



Role of Pulse Oximetry in Examining Newborns for Congenital Heart Disease: A Scientific Statement from the AHA and AAP

CONTRIBUTORS:

William T. Mahle, MD, FAHA, FAAP, Chair, Jane W. Newburger, MD, MPH, FAHA, FAAP, G. Paul Matherne, MD, FAHA, FAAP, Frank C. Smith, MD, Tracey R. Hoke, MD, FAAP, Robert Koppel, MD, FAAP, Samuel S. Gidding, MD, FAHA, FAAP, Robert H. Beekman, III, MD, FAHA, FAAP, Scott D. Grosse, PhD, on behalf of the AMERICAN HEART ASSOCIATION CONGENITAL HEART DEFECTS COMMITTEE OF THE COUNCIL ON CARDIOVASCULAR DISEASE IN THE YOUNG, COUNCIL ON CARDIOVASCULAR NURSING, AND INTERDISCIPLINARY COUNCIL ON QUALITY OF CARE AND OUTCOMES RESEARCH; AND THE AMERICAN ACADEMY OF PEDIATRICS SECTION ON CARDIOLOGY AND CARDIAC SURGERY, AND COMMITTEE ON FETUS AND NEWBORN

KEY WORDS

diagnostic techniques and procedures, outcomes research, health policy, pulse oximetry, heart defects, congenital, tests

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

The American Heart Association and the American Academy of Pediatrics make every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on November 14, 2008, and by the American Academy of Pediatrics on March 25, 2009.

The American Academy of Pediatrics requests that this document be cited as follows: Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R, Gidding SS, Beekman RH 3rd, Grosse SD; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research; and the American Academy of Pediatrics Section on Cardiology and Cardiac Surgery, and Committee on Fetus and Newborn. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the American Heart Association and American Academy of Pediatrics. *Pediatrics*. 2009;124(2):823–836.

This article has been copublished in *Circulation*.

www.pediatrics.org/cgi/doi/10.1542/peds.2009-1397

doi:10.1542/peds.2009-1397

Accepted for publication Jun 1, 2009

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2009 American Heart Association, Inc., and American Academy of Pediatrics

abstract

BACKGROUND: The purpose of this statement is to address the state of evidence on the routine use of pulse oximetry in newborns to detect critical congenital heart disease (CCHD).

METHODS AND RESULTS: A writing group appointed by the American Heart Association and the American Academy of Pediatrics reviewed the available literature addressing current detection methods for CCHD, burden of missed and/or delayed diagnosis of CCHD, rationale of oximetry screening, and clinical studies of oximetry in otherwise asymptomatic newborns. MEDLINE database searches from 1966 to 2008 were done for English-language papers using the following search terms: congenital heart disease, pulse oximetry, physical examination, murmur, echocardiography, fetal echocardiography, and newborn screening. The reference lists of identified papers were also searched. Published abstracts from major pediatric scientific meetings in 2006 to 2008 were also reviewed. The American Heart Association classification of recommendations and levels of evidence for practice guidelines were used. In an analysis of pooled studies of oximetry assessment performed after 24 hours of life, the estimated sensitivity for detecting CCHD was 69.6%, and the positive predictive value was 47.0%; however, sensitivity varied dramatically among studies from 0% to 100%. False-positive screens that required further evaluation occurred in only 0.035% of infants screened after 24 hours.

CONCLUSIONS: Currently, CCHD is not detected in some newborns until after their hospital discharge, which results in significant morbidity and occasional mortality. Furthermore, routine pulse oximetry performed on asymptomatic newborns after 24 hours of life, but before hospital discharge, may detect CCHD. Routine pulse oximetry performed after 24 hours in hospitals that have on-site pediatric cardiovascular services incurs very low cost and risk of harm. Future studies in larger populations and across a broad range of newborn delivery systems are needed to determine whether this practice should become standard of care in the routine assessment of the neonate. *Pediatrics* 2009;124:823–836

Congenital heart disease occurs in 9 of every 1000 livebirths.¹ Approximately one quarter of these children will have critical congenital heart disease (CCHD), which by definition requires surgery or catheter intervention in the first year of life.² Congenital malformations are one of the

leading causes of infant death in the United States and other developed nations, and CCHD is responsible for more deaths than any other type of malformation.^{3,4} Most newborns with CCHD can be diagnosed by echocardiography, palliated with prostaglandin infusion, and treated with surgery or transcatheter interventions. In the current era, congenital heart surgery allows for repair or palliation of nearly all types of congenital heart malformations. Congenital heart surgery, together with transcatheter interventions, has resulted in a marked improvement in survival for those with CCHD.⁵ Intervention is typically performed in the first weeks of life to optimize hemodynamics and prevent end-organ injury associated with delayed diagnosis. Because timely recognition of CCHD could improve outcomes, it is important to identify and evaluate strategies to enhance early detection. Pulse oximetry has been proposed as one such strategy, and legislation has been proposed to support this practice.⁶

