How to use saturation monitoring in newborns

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ABSTRACT

Pulse oximetry is a first-line monitoring tool, used in neonatal medicine routinely as a part of continuous monitoring during intensive care. It is also used to guide response to resuscitation and as a screening tool for congenital heart disease. Despite its widespread use, many healthcare providers are unaware of the underlying principles and limitations of pulse oximetry in neonates. In this article, we will discuss the physiological and technological principles behind the use of saturation monitoring and its use in neonatal practice.

INTRODUCTION

Pulse oximetry was introduced into clinical practice in the early 1980s. It is now a first-line monitoring tool and has been referred to as the 'fifth vital sign'.[1]

Within neonatology, pulse oximetry is used: for routine intensive care monitoring, to aid neonatal life support, to guide clinical decision-making in the critically ill and as a screening tool for congenital heart disease. However, despite widespread use, many healthcare providers are unaware of the principles, evidence for and limitations of pulse oximetry in neonates.[1]

PHYSIOLOGICAL CONSIDERATIONS

Oxygen is transported in two ways within the blood. The majority of oxygen is transported bound to haemoglobin within red blood cells as oxyhaemoglobin (HbO_2), with negligible amounts dissolved within plasma.[2]

The relationship between HbO_2 saturation and PaO_2 of oxygen is a sigmoid curve (figure 1).[2] At low oxygen tension, haemoglobin is maximally desaturated and has a low affinity for oxygen.[2] As oxygen tension increases the molecule undergoes conformational change revealing additional binding sites and increasing oxygen affinity.[2] Finally, at high oxygen tension, haemoglobin is maximally saturated and further increase in PaO_2 has limited effect on saturation.[2] In the context of a normal physiological state, arterial haemoglobin is greater than 95% saturated.[2] Oxygen is unloaded in peripheral tissues giving a mixed venous saturation level of 75%.[2]

At birth, transition occurs from placental to pulmonary gas exchange.[3] Transition describes a set sequence of lung aeration, pulmonary vasodilation and increasing pulmonary blood flow to replace umbilical blood flow as the source of left ventricular preload.[3] This suggests that the transitioning neonate's cardiac function can be supported by delayed cord clamping.[3] When placental circulation is removed, systemic blood pressure exceeds pulmonary and oxygenated blood shunts left to right across the ductus arteriosus.[3 4] Functional and anatomical closure of the foramen ovale and ductus arteriosus follows.[3 4]

Vascular pathways can be subdivided into preductal and postductal. This is based on their origin arising proximal or distal to the aortic insertion of the ductus arteriosus. Conventional wisdom recommends that the right arm is the preferred site to allow readings of preductal oxygenation; however, an observational study of 251 newborns demonstrated no statistically significant difference in saturation levels between upper limbs.[5] This means that with the exception of some infants with persistent pulmonary hypertension of the newborn (PPHN) and certain critical congenital heart disease, pulse oximetry on either upper limb can be considered preductal and the lower limb saturation assesses postductal oxygenation.[5]

In normal physiological circumstances, preductal and postductal arterial oxygen saturations are in equilibrium. A difference or gradient in the readings signifies pathological right to left shunting of deoxygenated blood across a patent ductus arteriosus (PDA) and is known as

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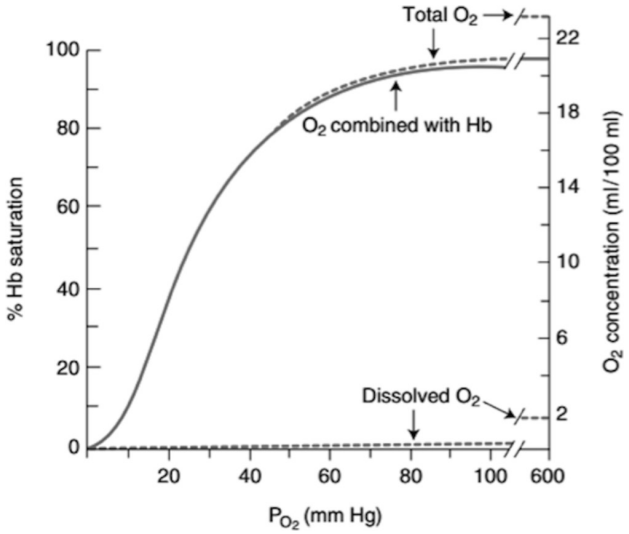

