THE EFFECT OF DYSHEMOGLOBINS ON PULSE OXIMETRY: PART I, THEORETICAL APPROACH AND PART II, EXPERIMENTAL RESULTS USING AN IN VITRO TEST SYSTEM

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Reynolds KJ, Palayiwa E, Moyle JTB, Sykes MK, Hahn CEW. The effect of dyshemoglobins on pulse oximetry: part I, theoretical approach and part II, experimental results using an in vitro test system.

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ABSTRACT. Pulse oximeters are known to be inaccurate in the presence of elevated concentrations of carboxyhemoglobin and methemoglobin. This paper attempts to alleviate some of the confusion that exists between fractional and functional saturation, and to clarify the comparison of each with SpO_2. A series of theoretical relationships between pulse oximeter reading (SpO_2) and actual oxygen saturation (both fractional and functional) is derived using simple absorption theory. The theoretical relationships are checked using an experimental in vitro test system. This consists of a blood circuit containing a model finger, capable of simulating the pulsatile transmission signals through a real finger. Theoretical predictions and experimental results are compared and are found to agree well in the presence of carboxyhemoglobin, but less well with methemoglobin. Possible reasons are discussed.

KEY WORDS. Equipment: pulse oximeter. Complications: carboxyhemoglobinemia; methemoglobinemia.

Pulse oximetry has become widely accepted as a method of continuously monitoring arterial oxygen saturation in the operating room and the intensive care unit. The operation of the pulse oximeter is based on two physical principles: the different absorption spectra of reduced hemoglobin and oxyhemoglobin (HbO_2), and the pulsatile change in absorption of arterial blood. This pulsatile component is recorded by the pulse oximeter as an AC signal. The monitor works by measuring the pulsatile AC signals across perfused tissue at two discrete wavelengths, using the constant component of absorption (that due to everything except arterial blood) at each wavelength to normalize the signals. It then computes the ratio between these two normalized AC signals and relates this ratio to the arterial oxygen saturation using an empirical algorithm.

Since the pulse oximeter measures at two wavelengths, it can analyze a two-component system only. In other words, it can only distinguish reduced hemoglobin and HbO_2. Unfortunately, adult blood contains other species of hemoglobin, in particular, carboxyhemoglobin (HbCO) and methemoglobin (MetHb). Carboxyhemoglobin exists in varying degrees (approximately 10%) as a consequence of smoking and of urban pollution [1,2], but may occur in concentrations as high as 45% as a result of smoke inhalation [3]. Methemoglobin is formed when the heme ion in hemoglobin is oxidized from the ferrous to the ferric state by, for example, the use of drugs (e.g., nitrites and aniline) or by certain anesthetics (e.g., prilocaine, benzocaine) [4,5]. It can be found in concentrations up to approximately 70%, above which it can be fatal [6].

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Pulse oximeters are calibrated empirically using data obtained from healthy adult volunteers. These volunteers typically have low HbCO and MetHb values. Since both HbCO and MetHb absorb light at the two wavelengths used in pulse oximetry (660 and 940 nm), their presence will cause errors in the oxygen saturation value produced by the pulse oximeter (SpO_2). These dyshemoglobins are usually present in such small amounts that the errors can be ignored, but with increased concentrations of HbCO and MetHb, there is a distinct possibility of the pulse oximeter giving erroneous readings for the arterial oxygen saturation.

Historically, oxygen saturation was defined as oxygen content expressed as a percentage of oxygen capacity. Since HbCO and MetHb do not bind oxygen, this is effectively

$$SaO_2^{fu} = c_{HbO2}/(c_{Hb} + c_{HbO2}),$$

where c is the concentration of the hemoglobin species given in the subscript. This value is referred to as the functional oxygen saturation (SaO_2^{fu}). This must be differentiated from the fractional oxygen saturation (SaO_2^{fr}), or HbO_2 percentage, which takes account of the dyshemoglobins present; i.e.,

$$SaO_2^{fr} = c_{HbO2}/(c_{Hb} + c_{HbO2} + c_{HbCO} + c_{MetHb}).$$

For patients with low dyshemoglobin levels, the difference between fractional and functional saturation is very small. However, when the dyshemoglobin levels are elevated, the two values can vary greatly, and the pulse oximeter readings are unlikely to agree with either the true fractional or functional saturation values [7].

The aim of Part I of this paper is to investigate theoretically the effect of dyshemoglobins on the saturation recorded by the pulse oximeter. It is hoped that the theoretical treatment will help eliminate any confusion between the comparison of pulse oximeter reading with fractional or functional saturation in the presence of dyshemoglobins. The theoretical predictions are checked experimentally using an in vitro test system, and the results presented in Part II of the paper.

PART I: THEORETICAL EFFECT OF DYSHEMOGLOBINS ON PULSE OXIMETER SATURATIONS

To assess the oxygen saturation as measured by the pulse oximeter in the presence of dyshemoglobins of various concentrations, a simple mathematical relationship is derived based on the Beer-Lambert law. This law relates the optical density (OD) of an absorbing, nonscattering solution to the concentration of absorber by

$$OD = \log_{10}(I_0/I) = \epsilon cd$$

where I_0 and I are the incident and transmitted light intensities through a sample of depth (d), concentration (c), and having an extinction coefficient (ϵ). It is assumed, to a first approximation, that this law can be used to describe the change in optical density of a pulsating arterial bed.