The present statement reviewed the existing data to evaluate the potential role of pulse oximetry in examining newborns for CCHD. A writing group was appointed by the American Heart Association (AHA) and the American Academy of Pediatrics to evaluate the available literature addressing current detection methods for CCHD, burden of missed and/or delayed diagnosis of CCHD, rationale of oximetry screening, and clinical studies of oximetry in otherwise asymptomatic newborns. Comprehensive searches of the MEDLINE database from 1966 to 2008 were done for English-language publications in scientific journals using the following search terms: congenital heart disease, pulse oximetry, physical examination, murmur, echocardiography, fetal echocardiography, and newborn screening. The reference lists of

identified papers were also searched. Published abstracts from major pediatric scientific meetings in 2006 to 2008 were also reviewed. The AHA classification of recommendations and levels of evidence for practice guidelines were used. The classification of recommendations and levels of evidence are shown in Table 1.

PREVALENCE AND SCOPE OF THE PROBLEM

Currently, children with CCHD are diagnosed by a variety of mechanisms. Neonates with CCHD may be diagnosed in the newborn nursery on the basis of physical examination findings, such as heart murmurs, tachypnea, or overt cyanosis. These findings are not always evident before hospital discharge, which may occur before 48 hours of life. A recent study from the United Kingdom suggested that 25% of infants with CCHD were not diagnosed with heart disease until after discharge from the newborn nursery.⁷ The median age of diagnosis in these cases was 6 weeks. A recent publication from the United States suggested that delayed or missed diagnosis occurs in 7 per 100 000 livebirths.⁸ However, because these data are derived

from a birth defect surveillance program with passive and thus incomplete case ascertainment, this calculation most likely represents a minimum estimate.

Newborns with CCHD are susceptible to profound, sudden worsening in clinical status in the first days and weeks of life. These acute physiological changes correspond to changes in pulmonary vascular resistance and closure of the ductus arteriosus. In neonates with CCHD, the ductus arteriosus is often essential for maintaining either pulmonary or systemic blood flow. These CCHD defects are considered *ductus arteriosus-dependent lesions* (Table 2). The newborn hospitalization provides a critical window for caregivers to identify CCHD lesions in order to avoid hemodynamic embarrassment. The timing of constriction or closure of the ductus arteriosus also explains why children with CCHD may be particularly vulnerable to cardiovascular collapse soon after discharge from the newborn nursery.

Morbidity and Sequelae

With the advent of prostaglandin therapy for ductus arteriosus-dependent lesions, many previously lethal con-

TABLE 1 Classification of Recommendations and Level of Evidence

Classification of recommendations	
Class I:	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective and should be performed. Benefit >>> risk.
Class II:	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa:	Weight of evidence/opinion is in favor of usefulness/efficacy. It is reasonable to perform procedure/administer treatment. Benefit >> risk. Additional studies with focused objectives needed.
Class IIb:	Usefulness/efficacy is less well established by evidence/opinion. Procedure/treatment may be considered. Benefit ≥ risk. Additional studies with broad objectives needed; additional registry data would be helpful.
Class III:	Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful. Risk ≥ benefit. No additional studies needed. Procedure/treatment should not be performed/administered because it is not helpful and may be harmful.
Level of evidence	
A:	Data derived from multiple randomized clinical trials or meta-analyses
B:	Data derived from a single randomized trial or nonrandomized studies
C:	Only consensus opinion of experts, case studies, or standard of care

TABLE 2 CCHD Lesions and Associated Clinical Characteristics

Lesion	Prevalence ^a	Hypoxemia	Ductus Arteriosus Dependent
Outflow tract defects			
Tetralogy of Fallot	6.1	Most	Uncommon
D-transposition of the great arteries	4.0	All	Uncommon
Double-outlet right ventricle	1.7	Some	Some
Truncus arteriosus	1.0	All	None
TAPVC	1.2	All	None
Ebstein anomaly	0.6	Some	Some
Right obstructive defects			
Tricuspid atresia	0.5	All	Some
Pulmonary atresia, intact septum	0.8	All	All
Pulmonic stenosis, atresia	6.3	Some	Some
Left obstructive defects			
Hypoplastic left heart	3.3	All	All
Coarctation of the aorta	4.7	Some	Some
Aortic arch atresia or hypoplasia	1.0	Some	All
Aortic valve stenosis (critical)	1.6	Uncommon	Some
Other major heart defects	12.4	Some	Some

TAPVC indicates total anomalous pulmonary venous connection.