Figure 1 Oxygen dissociation curve (adapted from West[2] and used with permission from Wolters Kluwer Health).

differential cyanosis. A significant preductal to postductal saturation gradient can be defined as >5% with the gradient increasing in proportion to the magnitude of right to left ductal shunting.[4] However, lower gradients (2%–4%) may be deemed significant to maximise sensitivity during pulse oximetry screening for critical congenital heart disease.

TECHNICAL BACKGROUND

A pulse oximeter consists of a microprocessor and a probe. The probe is composed of two light-emitting diodes (LEDs) and a photodetector. The LEDs emit light at 660 nm (red spectrum) and 940 nm (infrared spectrum).[1] The photodetector is positioned directly opposed to the diodes to measure tissue light absorption.[1]

Pulse oximetry utilises the principles of spectral analysis where different components in a solution are quantified based on their differing light absorption characteristics.[1] In the case of blood, these components are HbO_2 and deoxyhaemoglobin (Hb). HbO_2 primarily absorbs infrared light while Hb primarily absorbs red light.[1]

The varied wavelengths of the diodes allow two points of reference for the microprocessor to differentiate Hb and HbO_2. Light absorption varies with arterial pulsation and oxygenation level.[1] The microprocessor utilises the difference in absorption with wavelength and pulsation to derive a ratio. Arterial oxygenation is calculated following non-variable absorption elimination and comparison to experimentally derived reference data (figure 2).[1] This is thereafter expressed as a saturation level (SpO_2). Fluctuation with arterial pulsation allows the pulse oximeter to also detect and report a heart rate along with a pulse waveform (figure 2).[1] SpO_2 becomes inaccurate below 70% due to a lack of