For a solution containing n absorbers,

$$\text{total absorption} = \sum_{i=1}^{n} \epsilon_i c_i d_i.$$

Pulse oximeters measure the ratio between the normalized AC signals measured at two discrete wavelengths, 1 and 2. This ratio, β, will be

$$\beta = \frac{\sum_{i=1}^{n} \epsilon_{1i} c_i d_i}{\sum_{i=1}^{n} \epsilon_{2i} c_i d_i}. \quad (1)$$

The AC signals are a consequence of pulsatile arterial blood. If we assume blood contains two species of hemoglobin, oxygenated (subscript o) and reduced (subscript r), each occupying the same depth, then equation 1 becomes

$$\beta = \frac{\epsilon_{1o} c_o + \epsilon_{1r} c_r}{\epsilon_{2o} c_o + \epsilon_{2r} c_r}.$$

If we define the saturation of a hemoglobin species i as $S_i = (c_i/c)$, where c is the total hemoglobin concentration, then we have

$$\beta = \frac{S_r \epsilon_{1r} + S_o \epsilon_{1o}}{S_r \epsilon_{2r} + S_o \epsilon_{2o}}. \quad (2)$$

Now $S_r = 1 - S_o$. Substituting into equation 2 and rearranging gives

$$S_o = SpO_2 = \frac{\epsilon_{1r} - \beta \epsilon_{2r}}{\epsilon_{1r} - \epsilon_{1o} + \beta(\epsilon_{2o} - \epsilon_{2r})} \quad (3)$$

which is the theoretical calibration curve for the pulse oximeter. It should be remembered that SpO_2 is normally expressed as a percentage, and equation 3 should therefore be multiplied by 100.

If we now consider blood containing a dyshemoglobin (subscript x), in addition to reduced hemoglobin and HbO_2, equation 1 gives

$$\beta = \frac{S_r\epsilon_{1r} + S_o\epsilon_{1o} + S_x\epsilon_{1x}}{S_r\epsilon_{2r} + S_o\epsilon_{2o} + S_x\epsilon_{2x}}. \quad (4)$$

The pulse oximeter measures this ratio, and then uses its calibration curve, equation 3, to calculate a value for oxygen saturation. We can therefore obtain the saturation value given by the pulse oximeter by putting equation 4 into equation 3, which on arranging gives

$$SpO_2 = \frac{S_o + AS_x}{S_r + S_o + BS_x} \quad (5)$$

where $$A = \frac{\epsilon_{1r}\epsilon_{2x} - \epsilon_{2r}\epsilon_{1x}}{\epsilon_{1r}\epsilon_{2o} - \epsilon_{2r}\epsilon_{1o}}$$

and $$B = \frac{\epsilon_{2x}(\epsilon_{1r} - \epsilon_{1o}) - \epsilon_{1x}(\epsilon_{2r} - \epsilon_{2o})}{\epsilon_{1r}\epsilon_{2o} - \epsilon_{2r}\epsilon_{1o}}.$$

Now fractional saturation, SaO_2^{fr} is given by $SaO_2^{fr} = 1 - S_r - S_x$, whereas functional saturation is $SaO_2^{fu} = (1 - S_r - S_x)/(1 - S_x)$. These expressions in equation 5 give

$$SpO_2 = \frac{SaO_2^{fr} + AS_x}{1 + (B - 1)S_x} \quad (6)$$

and

$$SpO_2 = \frac{SaO_2^{fu}(1 - S_x) + AS_x}{1 + (B - 1)S_x}. \quad (7)$$

The wavelengths 1 and 2 used in pulse oximetry are typically 660 (red) and 940 (near infrared), respectively. Using the values obtained by van Assendelft [8] for the extinction coefficients of hemoglobin and its derivatives at these wavelengths, given in Table 1, to obtain A and B, we get

$$SpO_2 = \frac{SaO_2^{fr} - 0.062S_{HbCO}}{1 - 0.969S_{HbCO}}, \quad (8)$$

$$SpO_2 = \frac{SaO_2^{fu}(1 - S_{HbCO}) - 0.062S_{HbCO}}{1 - 0.969S_{HbCO}}, \quad (9)$$

$$SpO_2 = \frac{SaO_2^{fr} + 1.562S_{MetHb}}{1 + 1.419S_{MetHb}}, \quad (10)$$

and

$$SpO_2 = \frac{SaO_2^{fu}(1 - S_{MetHb}) + 1.562S_{MetHb}}{1 + 1.419S_{MetHb}}. \quad (11)$$

Table 1. Extinction Coefficients for Reduced hemoglobin, Oxygenated hemoglobin, Carboxyhemoglobin and Methemoglobin according to Van Assendelft [8]

	Hb	HbO_2	HbCO	MetHb
660	$\epsilon_{1r} = 0.80$	$\epsilon_{1o} = 0.08$	$\epsilon_{1c} = 0.07$	$\epsilon_{1m} = 0.81$
940	$\epsilon_{2r} = 0.20$	$\epsilon_{2o} = 0.30$	$\epsilon_{2c} = 0.00$	$\epsilon_{2m} = 0.64$

Values are given as liters per millimole per centimeter (L/mmoL/cm).

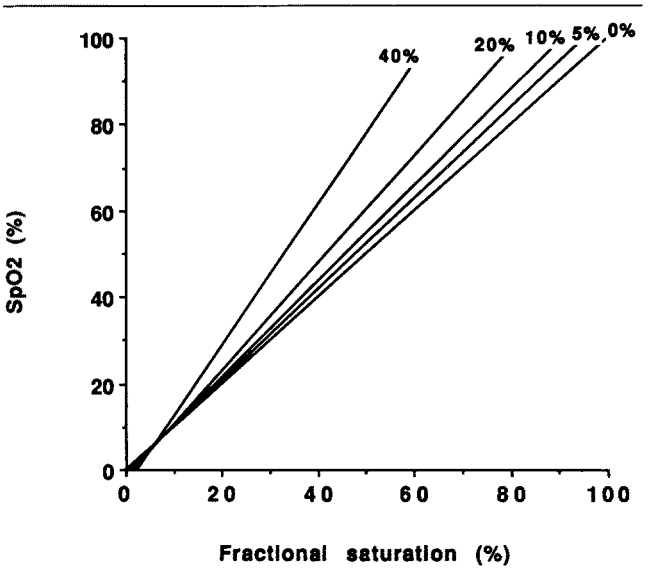

Fig 1. Pulse oximeter reading (SpO_2) compared with fractional saturation (SaO_2^{fr}) in the presence of various concentrations of HbCO, as predicted using the Beer-Lambert law and equation 8. Pulse oximeter wavelengths are 660 and 940.