^a Per 10 000 livebirths. Data are derived from the Metropolitan Atlanta Congenital Defects Program.¹

genital heart conditions that present with severe hypoxemia, shock, and acidosis in the newborn period are now survivable. The severity of organ damage is a function of the extent of insult, differential flow to organs as the neonatal circulation responds to the hypoxic/ischemic insult, and the oxygen requirement of each organ.

Among sequelae of neonatal hemodynamic compromise, the most important long-term effects relate to the consequences of brain injury from ischemia and reperfusion, because the brain has the highest oxygen requirement of any organ. Cerebrovascular pressure autoregulation and reactivity to CO₂ are affected by hypoxic/ischemic injury, which renders the brain particularly vulnerable to hypotension and decreased cardiac output.⁹ Such hemodynamic instability is prevalent among neonates with CCHD who present with shock. Furthermore, preoperative events may interact with genetic mutations and both intraoperative and postoperative factors in determining later neurodevelopmental outcome.¹⁰

Using brain magnetic resonance imaging, a number of investigators have

demonstrated acute brain injury in the newborn with CCHD before surgical intervention. Periventricular leukomalacia, which occurs secondary to vulnerability of the immature oligodendrocyte to hypoxia/ischemia, free radical attack, and excitotoxicity, and likely circulating cytokines, has been found on magnetic resonance imaging in up to 39% of neonates with CCHD.^{11–14}

Children with CCHD are reported to experience more frequent impairments in motor function, speech and language, visual-motor-perceptual function, and executive function, as well as increased use of special services.^{10,15–22} The greatest frequency of adverse outcomes is found among those with a single ventricle with obstruction to systemic outflow, such as hypoplastic left heart syndrome.²³ In this lesion, systemic perfusion occurs through the patent ductus arteriosus, and ductus closure results in shock and end-organ damage. Prenatal diagnosis of hypoplastic left heart syndrome has been reported in certain studies to reduce early neurological morbidity, with fewer adverse perioperative neurological events such as coma,²⁴ although earlier age at surgery

has not been shown to result in better long-term neurodevelopmental outcomes.²⁵ One could infer that because delayed diagnosis is associated with damage to various end organs, it might also lead to hypoxic/ischemic brain injury; however, further studies are needed to demonstrate a true causal relationship.

Death Due to Delayed Diagnosis

A number of children with CCHD are so severely compromised at presentation that they die before surgical intervention. For example, investigators have reported that between 3% and 6% of neonates with dextro-transposition of the great arteries died because of hemodynamic compromise before surgical intervention could be offered.^{25,26} In a study from the Baltimore-Washington metropolitan area in the 1980s, Kuehl and colleagues²⁷ reported that among 4360 children with any form of congenital heart disease, 76 (1.7%) died before the identification of heart disease. Delayed or missed diagnosis of CCHD accounted for 1.4 deaths per 10 000 livebirths in that series. In 1994, Abu-Harb and colleagues²⁸ reported on death due to unrecognized CCHD in infancy over a 6-year period in a region of northern England. Fifty-six of 185 children died in infancy, and 27 (48%) of these deaths resulted from sequelae of undetected CCHD. The great majority of these subjects had CCHD lesions that might have manifested hypoxemia. In another study from the United Kingdom, Wren and colleagues²⁹ reported that 25% of CCHD lesions were not diagnosed until after hospital discharge, even in the most recent era. The data from these United Kingdom studies suggested that delayed or missed diagnosis of CCHD accounted for 0.4 to 2.0 deaths per 10 000 livebirths.

With the increased use of prenatal ultrasound and a better understanding

of the presentation of CCHD in the past decade, the risk of death before diagnosis has undoubtedly declined, although it is still likely to be important.³⁰ Two recent studies have reported that the rate of mortality due to delayed diagnosis of CCHD is an order of magnitude lower than in the older studies discussed in the previous paragraph. First, a presentation from a study from metropolitan Atlanta, Ga, that used a population-based surveillance system reported that death due to delayed diagnosis of CCHD occurred in 1.0 of every 100 000 livebirths and may be decreasing with time³¹; however, this estimate could be understated, because in that study, only deaths that occurred before arrival at a hospital or before the child could be stabilized were attributed to delayed diagnosis. Another preliminary study from California reported 2.0 deaths per 100 000 livebirths related to delayed diagnosis of CCHD.³² Presumably, earlier recognition of CCHD in these patients could have prevented death in at least some of these cases.