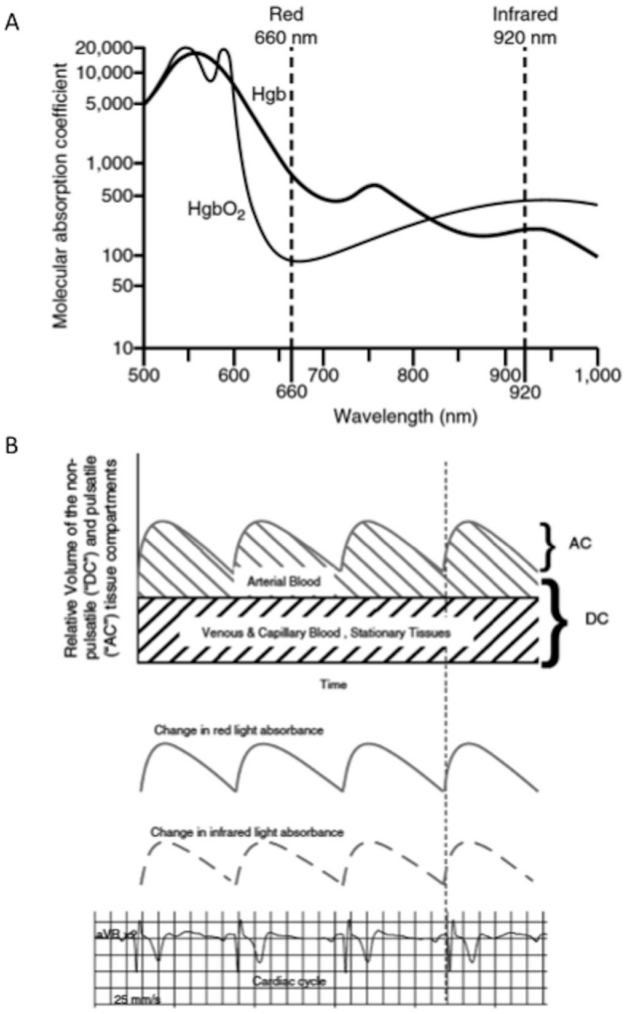

Figure 2 (A) Light absorption pattern of oxyhaemoglobin and deoxyhaemoglobin. (B) Light absorption pattern variance with pulsation (adapted from Wheeler *et al*[1] and used with permission from Springer).

experimentally derived reference data for such low oxygen saturations.[1]

Quality of the pulse oximetry reading is dependent on correct alignment of the diode and photodetector. The best site is somewhere relatively immobile, well perfused, easily accessible and comfortable for the infant such as the hands, wrists and feet. Saturation probes generate a small amount of heat which in combination with pressure, particularly in preterm infants, can result in burns, pressure ulceration, necrosis and deformity.[6] Saturation probes should therefore be positioned with care and rotated regularly between sites.[6]

Numerous factors can affect the accuracy of pulse oximeters.[1] Patient motion and ambient light are perhaps the most common causes of falsely low saturations. This can be overcome by gently wrapping the probe in an opaque material. SpO_2 is also unreliable in low perfusion states, leading to falsely low levels. A falsely low SpO_2 can often be differentiated

from true desaturations by inspecting the quality of the pulse waveform displayed.

Inhaled nitric oxide therapy used in the treatment of PPHN can result in the development of methaemoglobinaemia via oxidisation of haemoglobin.[1] Methaemoglobin absorbs light in a similar pattern to deoxyhaemoglobin and when present in significant amounts can result in a persistent saturation reading of 80%–85%.[1]

Table 1 Acceptable preductal oxygen saturation (SpO2) following delivery.[7]

Age	Acceptable preductal SpO_2 limit
2 min	60%
3 min	70%
4 min	80%
5 min	85%
10 min	90%

CLINICAL QUESTIONS

What are acceptable saturations in newborn babies?

Neonates must transition from placental to pulmonary gas exchange at birth. Most make this transition without the need for support. Of those over 2.5 kg, 8 per 1000 require mask ventilation and 2 per 1000 intubation.[7] Historically, the need for resuscitation and supplemental oxygen was guided by assessing heart rate, respiratory effort, colour and tone, with high oxygen concentrations used for lung inflation.[7 8] Clinical determination of oxygen saturation is highly subjective and pulse oximetry can accurately determine saturation levels within 90 s of birth.[8]

Umbilical venous blood is 60% saturated dropping to 30% during contractions.[8] Dawson *et al*[9] demonstrated how oxygen saturation levels rise gradually during the first 10 min of life in healthy term and preterm infants.[9] Based on this, neonatal resuscitation guidelines incorporate acceptable preductal saturation ranges for this period (table 1).[7]

A recent prospective observational study conducted by Smit *et al*[10] assessed whether these saturation limits held true in term infants born in a community setting where delayed cord clamping was practised.[10] Their results demonstrated comparable, but higher, saturation ranges within the first 3 min of life, which increased slower than traditionally acceptable ranges.[10] Given the increasing utilisation of delayed cord clamping within routine care, acceptable saturation ranges are likely to be revised in future.