These theoretical equations relate the pulse oximeter saturation, SpO_2, to the actual saturation (fractional or functional) in the presence of HbCO or MetHb. The relationships are plotted in Figs 1 to 4.

Discussion of Part I

Erroneous pulse oximeter readings have been reported on several occasions in the presence both of HbCO and of MetHb [9–12]. However, it has not always been made clear whether the word "saturation" refers to fractional or functional oxygen saturation. Kelleher, for example, in his comprehensive review of pulse oximetry [13], reported that in the presence of HbCO the pulse oximeter will give a value for saturation higher than the actual fractional saturation, and in the presence of MetHb the pulse oximeter will either underread or overread fractional saturation depending on the saturation of the blood. This is incorrect, since in the presence of MetHb, it is true only when compared with func-

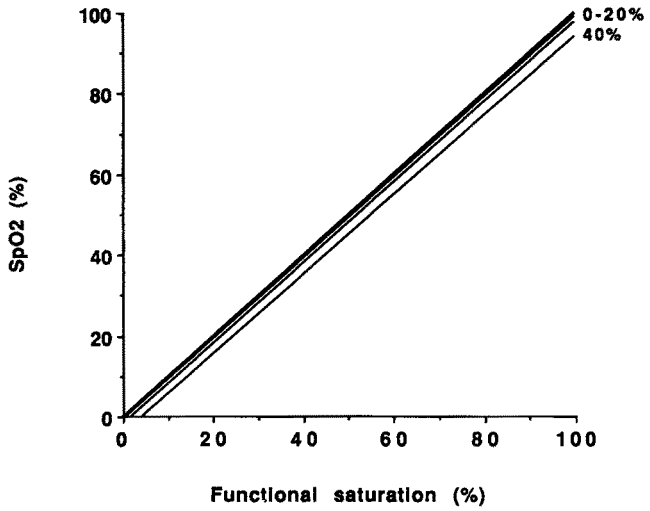

Fig 2. Pulse oximeter reading (SpO_2) compared with functional saturation (SaO_2^{fu}) in the presence of various concentrations of HbCO, as predicted using the Beer-Lambert law and equation 9. Pulse oximeter wavelengths are 660 and 940.

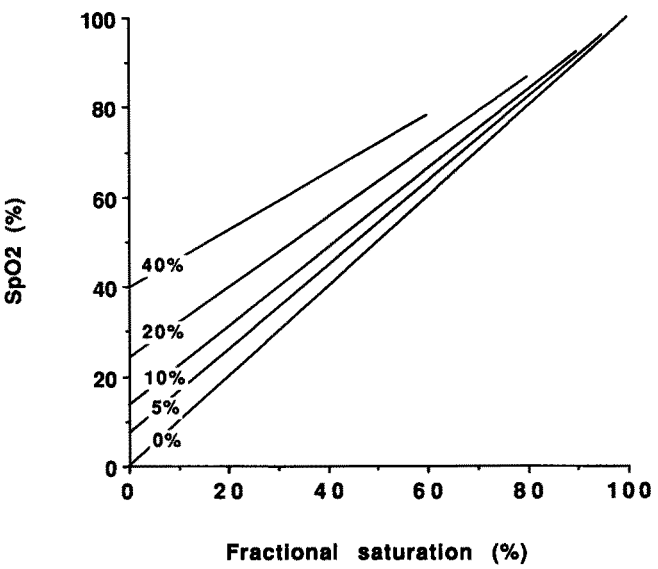

Fig 3. Pulse oximeter reading (SpO_2) compared with fractional saturation (SaO_2^{fr}) in the presence of various concentrations of MetHb, as predicted using the Beer-Lambert law and equation 10. Pulse oximeter wavelengths are 660 and 940.

tional saturation (Fig 4). All two-wavelength pulse oximeters will always overread when compared with the fractional saturation (Fig 3). This misconception was duplicated by Ralston et al [14].

To add to the confusion, pulse oximeter manufacturers often claim that their instruments measure functional saturation. For example, the Nellcor-200

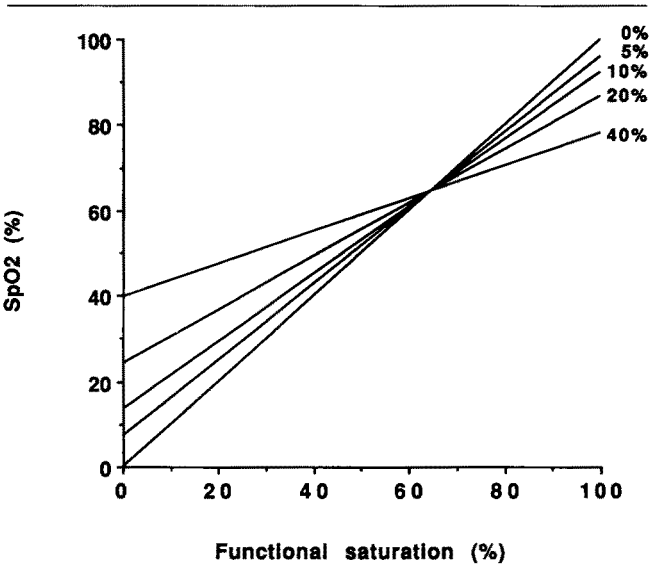

Fig 4. Pulse oximeter reading (SpO_2) compared with functional saturation (SaO_2^{fu}) in the presence of various concentrations of MetHb, as predicted using the Beer-Lambert law and equation 11. Pulse oximeter wavelengths are 660 and 940.

handbook claims that "because the N-200 measures functional oxygen saturation, it may produce measurements that differ from those of instruments that measure fractional saturation" [15]. This is misleading. Each manufacturer must initially calibrate its instrument against either functional or fractional saturation, but the oximeter will not measure either unless the dyshemoglobin levels in the subject's blood are equivalent to those present in the initial calibration. While attempting to clarify the distinction between functional and fractional saturation, Zijlstra and Oeseburg [16] unfortunately also claimed that, by definition, pulse oximeters measure functional saturation. However, we would argue that "by definition" pulse oximeters purely measure the ratio of pulsatile light absorbance at two discrete wavelengths.