Impairment in cardiovascular function from delayed diagnosis may also adversely impact survival during neonatal cardiovascular surgery and recovery. Certain studies that compared outcomes in prenatal and postnatal diagnosis of CCHD have reported better short-term results for those who were diagnosed prenatally.^{25,33} However, numerous other studies have failed to document any survival benefit of prenatal diagnosis among infants undergoing congenital heart surgery.^{34,35}

In summary, delayed or missed diagnosis is associated with significant morbidity, the most significant being hypoxic/ischemic brain injury. In addition, delayed diagnosis appears to lead directly and indirectly to higher mortality in this population, although the number of deaths that might be pre-

vented through pulse oximetry screening remains to be determined. Methods to improve early detection of CCHD appear warranted.

Customary Practice

Children with CCHD are identified in a variety of ways. Since the late 1980s, prenatal ultrasound has been used to screen for congenital anomalies. An anatomic ultrasound is typically performed at 18 to 20 weeks' gestation. During this process many, but not all, cases of CCHD can be identified by a methodical scan.³⁶ When CCHD is identified by this approach, the patient is often referred to a pediatric cardiologist for confirmatory imaging and counseling. With knowledge that the fetus has CCHD, the newborn can be delivered in a hospital capable of providing intensive care, including prostaglandin, as well as mechanical ventilation. The newborn can be stabilized and transferred to a congenital heart center.

Prenatal ultrasound, performed by those with specific training in congenital heart disease, can identify a variety of CCHD lesions; however, numerous studies have reported that even when fetal ultrasound is routinely performed during pregnancy, fewer than 50% of cases of CCHD are identified. Most of the published literature comes from European countries, which tend to have more centralized healthcare systems and uniform practices vis-à-vis prenatal ultrasound.^{30,37–41} As such, these systems may represent the best-case scenario for population prenatal ultrasound screening. In the United States, many congenital surgery referral centers have reported prenatal detection rates >50% for functional single-ventricle lesions,^{35,42} although the detection rate is generally <30% for CCHD lesions with 2-ventricle circulation.^{43,44} These studies from referral centers may be bi-

ased toward higher detection rates, and population-based data on prenatal detection of CCHD in the United States are sparse.

There are several factors that might account for the relatively low prenatal CCHD detection rate. The quality of anatomic ultrasounds varies considerably.^{45,46} A number of medical professionals, including radiologists, perinatologists, and general obstetricians with varying degrees of training, as well as technicians, perform these ultrasounds.⁴⁷ In addition to concerns about the quality, there may be limited access to prenatal ultrasound. In the United States, an anatomic ultrasound is not performed in all women.⁴⁸ The availability of anatomic ultrasound is likely to be particularly limited in certain racial/ethnic or low-socioeconomic-status groups.⁴⁹ Therefore, although prenatal ultrasound plays an important part in the timely identification of CCHD, population-based data demonstrate that this methodology by itself is insufficient to identify a high proportion of cases.

After birth, screening for congenital heart disease by primary care providers is currently accomplished by physical examination within the first 24 hours of life and on subsequent nursery visits. Supplemental tests, including electrocardiograms, pulse oximetry, and chest radiographs, are often obtained in suspicious cases. Echocardiograms can be done either with or without pediatric cardiology consultation. This strategy blends diagnostic assessment approaches from the 1950s to 1970s with the increasing availability of echocardiography. It results in substantial case identification but is regarded as inefficient and costly and misses a significant number of newborns with CCHD.⁵⁵

Skilled physical examination, a sensitive and specific screening tool in

older children, does not always distinguish between neonates with and without congenital heart disease.^{50,56} Hypoxemia is difficult to detect in newborns, and the transitional circulation masks important clinical findings such as absent femoral pulses while the ductus arteriosus remains patent. Reports of the late detection of coarctation of the aorta have been published since the 1960s.⁵¹ Perhaps most importantly, physical examination skills are on the decline in current trainees.⁵²

Heart murmurs have a prevalence of between 0.6% and 4.2% in newborns and are mistakenly considered a hallmark of heart disease.^{53,54} They often do not accompany critical heart defects, particularly those with valve atresia and transposition. Flow murmurs of the transitional circulation, transient tricuspid regurgitation, and small ventricular septal defects are common and of no clinical importance in newborns. Conversely, murmurs of many important complex heart defects, such as tricuspid atresia with ventricular septal defect, double-outlet right ventricle, and total anomalous pulmonary venous return, emerge only after the decline in pulmonary resistance and after neonatal discharge and are often heard but not considered pathological. Practicing pediatricians currently have limited experience in discriminating innocent from pathological murmurs. In a contemporary series in which echocardiography was performed to evaluate for possible heart disease based on suspicious physical examination, fewer than 15% of subjects were found to have significant congenital heart disease.⁵⁵

Clinical experience and epidemiological observations suggest that although physical examination, electrocardiogram, and chest radiograph are useful in identifying many cases of serious congenital heart disease postnatally,

they do not have sufficient sensitivity and specificity to detect all cases. Echocardiography, although an essential diagnostic tool, has serious limitations as a universal screening tool, particularly its cost.⁵⁶ When used as a screening tool, echocardiography has a high frequency of either false-positive results (usually related to the transitional circulation) or recognition of clinically benign diagnoses (eg, small muscular ventricular septal defects). In addition, there may be an inadequate supply of trained personnel who could perform this screening with a reasonable degree of accuracy. Therefore, there is considerable interest in improving the detection of CCHD with novel diagnostic techniques.

