and cyanosis due to low oxygen
affinity or methaemoglobinaemia. Methaemoglobin is
the most frequent dyshaemoglobin resulting in cyanosis
and is well known to confound pulse oximetry as a result
of its absorption spectrum: in most cases, this is acquired
(e.g. prilocaine); congenital forms are rare.13 Some hae-
moglobinopathies labelled haemoglobin M (because they
resemble methaemoglobin to some degree) have differing
absorption spectra leading to inaccurate readings when
using pulse oximetry. Kuji and colleagues have previ-
ously described the anaesthetic management of a patient

![Fig 1](image_url)

Fig 1 Mass spectrometry of patient’s haemoglobin (mass vs percentage of total haemoglobin).
with haemoglobin $M_{\text{Hb}}$. The oxygenation of this dyshaemoglobin (which constitutes 30% of the total) is only 60% at $P_{\text{O}_2}$ of 13.3 kPa. Their patient was centrally cyanosed but asymptomatic. Arterial blood gas analysis revealed a $P_{\text{O}_2}$ of 11.2 kPa when breathing room air, but pulse oximetry was completely unreliable: they also depended upon co-oximetry. The anaesthetic course of their patient, as with ours, was uneventful.

Other haemoglobin variants have been described that have rendered pulse oximetry undependable. Gottschalk and Silverberg\textsuperscript{15} reported a patient with haemoglobin Köln. HbKöln itself actually exhibits increased oxygen affinity and is unstable resulting in haemolysis. Pulse oximetry was inaccurate: $S_b_{\text{O}_2}$ 89% on room air, $P_{\text{O}_2}$ 13.5 kPa from an arterial blood gas sample. Methaemoglobin levels were 3.7%, but the authors did not feel that this was high enough to explain the inaccuracy. They proposed that the haemoglobin variant most probably possessed abnormal absorption spectra.\textsuperscript{15} This was subsequently verified in another patient with HbKöln.\textsuperscript{16} In addition, the authors of other case reports of patients with HbHammersmith and HbCheverly (both unstable haemoglobins) have suggested that inaccurately low readings have precluded the use of pulse oximetry.\textsuperscript{17,18} Furthermore, what is more interesting is that HbHammersmith exists almost entirely in the oxidized form but, in contrast, HbCheverly has reduced affinity for oxygen. This would seem to add more weight to the argument that these unstable haemoglobins have abnormal absorptive spectra.\textsuperscript{18} But how do we begin to explain why CO-oximetry is able to provide a measure of what is thought to be the true arterial oxygen saturation?

Modern pulse oximeters rely on the principle of spectrophotometry, the basis of which is the Beer–Lambert law. An alteration in the quantity of oxygen bound to haemoglobin results in a change in the absorption of light by the molecule. There are a number of differences between how pulse oximeters and CO-oximeters calculate and produce an arterial oxygen saturation measurement. For example, CO-oximeters measure haemoglobin oxygen saturation by the same spectrophotometric principle as the pulse oximeter, but they use an in vitro technique rather than an in vivo technique to evaluate haemoglobin: it is analysed in solution (the sample is haemolysed) and only for the moment it is taken from the patient.\textsuperscript{19} More importantly, CO-oximeters utilize more than two wavelengths for analysis, affording the ability to measure additional haemoglobins, such as carboxyhaemoglobin, methaemoglobin, and sulphhaemoglobin. They also function primarily in the visible range of the electromagnetic spectrum—avoiding the near infrared (940 nm) wavelength adopted in pulse oximeters.\textsuperscript{19} It could be argued that the dyshaemoglobin identified in our patient may have a similar absorption spectrum to normal oxyhaemoglobin in the visible range and only differs at the 940 nm wavelength; therefore, the CO-oximeter was able to actually measure it.

In the clinical situation, the CO-oximeter reassured us, but the drawback of this technique is that it was not able to indicate how much of the haemoglobin was abnormal. The ability to measure haemoglobin variants depends on the calibrated absorption spectra of the particular machine. In addition, we have no way of measuring the degree of oxygen affinity a dyshaemoglobin possesses. This may have significant clinical implications in the perioperative period in terms of oxygen delivery, placing the patient at risk of tissue hypoxia. In addition to CO-oximetry, modern arterial blood gas analysers are also able to provide a direct measurement of $P_{\text{O}_2}$. In our patient, the normal $P_{\text{O}_2}$ values again reassured us, but this could be short-sighted. A normal $P_{\text{O}_2}$ does not signify normal oxygen transport capacity and in the context of a haemoglobinopathy with reduced oxygen affinity and where a large proportion of the patient’s haemoglobin is abnormal, this could again place the patient at risk of significant tissue hypoxia. Fortunately in this case, the dyshaemoglobin constituted only 7% of the total Hb.

To conclude, what have we learnt? We have revised some of the limitations of both pulse oximeters and CO-oximeters and have described how low pulse oximetry readings may be the result of a haemoglobinopathy. Through this, we have been informed of the presence of numerous haemoglobinopathies and their variable clinical significance. Ultimately, most haemoglobinopathies are benign and clinically inconsequential, but it must be remembered that some are associated with haemolysis, impaired oxygen binding, and secondary polycythaemia. In this case, we have been reassured that this potentially new haemoglobin variant has a benign pathology. One of the most pertinent issues when identifying a haemoglobinopathy is the counselling of the patient and subsequent family screening. Unfortunately, we were unable to commence this, but Bruns and colleagues\textsuperscript{20} have reasoned that pulse oximetry could easily be utilized to identify family members in these conditions where $S_b_{\text{O}_2}$ values are low. However, knowledge of this patient’s previously undiagnosed haemoglobinopathy may avoid future needless investigations, such as chest radiographs, and unnecessary referral to a physician. It may also limit the use of oxygen therapy, and avoid the unwarranted occupation of a post-operative bed in a higher dependency setting, thus ultimately reducing patient distress.

References
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