It is important to remember that the relationships of equations 8 to 11 are derived theoretically, and it has been assumed that the Beer-Lambert law is valid for a pulsating vascular bed. In reality, however, the presence of the red blood cells in whole blood causes a discrete change in refractive index at the red cell/plasma interface. This causes the light to be scattered repeatedly and, consequently, the optical density of the substance is a result not only of absorption but also of multiple scattering of the incident light. The pulse oximeter is calibrated empirically and not simply by using the Beer-Lambert law; thus, our theoretical predictions may not be accurate. Equations 8 to 11 will be compared with

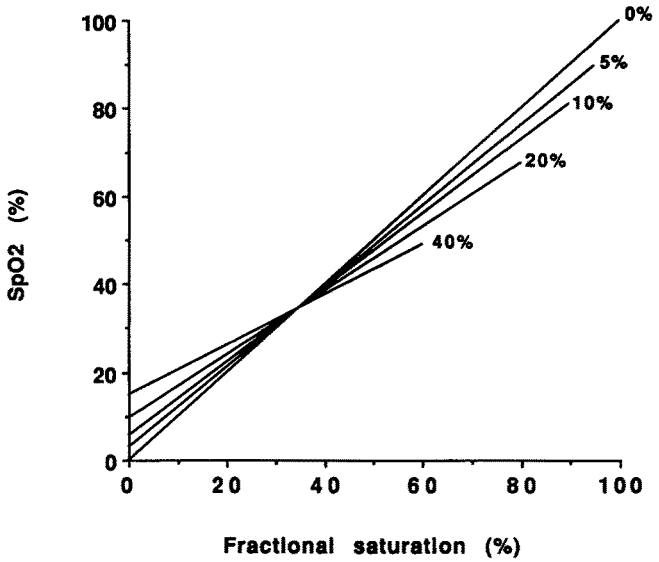

Fig 5. The same as Fig 3, SpO_2 versus SaO_2^{fr} with MetHb present, but pulse oximeter wavelengths are 650 and 940.

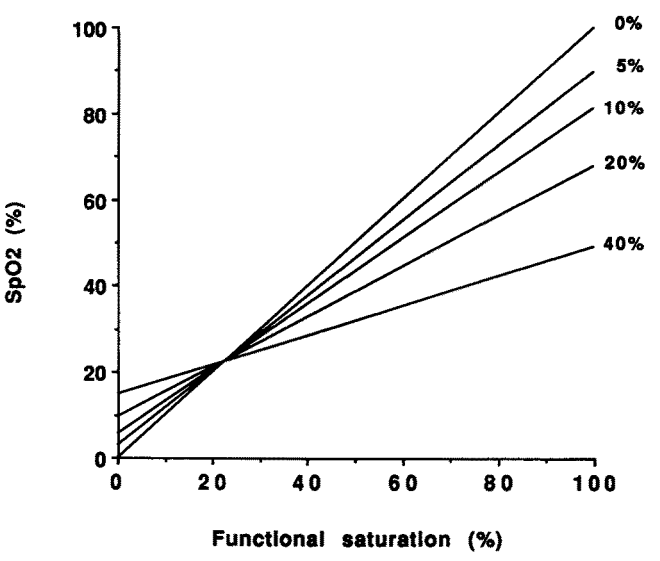

Fig 6. The same as Fig 4, SpO_2 versus SaO_2^{fu} with MetHb present, but pulse oximeter wavelengths are 650 and 940.

experimental results obtained in an in vitro test system, and other reported observations in Part II of this report.

The theoretical treatment also can be used to examine the effect of a change in probe light-emitting diode (LED) wavelength on SpO_2 in the presence of dyshemoglobins. It is known that the peak emission wavelength of an LED will vary depending on the drive current of the LED. Some pulse oximeters are designed to alter the drive current of their LEDs to compensate for different finger thicknesses, and therefore peak LED wavelength may vary with finger thickness [17]. Variations also may occur with ambient temperature [18], and there can be variations of up to ±15 in peak wavelengths of LEDs due to production tolerances [19]. Any shift in wavelength will leave the pulse oximeter working with a different set of extinction coefficients. This is less important either with no dyshemoglobins present [17,18] or in the presence of HbCO; however, the extinction coefficient of MetHb varies greatly around 660, and a wavelength shift will thus effect the pulse oximeter reading in the presence of MetHb. If, for example, we consider a red LED wavelength of 650 and use appropriate extinction coefficients in equations 6 and 7, we obtain the theoretical results shown in Figs 5 and 6 for SpO_2 in the presence of MetHb. Similarly, using extinction coefficients at 670 we obtain the results shown in Figs 7 and 8. Comparing these with Figs 3 and 4 we can see that for a pulse oximeter working at 650 or 670, the dependence of SpO_2 on %MetHb changes considerably with red LED wavelength; on the other hand, the dependence on %HbCO is not greatly affected.

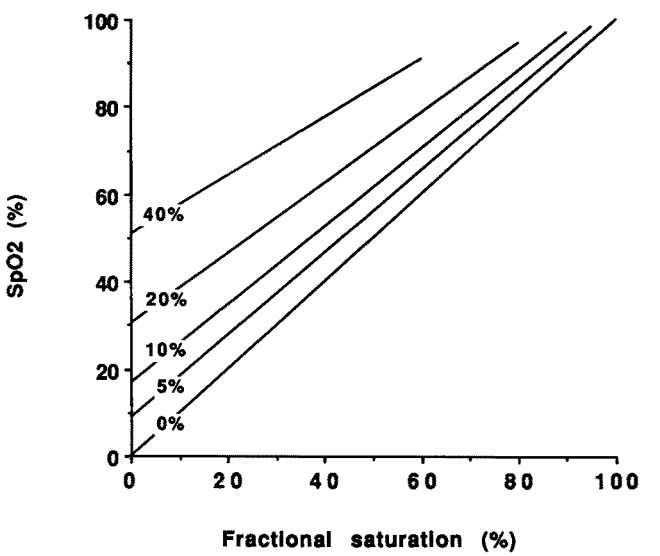

Fig 7. The same as Fig 3, SpO_2 versus SaO_2^{fr} with MetHb present, but pulse oximeter wavelengths are 670 and 940.