PULSE OXIMETRY AND DETECTION OF CCHD

A common feature of many forms of congenital heart disease is hypoxemia. Hypoxemia results from the mixing of systemic and venous circulations or parallel circulations as one might see in dextro-transposition of the great arteries. Hypoxemia may result in obvious cyanosis. However, generally, 4 to 5 g of deoxygenated hemoglobin is needed to produce visible central cyanosis, independent of hemoglobin concentration.⁵⁷ For the typical newborn with a hemoglobin concentration of 20 g/dL, cyanosis will only be visible when arterial oxygen saturation is <80%; if the infant only has a hemoglobin concentration of 10 g/dL, the saturation must be <60% before cyanosis is apparent.⁵⁸ Importantly, those children with mild hypoxemia, with arterial oxygen saturation of 80% to 95%, will not have visible cyanosis. Moreover, the identification of cyanosis is particularly problematic in black and Hispanic neonates because of skin pigmentation.⁵⁷

The majority of CCHD lesions present with some degree of hypoxemia in the

newborn period. Table 2 demonstrates the frequency of the most common forms of CCHD based on data from the Metropolitan Atlanta Congenital Birth Defects Surveillance Program⁵³ and the likelihood of having some degree of hypoxemia in the newborn period. To improve timely detection of CCHD, a number of investigators have proposed that pulse oximetry be considered as a complementary modality to the newborn physical examination.^{59,60}

Pulse oximetry was developed in the early 1970s based on the different absorption spectra between oxygenated and deoxygenated hemoglobin.⁶¹ Deoxygenated hemoglobin absorbs light in the red band (600 to 750 nm), whereas oxygenated hemoglobin absorbs light in the infrared band (850 to 1000 nm). The ratio of light absorbance at these 2 wavelengths correlates with the saturation of hemoglobin in the capillaries.⁶² Pulse oximetry has the potential to identify hypoxemia that might not otherwise produce visible cyanosis, especially among darkly pigmented newborns.

Pulse oximetry is used routinely in the assessment of young children in neonatal intensive care units and emergency departments and has been proposed as an adjunct to the assessment of the newborn in the delivery room.⁶³ As such, some have proposed that pulse oximetry be considered as a vital sign equivalent in importance to pulse, respirations, and blood pressure.⁶⁴ Contemporary use of pulse oximetry has thus already contributed to heightened recognition of congenital heart disease in neonates.

Clinical Studies of Oximetry Screening

Pulse oximetry has gained wide acceptance as a noninvasive method to determine oxygen saturation (SpO₂). The method does not require calibration and is able to provide instantaneous

data that correlate well with blood gas measurements. O'Brien and colleagues⁶⁵ have defined reference data for oxygen saturation in healthy full-term infants during their first 24 hours of life. The median value at 20 to 24 hours of life (97.8%) is similar to the results for healthy full-term infants between 2 and 7 days of age (97.6%).⁶⁶ Other investigators have reported similar results.^{67,68} Beginning in the 1990s, investigators began to explore the possible role of neonatal oximetry in identifying CCHD that might otherwise go undetected. Initially, investigators demonstrated that in neonates with known CCHD, pulse oximetry measurements were significantly lower than in age-matched control subjects. Using a cutoff of 95% in lower-extremity saturation, Hoke and colleagues⁵⁹ suggested that 81% of neonates with CCHD could be identified. Given this association, the question arose as to whether oximetry can successfully identify CCHD in a population of newborns not otherwise suspected of having heart disease. To date, several published studies^{55,59,60,69–75} have used newborn oximetry to screen for CCHD (Table 3). Most studies were relatively small, and screening protocols differed with respect to both age at screening and cutoff levels for an abnormal screen. Nonetheless, the cumulative experience

of these investigations provides a framework for evaluation of the test characteristics of newborn oximetry screening. The results of these studies and differences in study protocols are described below.