The aim of acceptable saturation targets is to avoid potentially harmful and unnecessary oxygen therapy. A meta-analysis conducted by Saugstad *et al*[11] compared high versus low oxygen use during preterm (<32 weeks) transition and demonstrated a reduced mortality approaching statistical significance when 21%–30% oxygen was used compared with higher levels (>60%).[11] An earlier meta-analysis by Davis *et al*[12] had demonstrated an association between high oxygen delivery, increased mortality and delayed onset of spontaneous breathing in term infants with apnoea and bradycardia.[12] Initial resuscitation with 21% in term and 21%–30% oxygen in

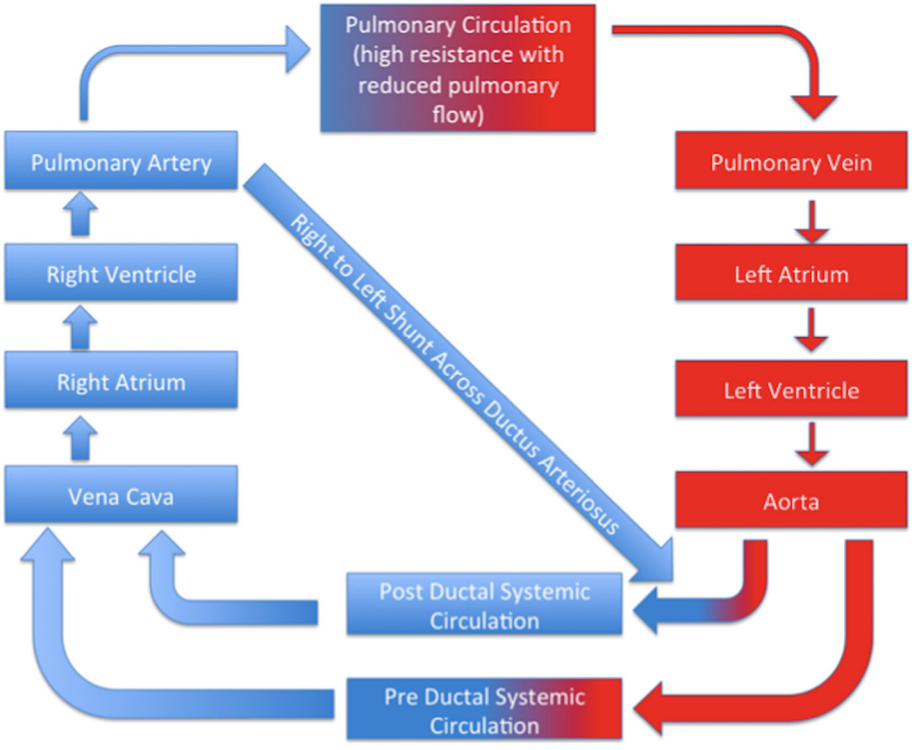

Figure 3 Haemodynamics in persistent pulmonary hypertension of the newborn with patent ductus arteriosus.