PART II: EXPERIMENTAL INVESTIGATION USING AN IN VITRO TEST SYSTEM

The aim of Part II of this paper is to investigate experimentally the effect of dyshemoglobins on the saturation recorded by the pulse oximeter using an in vitro test system, and to compare the experimental results with

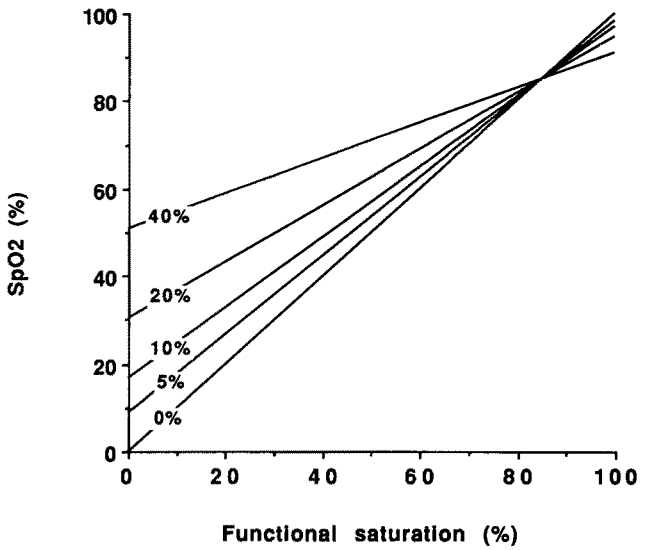

Fig 8. The same as Fig 4, SpO_2 versus SaO_2^{fu} with MetHb present, but pulse oximeter wavelengths are 670 and 940.

the theoretical relationships derived in Part I and given by equations 8 to 11.

The test system has been shown previously [20] to be capable of testing the accuracy, reproducibility, and linearity of pulse oximeters. The response of 10 different pulse oximeters was tested and was found to be highly variable. However, the results for each oximeter were reproducible and were in agreement with results obtained using the same oximeters on hypoxic patients. For the following dyshemoglobin experiments, we first tested the pulse oximeter in the absence of dyshemoglobins (total dyshemoglobin concentration <1.5%) to check that it gave an accurate, linear, and reproducible response to the test system.

Methods

DESCRIPTION OF IN VITRO TEST SYSTEM. Whole blood is pumped around a circuit (Fig 9) by a computer-controlled peristaltic pump capable of generating waveforms similar to those seen in arterial blood. The blood passes through a cuvette representing a human finger, and a pulse oximeter probe (Ohmeda Biox 3740 finger probe, Ohmeda, Englewood, CO) is positioned over this model finger. The cuvette (Fig 10) consists of two thin (0.5-mm) silicone rubber membranes, which allow pulsatile expansion of the blood channels, and a rigid Perspex central section. The blood enters from one end of the cuvette and flows in a thin (1-mm) layer through the cuvette, over the finger tip end, and back in a similar fashion along the underside. A diffuser made from translucent paper simulates the properties of the skin, scattering the incident light.

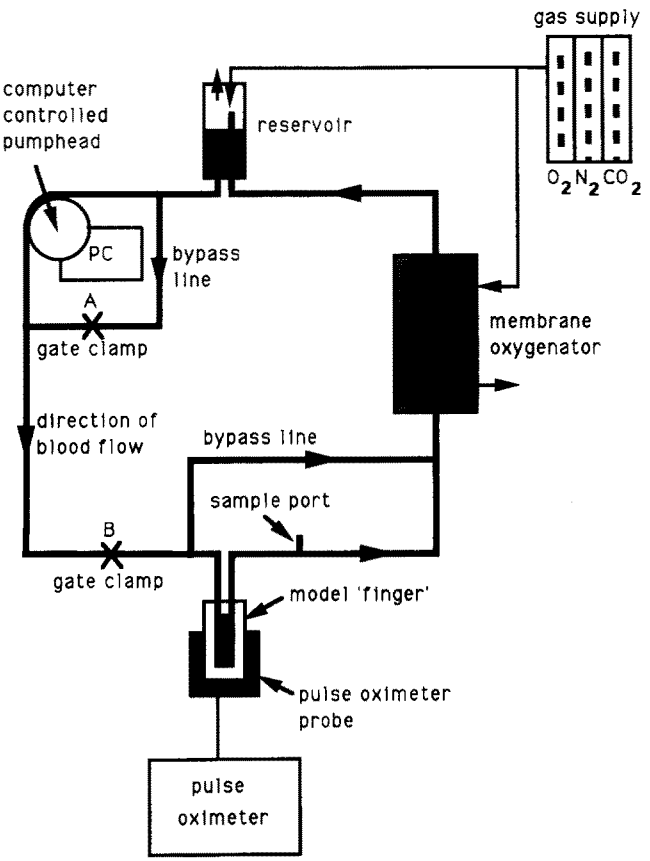

Fig 9. In vitro test system for pulse oximeters. (PC = personal computer for controlling pump; A, B = gate clamps to adjust blood flow.)

The saturation of the blood flowing through the circuit can be controlled by a small parallel plate membrane oxygenator. Nitrogen (N_2), oxygen (O_2), and carbon dioxide (CO_2) pass by diffusion across the membrane, and the blood saturation is altered by changing the percentage of oxygen in the gas mixture.

EXPERIMENTAL METHODS. In-date bank blood anticoagulated with CPD Adenine 1 solution was obtained from the Blood Transfusion Service and additionally anticoagulated with heparin. This was introduced to the test system. The saturation measurement displayed by the Ohmeda Biox 3740 pulse oximeter was compared with the saturation of a blood sample withdrawn simultaneously from a sampling port beyond the outlet of the model finger. This was analyzed immediately using an OSM3 Hemoximeter (Radiometer Ltd, Copenhagen, Denmark) to obtain values of both functional and fractional saturation. Unlike a pulse oximeter, the Hemoximeter is capable of distinguishing HbCO and MetHb since it uses six discrete wavelengths of visible light.