Because newborns with CCHD may have clinical deterioration in the first 48 hours of life, one would ideally use oximetry screening soon after delivery. However, arterial oxygen saturation varies considerably in the first 24 hours, with many healthy newborns having arterial saturations of less than 95%. As such, oximetry screening before 24 hours of life can result in a significant number of false-positive results. A study from the United Kingdom reported that the false-positive rate was as high as 5% when oximetry screening was performed in the first 24 hours compared with 1% at the time of hospital discharge.⁷⁶ Therefore, to achieve an acceptable specificity, testing >24 hours after birth would appear to be the most reasonable strategy. This screening strategy assumes that the majority of newborns will not be discharged on the first day of life. With early discharge at less than 24 hours of age, many infants would not be screened.

The establishment of a cutoff threshold for an abnormal Sp_{o2} is important.

Other factors being constant, a higher threshold will increase sensitivity and at the same time decrease specificity. Setting the Sp_{o2} cutoff value closer to the normal level will decrease the number of false-negative screening results at the cost of increasing the number of false-positive screening results. Conversely, a lower Sp_{o2} threshold will lower sensitivity and raise specificity. Although a number of Sp_{o2} thresholds have been proposed, many investigators believe that an Sp_{o2} of ≤95% is appropriate. In studies of healthy populations, the distribution of Sp_{o2} measured in a lower extremity at 24 hours was reported to be 97.3±1.3%.⁶⁸ One study suggested that Sp_{o2} <92% be considered a positive sign of hypoxemia; however, others have argued that a low threshold is likely to result in a number of infants with CCHD being misclassified as normal without markedly improving specificity.⁷⁷

Most published studies of oximetry screening for CCHD have been performed at relatively low altitude. It is known, however, that arterial saturation in children and adults is lower at high altitudes, especially above 5000 ft. Several investigators have reported the normal Sp_{o2} values for neonates at high altitude.^{77,78} Bakr and colleagues⁷⁸ reported a mean Sp_{o2} of

TABLE 3 Results of Studies Examining Oximetry Screening for CCHD

Study's First Author	n	Age at Screening, h	Probe Location	Cutoff for Normal	FP	FP Rate, %	TP	FN	TN	PPV, %	NPV, %	Sensitivity, %	Specificity, %
Hoke ⁵⁹	2876	<24	H+F	≥92/<7	53	1.84	4	0	2819	7.0	98.1	100.0	100
Richmond ⁷¹	5626	11.7	F	≥95	51	0.91	9	4	5621	15.0	99.9	69.2	99.8
Koppe ⁶⁰	11 281	72	F	≥96	1	0.01	3	2	11 275	75.0	99.98	60.0	99.9
Reich ⁵⁵	2114	>24	H+F	≥95/<4	2	0.09	1	1	2110	33.3	99.95	50.0	99.9
Bakr ⁷²	5211	31.7	H+F	≥94	1	0.02	3	2	5211	75.0	99.9	60.0	99.9
Rosati ⁷³	5292	72	F	≥96	1	0.02	2	1	5288	66.7	100	66.7	100
Arlettaz ⁶⁹	3262	8	F	≥95	7	0.21	17	3	3235	70.8	99.9	85.0	99.8
Kawalec ⁷⁰	27 200	26	F	≥95	13	0.05	7	1	27 179	35.0	99.9	87.5	99.9
Meberg ⁷⁴	50 008	6	F	≥95	324	0.65	43	NA	NA	11.7	NA	NA	NA
Sendelbach ⁷⁵	10 976	4	F	≥96	636	4.5	0	1	10 340	0	99.9	0	95.5
All studies	123 846				1089	0.87	89	15	122 762	16.4	99.9	75 ^a	99.3
Studies >24 h	51 098				18	0.035	16	7	51 063	47.0	99.9	69.6	99.9

FP indicates false-positive; TP, total positive; FN, false-negative; TN, total negative; PPV, positive predictive value; NPV, negative predictive value; H+F, hand and foot; F, foot; and NA, not available.

^a Excludes study by Meberg et al⁷⁴ because false-negative data were not included.

95.4% at 24 hours of life from a population evaluated at 5300 ft. Presumably, one would need to establish a different threshold for high-altitude populations to maintain a reasonable balance between sensitivity and specificity of oximetry screening. Pilot projects are currently under way to examine how high altitude impacts newborn screening with oximetry.