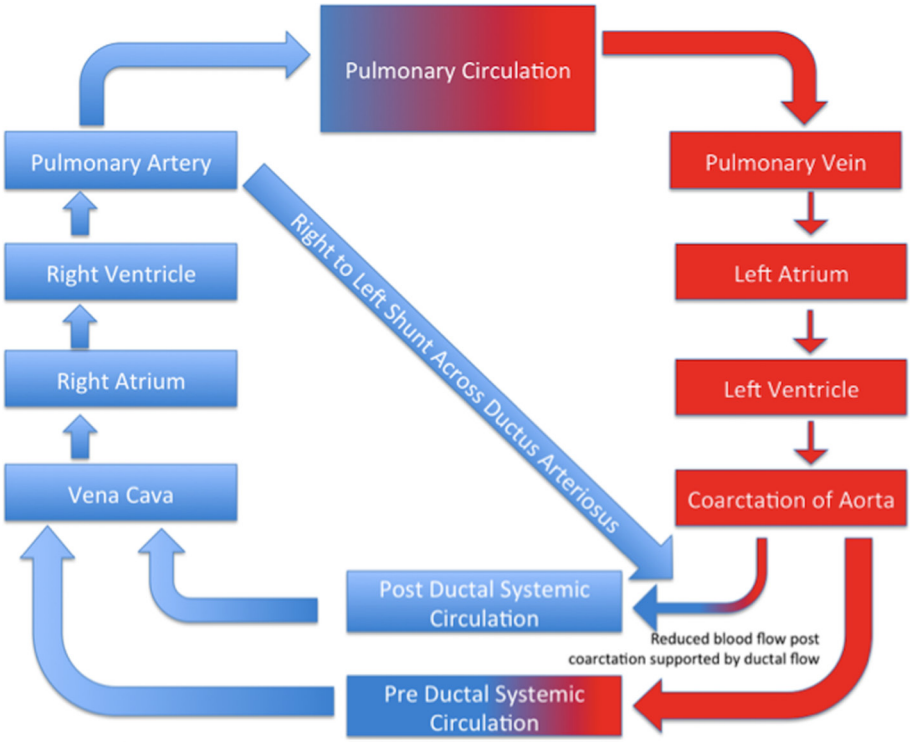

Figure 4 Haemodynamics of left heart obstructive congenital cardiac disease.

preterm neonates with subsequent escalation based on pulse oximetry is currently advocated.[7]

What saturation range should we target for preterm infants in the neonatal intensive care unit?

As early as the 1950s, a need to balance hyperoxia and hypoxia in prematurity was recognised.[13] The association of hyperoxia with morbidity (chronic lung disease and retinopathy of prematurity (ROP)) and hypoxia with mortality meant a clinically appropriate range of oxygen saturation for neonates was unknown.[13] This uncertainty inspired several clinical trials investigating appropriate neonatal saturation targeting beyond the first 10 min of life.[13 14]

The first Benefits of Oxygen Saturation Targeting (BOOST) trial allocated babies born at <30 weeks gestation who remained on oxygen therapy beyond 32 weeks corrected gestation to SpO_2 target 91%–94% versus 95%–98% and showed no significant difference in growth or major developmental abnormality at 12 months corrected age.[14] The BOOST 2 trial was halted early when pooled interim

Table 2 Differentiating persistent pulmonary hypertension of the newborn (PPHN) from ductus arteriosus (ductus botalli) dependent cardiac lesions

	PPHN	Ductus arteriosus dependent left heart obstructive lesions
Risk factor	Birth asphyxia Meconium liquor Sepsis/pneumonia Pulmonary hypoplasia Respiratory distress syndrome	Abnormal fetal anomaly scan/echocardiogram
Illness timing	Typically in the first 24 hours of life	With ductus arteriosus closure
Respiratory distress	Present	Minimal
Pulses	Normal or globally reduced	Reduced pulses post ductus arteriosus (absent femorals with brachiofemoral delay)
Blood pressure	No preductus and postductus arteriosus gradient.	Significant pre–post ductus arteriosus gradient (systolic >20 mm Hg, diastolic >10 mm Hg)
Saturations	Elevated saturation gradient	Elevated saturation gradient
Chest X-ray	Normal cardiac shadow Reduced pulmonary blood flow Pulmonary pathology features (eg, meconium aspiration)	Abnormal cardiac shadow Increased pulmonary vascularity Absent pulmonary pathology
ECG	Nil specific	Lesion-specific changes

safety analysis showed a significantly increased mortality risk in the 85%–89% group compared with 91%–95%.[13]

A subsequent Cochrane meta-analysis of five randomised control trials by Askie *et al*[15] found that targeting SpO_2 91%–95% versus 85%–89% in extremely preterm infants significantly increased the incidence of death at 18–24 months corrected age (p=0.01), death before hospital discharge (p=0.02) and necrotising enterocolitis (p=0.01).[15] Although the rate of severe or treated ROP significantly decreased (p=0.004), there was no significant reduction in blindness (p=0.65).[15] Current recommendations are that SpO_2 should be targeted between 91% and 95% in infants born at less than 32 weeks.[15]

There are no data to guide target saturations in mature term babies. However, as ROP and chronic lung disease are uncommon in infants born after 37 weeks gestation, a saturation target of >95% is commonly adopted.

What are the causes of a preductal and postductal saturation gradient?