The saturation of the blood was then reduced by de-

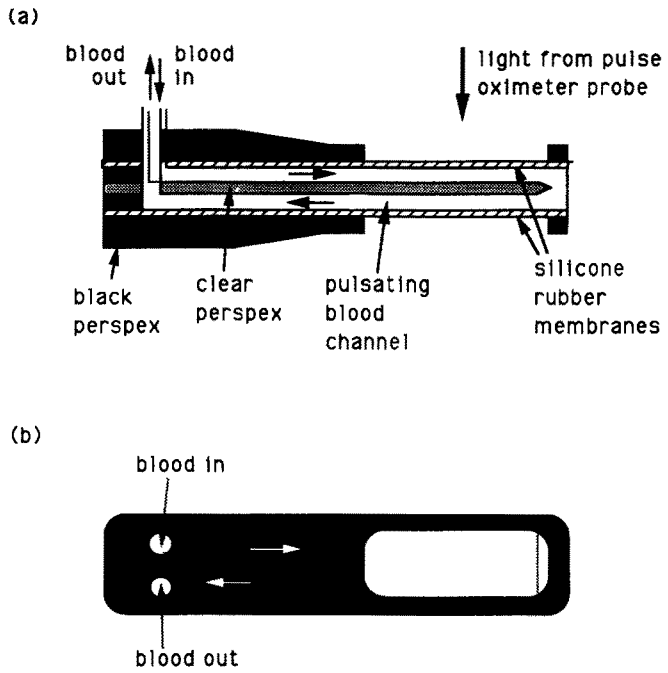

Fig 10. "Model finger" used in pulse oximeter test system. (a) *View from above.* (b) *Side view. Blood flows in a pulsatile fashion through a channel at the top of the finger, over the fingertip end, and back through the underside. The silicon rubber membranes allow pulsatile expansion of the blood channels, from which a pulse oximeter probe, placed over the finger, obtains its signals.*

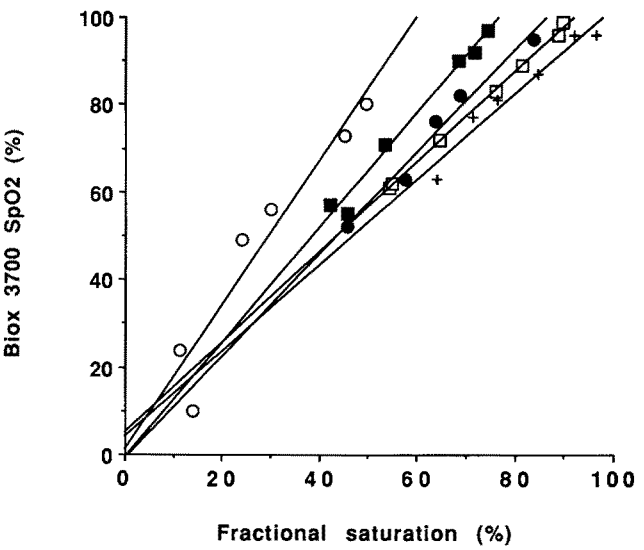

Fig 11. Pulse oximeter reading (SpO_2) across model finger plotted against fractional saturation (SaO_2^{fr}) measured with an OSM3 Hemoximeter in the presence of various concentrations of HbCO (+ = 0.5%, □ = 4.3%, ● = 11.3%, ■ = 22.5%, and ○ = 39.3%). The solid lines indicate linear regression of each data set (given in Table 2).

creasing the percentage of O_2 in the gas mixture, which also contained 5% CO_2, balance N_2. To test the response of the pulse oximeter to the test system, SpO_2, SaO_2^{fr}, and SaO_2^{fu} were recorded over a wide range of saturations.

Carboxyhemoglobin was formed by passing a small amount of carbon monoxide through the membrane oxygenator. Results were obtained at HbCO concentrations of approximately 0%, 5%, 10%, 20%, and 40%.

Methemoglobin was created by the addition of a small quantity of sodium nitrite to the blood, and pulse oximeter and Hemoximeter measurements were again compared over a range of saturations. This procedure was repeated for four concentrations of MetHb, approximately 0%, 5%, 10%, 20%, and 40%. Before each set of results, the pH of the blood was checked using an ABL2 blood gas analyzer (Radiometer Ltd.) and its value was adjusted to 7.2 ± 0.1 by the addition of isotonic sodium bicarbonate. It was necessary to maintain a constant pH, since the absorption spectrum of MetHb varies with pH [8]. A value of 7.2 was chosen because equations 8 to 11 were derived using van Assendelft's extinction coefficients for MetHb [8], which he obtained using a median pH value of 7.2.

Results

In the absence of dyshemoglobins (total dyshemoglobin concentration <1.5%), the pulse oximeter was found to give an accurate, linear, and reproducible response to the test system (slope = 0.96, correlation coefficient = 0.97, number of data points = 53).

Pulse oximeter reading (SpO_2) is plotted against fractional saturation in Fig 11 and against functional saturation in Fig 12 for each concentration of HbCO. Results obtained in the presence of elevated concentrations of MetHb are shown in Figs 13 and 14.

Linear regression analysis was performed on the experimental results, and the results of this analysis are compared with the predicted results from equations 8 to 11 in Table 2. The regression lines are shown on Figs 11 to 14 as solid lines.