Another variation among published oximetry screening studies has been the position of the pulse oximetry probe with respect to the upper or lower extremity. Previous investigators have demonstrated slightly lower SpO₂ measurements in the lower extremity than in the upper extremity in the newborn at 24 hours of life due to shunting at the level of the ductus arteriosus.⁶⁸ In general, the mean difference between the SpO₂ in the upper and lower extremities is <1%; however, some newborns with CCHD may have a more profound difference in saturation between the upper and lower body. For example, neonates with some forms of left obstructive heart lesions, such as critical coarctation of the aorta, in which the ductus arteriosus supplies a portion of the systemic flow, may have lower SpO₂ readings in legs than in the arm.⁵⁹

Some investigators proposed that oximetry screening should include measurements of both upper and lower extremities and that differences in SpO₂ of more than 3% or 4% be used to identify newborns with CCHD who might otherwise be missed by measuring lower-extremity SpO₂ alone.^{55,79} One study that examined newborns with known CCHD suggested that the addition of upper and lower measurements would increase sensitivity from 89.4% to 92.4% without a decrease in specificity.⁷⁹ However, these data were not obtained in the setting of a screening birth cohort but rather among those with known CCHD. It is possible

that the inclusion of both upper and lower SpO₂ measurements would result in a significantly higher false-positive rate. Moreover, screening both upper and lower extremities would increase the time required to screen a single newborn. Therefore, a single lower-extremity reading would appear to be the most appropriate for the purposes of large-scale screening.

The results of published studies using oximetry screening to detect CCHD in a representative birth population are shown in Table 3. Ten studies with a total of 123 846 infants screened reported a mean of 0.87% of infants with false-positive screens but a false-positive rate of 0.035% when screening was done after 24 hours; however, there was remarkable dispersion in reported screening performance. Five studies reported a low false-positive rate ($\leq 0.1\%$) when measurements were made after 24 hours of life. The low false-positive rate is somewhat surprising given the reported variation of SpO₂ reported in normal newborn populations. It is not known whether there might be a publication bias in that only studies with favorable specificity might be published. A low false-positive rate would reduce the number of unnecessary echocardiograms. Nine of 10 studies listed in Table 3 reported sensitivity of <90%, ranging from 0% to 87%. This is explained in part by the fact that hypoxemia is not present in some forms of CCHD (Table 2).

False-positive results can be a cause for concern in public health newborn screening programs that are based on the laboratory analysis of dried blood spot specimens collected on filter paper cards. These false-positive results typically require families to be notified to bring their child in for further testing, and there can be a delay of several days before the results of such testing become available. False-positive new-

born screening results have been reported to sometimes result in lasting parental anxiety and possibly elevated use of healthcare services.⁸⁰ In the case of pulse oximetry, this type of psychosocial risk of harm is very unlikely to be a problem in the typical hospital setting for infants not subject to early discharge. A positive test result leads to an immediate referral for an echocardiogram, and the results are reported before discharge. However, when the birth center does not have ready access to cardiac consultation, delay in hospital discharge or transfer to another facility may result in anxiety and added stress.

Oximetry screening may be less effective at identifying some CCHD lesions at greatest risk for acute cardiovascular compromise, namely, obstructive left heart lesions. A published analysis of oximetry has suggested that the difficulty in detecting hypoplastic left heart syndrome, aortic stenosis, and coarctation of the aorta limits the usefulness of this screening tool.⁸¹ However, it should be noted that nearly all forms of CCHD—even those unrelated to left heart obstruction—can result in serious morbidity and even death when diagnosis is delayed.^{25,31} Moreover, oximetry can detect a significant number of newborns with obstructive left heart lesions and right-to-left shunting at the ductus arteriosus (Table 4). In published series, hypoplastic left heart syndrome was detected in all cases, and coarctation of the aorta was detected in just over half the cases. Studies that have obtained SpO₂ measurements on newborns with known CCHD have similarly reported that a lower-extremity SpO₂ of $\leq 95\%$ detected hypoplastic left heart syndrome in all cases and critical coarctation of the aorta in the majority of cases.^{59,79}

Several studies of screening oximetry have reported incidental findings of

TABLE 4 Detection of CCHD Lesions From Screening Studies, Assuming a Positive Screen as SpO₂ ≤95%

	Kao ⁸²	Hoke ⁵⁹	Richmond ⁷¹	Koppel ⁶⁰	Reich ⁵⁵	Bakr ⁷²	Rosati ⁷³	Arlettaz ⁶⁹	Kawalec ⁷⁰	Total	Percent	95% CI
DORV	0	0	0	0	0	0	0	3/3	0	3/3	100	44–100
HLHS	0	0	0	0	0	0	0	3/3	2/2	5/5	100	57–100
PA	0	0	3/3	0	0	1/1	0	1/1	0	5/5	100	57–100
d-TGA	2/2	1/1	3/3	0	1/1	0	0	2/2	0	9/9	100	70–100
TAPVC	0	0	0	2/2	1/2	1/1	1/1	0	1/1	6/7	85.7	47–97
Truncus	0	0	0/1	1/1	2/2	1/1	0	3/3	0	7/8	87.5	53–92
TA	0	0	0	0	0	0	0	0	1/1	1/1	100	21–100
AA/AS	2/3	0	0	0	0	0	0	1/1	0	3/4	75.0	30–100
TOF	5/5	1/1	1/4	0	2/3	0	0	0	0	9/13	69.2	49–87
AVSD	2/2	0	0	0	1/1	0	0	1/2	0	4/5	80.0	38–96
CoA	0/3	1/1	2/3	0/1	0	0	1/2	1/1	3/4	8/15	53.3	30–75
PS	0	1/1	0/1	0	0	0/1	0	1/3	0	2/6	33.3	10–70