A ductal saturation gradient of >5% is significant and represents pathological right to left shunting.[4] In neonates, the causes of an elevated saturation gradient include: PPHN with PDA, duct dependent left heart obstructive lesions and transposition of the great arteries (TGA).[16]

In PPHN, following an insult (respiratory distress syndrome, congenital pneumonia, meconium aspiration), pulmonary vasodilation does not occur, while in duct-dependent cardiac lesions (severe coarctation, critical aortic stenosis, hypoplastic left heart) obstruction to left ventricular outflow results in low aortic arterial pressures. In both situations, desaturated blood shunts from right to left across the ductus arteriosus leading to lower oxygen saturation within postductal circulations (figures 3 and 4).

Differential cyanosis is an accepted sign of both these pathologies but has not been subject to statistical investigation within symptomatic individuals to define test sensitivity, specificity and predictive probability. The finding of differential cyanosis helps in the diagnosis of PPHN and duct-dependent cardiac lesions when considered along with the whole clinical picture (table 2). However, in clinical practice, these two pathologies often overlap in presentation. Definitive diagnosis may be reached only with the aid of echocardiography.[4]

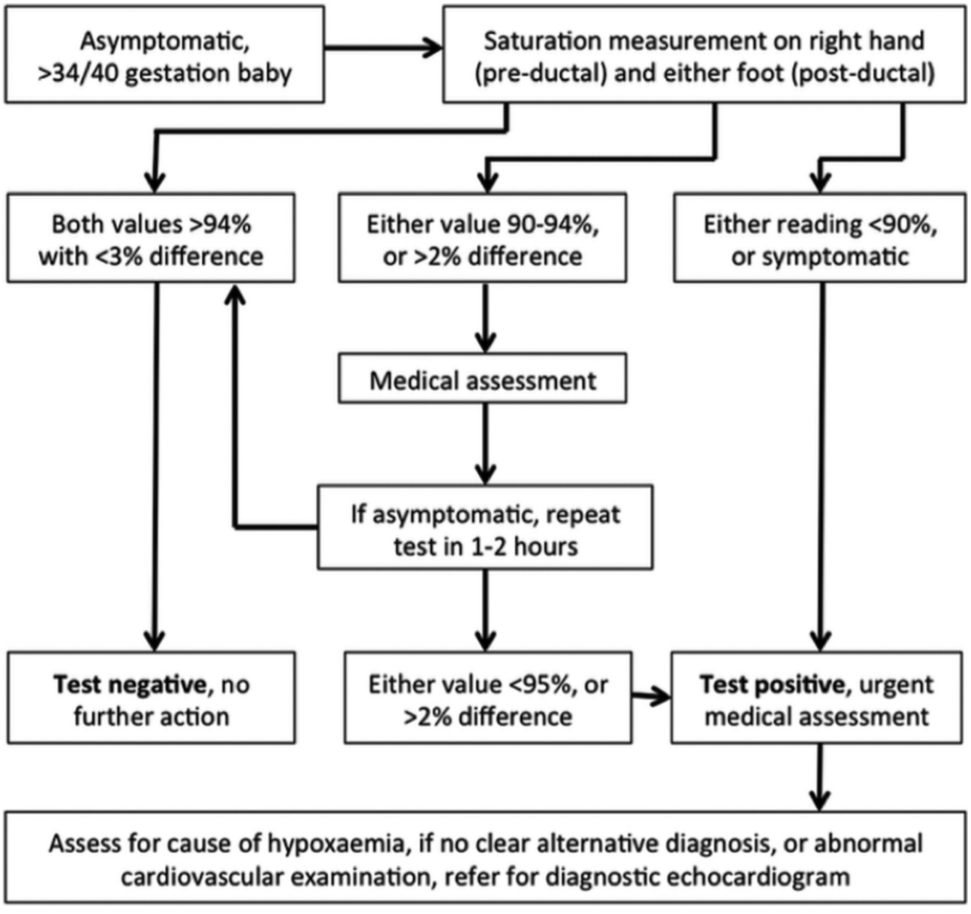

Figure 5 Suggested algorithm for newborn pulse oximetry screening from Ismail *et al*.[17]