Discussion of Part II

Figures 11 and 12 show the effect of HbCO on pulse oximeter reading. It can be seen (Fig 11) that the presence of HbCO tends to elevate the pulse oximeter reading to a value greater than the true fractional saturation and that this effect is smaller at low saturations. This is in agreement with the experimental results that Barker and Tremper obtained in dogs [9]. These investigators suggested that the degree of overestimation by SpO_2 is close to the percentage of HbCO present. This was

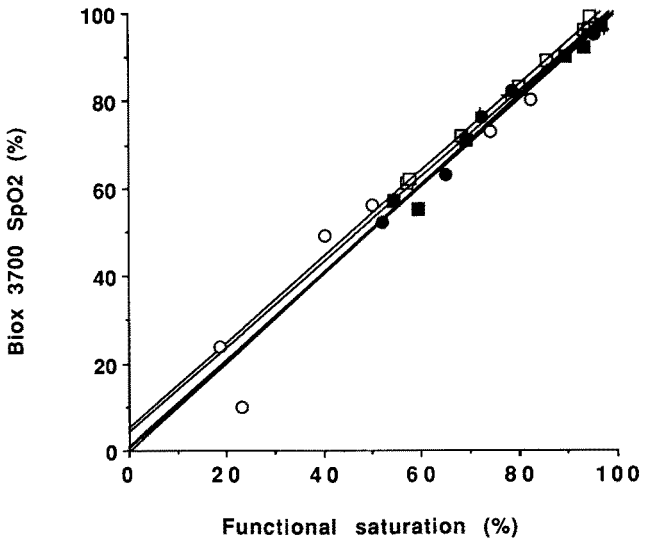

Fig 12. Pulse oximeter reading (SpO_2) across model finger plotted against functional saturation (SaO_2^{fu}) measured with an OSM3 Hemoximeter in the presence of various concentrations of HbCO (+ = 0.5%, □ = 4.3%, ● = 11.3%, ■ = 22.5%, and ○ = 39.3%). The solid lines indicate linear regression of each data set (given in Table 2).

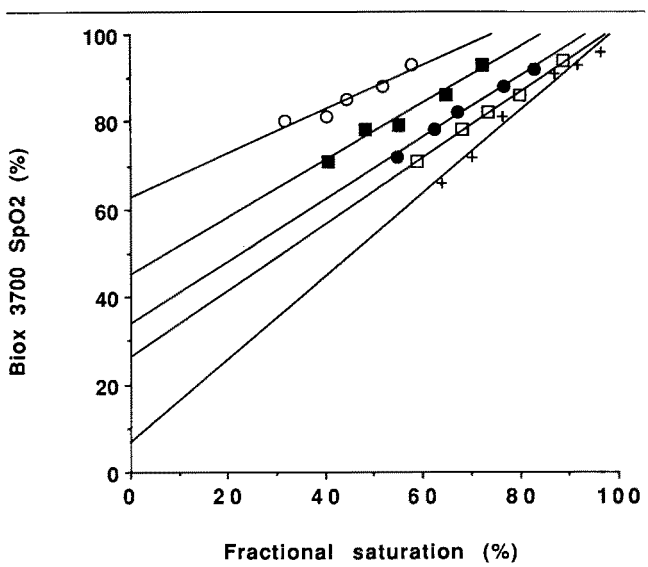

Fig 13. Pulse oximeter reading (SpO_2) across model finger plotted against fractional saturation (SaO_2^{fr}) measured with an OSM3 Hemoximeter in the presence of various concentrations of MetHb (+ = 1.0%, □ = 5.8%, ● = 9.6%, ■ = 21.5%, and ○ = 39.5%). The solid lines indicate linear regression of each data set (given in Table 2).

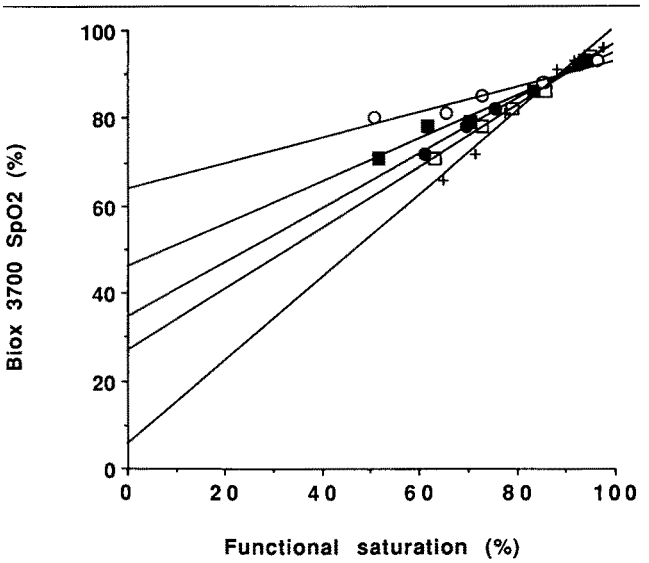

Fig 14. Pulse oximeter reading (SpO_2) across model finger plotted against functional saturation (SaO_2^{fu}) measured with an OSM3 Hemoximeter in the presence of various concentrations of MetHb (+ = 1.0%, □ = 5.8%, ● = 9.6%, ■ = 21.5%, and ○ = 39.5%). The solid lines indicate linear regression of each data set (given in Table 2).

supported recently by a clinical observation [10]. Using Fig 11 we suggest that this is true provided that all available hemoglobin is fully saturated and the fractional saturation is at a maximum for that concentration of HbCO. Carboxyhemoglobin often exists in concentrations of approximately 10% purely as a consequence of smoking, and this value can be greater [2]. Thus, fractional saturation will be overestimated by at least 10% in a healthy smoker.

On the other hand, the pulse oximeter should give an accurate estimate of functional saturation (Fig 12) for HbCO concentrations of up to approximately 20%. Concentrations greater than this will cause underestimation by the pulse oximeter, and the size of the effect is not affected greatly by the saturation. While the pulse oximeter appears to give an accurate estimation of functional saturation in the presence of HbCO, the fractional saturation is a more relevant value clinically since this gives an indication of the amount of oxygen available in the blood.

The experimental results obtained in vitro and plotted in Figs 11 and 12 are compared with the theoretical predictions (equations 8 and 9) in Table 2. From Table 2 we see that experimental and theoretical results compare well in the presence of HbCO.