In the setting of PPHN, inhaled nitric oxide may successfully vasodilate the pulmonary vascularity. This will result in a lower pulmonary artery pressure, less right to left shunting and a narrowing of the saturation gradient. Little effect would be expected in duct-dependent left heart obstructive lesions. In duct-dependent left heart obstructive lesions, prostaglandin E1 or E2 is used to reverse ductal closure, increasing right to left ductal flow, which supports the circulation, but widens the saturation gradient.

Reverse differential cyanosis (preductal SpO_2 < post ductal SpO_2), may occur in the setting of TGA.[16] In TGA, the right ventricle receives deoxygenated systemic blood and supplies the systemic circulation via the aorta, while the left ventricle receives oxygenated pulmonary venous blood and supplies the pulmonary circulation. If, in combination with this parallel arrangement, a PDA exists and pulmonary pressures exceed systemic (obstructive total anomalous pulmonary venous drainage, left heart obstructive lesions), then oxygenated blood will shunt from the pulmonary to systemic circulation.[16] This oxygenates the postductal blood giving a reversed differential saturation pattern. This finding has not been subject to statistical investigation to define test sensitivity, specificity or predictive probability and corroboration of the diagnosis of TGA can only be definitively made with the use of echocardiography.

In asymptomatic neonates, can we use saturation monitoring to screen for congenital heart disease?

Critical congenital heart disease (CCHD) occurs in 2–3/1000 live births and accounts for 3%–7.5% of infant deaths.[17] Current CCHD screening consisting of antenatal ultrasound and postnatal clinical examination is not consistent in identifying CCHD. Overall, UK antenatal detection rates are <50% and a third of cases are missed on postnatal examination.[17] Acute collapse in a previously well infant, at the time of ductal closure, remains a significant factor in morbidity with worse surgical and neurodevelopmental outcomes.[17]

Since preliminary study in 2002, pulse oximetry screening (POS) has become well established and refined.[18–20] POS's guiding principle remains that objective measurement of pulse oximetry is better than subjective clinical determination on examination. POS has been tested in large numbers (some studies include 50–75 000 live births), in different parts of the world, with different pieces of equipment and staff of varying levels of experience.[19] Despite these variations, POS continues to identify asymptomatic infants with CCHD before ductal closure and acute collapse.

In a systematic review and meta-analysis in 2012, sensitivity and specificity of POS were calculated.[20] While the sensitivity (true positive) rate was moderate at 76.5% (95% CI 67.7% to 83.5%), the specificity (true negative) was exceptionally high at 99.9% (95% CI 99.7% to 99.9%).[20] Reasons for false-positive screening include sepsis and PPHN. POS has been found to help close the CCHD diagnostic gap by increasing detection rates to >90%.[17]

The PulseOx study has lead to the development of a POS screening algorithm consisting of measurement of preductal and postductal pulse oximetry in asymptomatic neonates beyond 34 weeks of gestation to identify those with unsuspected CCHD.[17] Previously, screening was advocated at 24 hours or beyond. However, this is not practical in the current climate of early postnatal discharge.[17] The PulseOx study showed that early screening (<24 hours) did have a higher false-positive rate (0.5% vs 0.05% compared with POS at >24 hours).[17] The level of saturation then defines the action to be taken. In those whose POS saturations are >94% and gradient <3%, the screening was negative.[17] In those whose saturations lie between 90% and 94% or gradient exceeds 2%, then retest in 1 hour was advocated.[17] While those with saturations <90% initially, or <95% on retest should be urgently evaluated for CCHD.[17] Evaluation should include at least a full clinical examination, chest radiograph and partial septic screening.[17] Echocardiograms are reserved for those with an abnormal cardiovascular examination, persistent hypoxia despite oxygen and where an alternative diagnosis is not evident (figure 5).[17]

Clinical bottom line

- Preductal pulse oximetry should be applied in delivery suite to all neonates requiring newborn life support and all preterm deliveries to allow safe O_2 escalation to achieve acceptable saturation levels within the first 10 min of life.
- In preterm infants, following the first 10 min of life, a saturation target of 91%–95% has been shown to reduce morbidity (chronic lung disease and retinopathy of prematurity) without elevating mortality.
- A saturation gradient of >5% in the acutely unwell neonate warrants assessment for pulmonary hypertension of the newborn and critical congenital cardiac disease.
- Technical limitations of pulse oximetry include movement, ambient light, poor perfusion, skin pigmentation and dyshaemoglobinaemia.
- The use of pulse oximetry screening is well evidenced and has been shown to identify infants with critical congenital heart disease while they are asymptomatic and thus before acute collapse at the time of ductal closure.

Test your knowledge

1. Which of the following statements are true? (Multiple answers)
   A. The Benefits of Oxygen Saturation Targeting II trial demonstrated an increased risk of mortality in preterm infants associated with target pulse oximetry saturations of 85%–89%.
   B. Pulse oximetry has been shown to identify critical congenital heart disease only in ideal conditions with specially calibrated saturation monitors in tertiary hospitals.
   C. In persistent pulmonary hypertension of the newborn, the increased pulmonary vascular resistance leads to shunting of deoxygenated blood to the systemic circulation causing lower preductal saturations compared with postductal measurements.
   D. Pulse oximetry screening can increase detection of critical congenital heart disease to more than 90% compared with around 80% by prenatal ultrasound and clinical examination alone.
   E. Saturations can be determined because deoxyhaemoglobin absorbs more light than oxyhaemoglobin.
2. Which of the following situations may affect the accuracy of pulse oximetry in the neonatal unit? (Multiple answers)
   A. A critically unwell neonate with necrotising enterocolitis, increased base excess and reduced urine output.
   B. An infant who is extremely unsettled with neonatal abstinence syndrome secondary to maternal opiate use.
   C. A term infant sedated and paralysed on mechanical ventilation and inhaled nitric oxide therapy for persistent pulmonary hypertension.
   D. Preterm infant with haemoglobin level of 95 g/dL.
   E. A neonate with physiological jaundice not requiring single phototherapy.
3. During neonatal life support, what is an acceptable saturation level in a 5-minute-old neonate? (Single best answer)
   A. 60%
   B. 70%
   C. 80%
   D. 85%
   E. 90%
4. Routine targeting of a saturation level of 90%–94% versus >95% in preterm infants is associated with (Single best answer)
   A. Higher incidence of retinopathy of prematurity (ROP).
   B. Higher incidence of necrotising enterocolitis (NEC).
   C. Higher mortality.
   D. Lower prevalence of chronic lung disease.
   E. Higher incidence of developmental delay.
5. An asymptomatic neonate with pulse oximetry screening showing SpO2 of 89% should receive the following investigations first line: (Multiple answers)
   A. Clinical examination.
   B. Chest radiograph.
   C. Echocardiogram.
   D. Blood culture.
   E. Full blood picture and C-reactive protein.

Answers are at the end of the references.

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Answers to the test your knowledge quiz

1. A and D are true.
2. A (poor perfusion state), B (excessive movement) and C (methaemoglobinaemia): all three situations have possible confounding factors, and pulse oximetry should be interpreted with caution, assessing clinical condition and pulse waveform.
3. D: 85% is an acceptable saturation level in this case.
4. D: targeting saturation levels of 90%–94% versus >95% is associated with lower chronic lung disease without increasing the incidence of ROP, NEC, mortality or developmental delay.
5. A, B, D and E: asymptomatic neonates with positive screening on pulse oximetry should receive clinical assessment, chest radiography and septic screening at a minimum. An echocardiogram is indicated second line in those where an alternative diagnosis to critical cardiac disease is not found.