The effects of methemoglobinemia on pulse oximetry are shown in Figs 13 and 14. When compared with fractional saturation values, values obtained from the in

Table 2. Comparison of Theoretical Predictions and Experimental Results

	Theoretical		Experimental			
%HbCO or %MetHb	Slope	Intercept (%)	Slope (b)	se(b)[a]	Intercept (%)	Correlation Coefficient, *r*
HbCO						
Regression of SpO_2 on fractional saturation						
0.5%	1.00	−0	0.98	(0.11)	+4	0.976
4.3%	1.04	−0	1.03	(0.02)	+5	0.999
11.3%	1.12	−1	1.16	(0.11)	−1	0.987
22.5%	1.28	−2	1.31	(0.09)	−1	0.990
39.3%	1.62	−4	1.65	(0.25)	+1	0.938
Regression of SpO_2 on functional saturation						
0.5%	1.00	−0	0.97	(0.11)	+4	0.976
4.3%	1.00	−0	0.98	(0.02)	+5	0.999
11.3%	1.00	−1	1.02	(0.09)	−1	0.989
22.5%	0.99	−2	0.99	(0.07)	+0	0.991
39.3%	0.98	−4	1.00	(0.20)	+1	0.957
MetHb						
Regression of SpO_2 on fractional saturation						
1.0%	0.99	+0	0.94	(0.07)	+7	0.990
5.8%	0.92	+8	0.76	(0.03)	+26	0.998
9.6%	0.88	+13	0.71	(0.02)	+34	0.998
21.5%	0.77	+26	0.65	(0.06)	+45	0.985
39.5%	0.64	+39	0.51	(0.08)	+62	0.965
Regression of SpO_2 on functional saturation						
1.0%	0.98	+0	0.94	(0.07)	+6	0.990
5.8%	0.87	+8	0.70	(0.03)	+27	0.998
9.6%	0.79	+13	0.62	(0.02)	+34	0.999
21.5%	0.62	+26	0.49	(0.05)	+46	0.987
39.5%	0.39	+39	0.29	(0.04)	+64	0.967

[a]se(b): The standard error of the regression slope.

vitro test-pulse oximeter system tend to overestimate the saturation, with the effect greatest at low saturations (Fig 13). As the MetHb concentration is increased, the pulse oximeter becomes less sensitive to changes in saturation. These effects also were observed by Barker et al during experiments on dogs [11].

On the other hand, our theory predicts that the presence of MetHb causes the underestimation of functional saturation at high saturations and overestimation at low saturations (Fig 14). This is in agreement with Barker and colleagues [11,21], with clinical observations [12], and also with our experimental results (Fig 14). The difference between SpO_2 and functional saturation increases with increasing MetHb concentration. This results in the pulse oximeter's becoming less sensitive to changes in functional oxygen saturation as MetHb increases, until at very high MetHb concentrations the pulse oximeter saturation reading is almost independent of the actual value of functional saturation. The experimental results plotted in Figs 13 and 14 are compared with the theoretical predictions (equations 10 and 11) in Table 2. It appears that experimental and theoretical results do not compare as well in the presence of MetHb as they do in the presence of elevated HbCO concentrations.

Barker et al [11] observed that in the presence of high concentrations of MetHb, the pulse oximeter saturation tended toward 85%, regardless of the relative amounts of hemoglobin and HbO_2 (i.e., the functional saturation) present. Similarly, our experimental in vitro results illustrated in Fig 14 suggest that the pulse oximeter reading tends toward 85 to 90% at high concentrations of MetHb. Barker et al explained this effect by suggesting that the presence of MetHb increases both the numerator and denominator of the red/infrared ratio, driving this ratio toward a value of 1, which corresponds to a saturation of approximately 85% on the pulse oximeter calibration curve. According to our theory, however, high concentrations of MetHb should force the ratio β toward 1.26 (equation 4), with a corresponding pulse oximeter reading of 65% (equation 3). The discrepancy between these values can be attributed to scattering of the light by red blood cells in Barker's experiments and in our test system. Our theory, on the other hand, was based on a simple nonscattering medium (i.e., hemoglobin solution).

Another possible explanation for the discrepancy between experimental values and those predicted by theory is a shift in red LED peak wavelength away from 660 either due to ambient temperature [18] or finger thickness [17], or perhaps a shifted LED wavelength during production [19]. As explained in Part I, this leaves the pulse oximeter working with a different set of extinction coefficients and can cause errors. The effect is relatively unimportant with HbCO, but in the presence of MetHb, a shift of 10 from 660 to 670 will cause the difference in the theoretical pulse oximeter response between Figs 3 and 4 and Figs 7 and 8.

In reality, however, it is unlikely that the LED wavelength will have shifted greatly. The Ohmeda pulse oximeter allows for variations in LED wavelength during production by the inclusion of a coding resistor in each probe at the time of manufacture. The coding resistor gives information to the pulse oximeter about the wavelengths of the LEDs within that probe, and appropriate calibration is performed by the pulse oximeter.

When comparing theoretical and experimental results, remember that the regression estimate is subject to sampling variation. Table 2 gives the standard error of the regression slope for each set of data points.

CONCLUSION

A series of theoretical relationships between pulse oximeter saturation and either fractional or functional saturation in the presence of HbCO or MetHb has been derived according to simple absorption theory. For most patients, the difference between fractional and functional saturation is very small. However, when dyshemoglobin concentrations are elevated, there is a significant difference between these two values, and the pulse oximeter reading is unlikely to agree with either.

Although the difference is usually insignificant, the clinician should be aware of the possibility of confusion between pulse oximeter reading, fractional saturation, and functional saturation. In the case of doubt, pulse oximeter readings should be confirmed by other methods, for example, a multi-wavelength co-oximeter capable of distinguishing HbCO and MetHb.

While it appears that the theoretical relationships based on a pure absorbing solution are not easily applicable to a clinical situation for a quantitative prediction (especially in the presence of MetHb), they provide a useful approximation and allow qualitative changes to be observed. Pulse oximeters should always be used with caution on patients with suspected high levels of dyshemoglobins.

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