CI indicates confidence interval; DORV, double-outlet right ventricle; HLHS, hypoplastic left heart syndrome; PA, pulmonary atresia; d-TGA, dextro-transposition of the great arteries; TAPVC, total anomalous pulmonary venous connection; Truncus, truncus arteriosus; TA, tricuspid atresia; AA/AS, aortic atresia/aortic stenosis; TOF, tetralogy of Fallot; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; and PS, pulmonary stenosis.

persistent fetal circulation, defined as elevated pulmonary vascular resistance and right-to-left shunting at the ductus arteriosus. In some reports, these cases have been reported as false-negative findings. In other studies, the investigators have emphasized the benefits of identifying these patients.⁶⁹ The finding of persistent fetal circulation in otherwise healthy newborns may be of benefit to medical care.⁸⁵ An understanding of the outcome of newborns who are asymptomatic with a decreased lower-extremity SpO₂ will be needed to understand whether identification of this population is a true benefit of oximetry screening.

LIMITATIONS AND CHALLENGES TO NEWBORN PULSE OXIMETRY IN DETECTION OF CCHD

There are technical limitations to oximetry measurement in the newborn. As noted above, the mean SpO₂ in the newborn at >24 hours of age is 97% to 98%; however, when continuous pulse oximetry is used, multiple investigators have demonstrated periodic and/or sustained desaturation below 95% during sleep, feeding, and crying.^{65,68,84,85} Sustained rather than variable hypoxemia is consistent with the diagnosis of cyanotic congenital heart disease. Low oximetry readings in the setting of normal arterial oxygen saturation have been reported by

multiple investigators.^{76,86,87} In fact, falsely low oximetry readings in the newborn population are known to be associated with low peripheral perfusion and motion artifact,^{88,89} probe placement site and partial probe detachment,⁹⁰ and hyperbilirubinemia or dyshemoglobinemias. It is known that technical differences between the various types of oximeters in general use include measurement of functional or fractional oxygen saturation, preset signal-averaging times, and methods for the exclusion of motion artifact.⁹¹ There has been some research into the variability among various commercially available pulse oximeters; however, most of the variability occurs in the cyanotic range (<90%) or at the highest saturations (99% to 100%). The peak performance of the commercially available oximeters occurs in the range of 92% to 97%.⁹² Therefore, in the critical range for oximetry screening (94% to 97%), the variability of the most commonly used oximeters should be negligible.

There has also been concern that pulse oximeters may not be as accurate in darkly pigmented adults and children. At low SpO₂ levels (<70%), commercially available oximeters appear to overestimate arterial saturation by 3% in darkly pigmented subjects.⁹³ However, when SpO₂ is >90%, measurement bias

related to skin pigmentation appears negligible (<0.2%). Lastly, the quality of oximetry measurements may be lower when performed in a screening setting.⁹⁴

When neonates are identified as having hypoxemia (SpO₂ ≤95%), it is necessary to evaluate them for CCHD. Although physical examination, chest radiography, and electrocardiography can assist in this process, echocardiography is now considered the definitive diagnostic modality. Whenever possible, the echocardiograms should be interpreted by pediatric cardiologists; major errors in the interpretation of a newborn echocardiogram by trained pediatric cardiologists are rare.⁹⁵

Although the majority of metropolitan areas in the United States have access to pediatric subspecialists, such as pediatric cardiologists, availability in rural areas can be limited. Approximately 15% of births in the United States occur in non-metropolitan areas.⁹⁶ In these settings, echocardiograms are often performed by sonographers without formal pediatric training and are interpreted by adult cardiologists. Several investigators have found that the accuracy of pediatric echocardiograms interpreted by adult cardiologists is low.^{95,97} One alternative is to use telemedicine, in which echocardiograms are interpreted distantly at a pediatric referral center.^{98,99} The accu-

racy may be improved by direct guidance of the sonographers by a pediatric cardiologist via videoconferencing. This approach, which has been shown to be efficient and accurate, may be required to enhance detection of CCHD in rural or underserved areas. Another option is for newborns with suspected CCHD to be transported to a tertiary center. This strategy, however, would be expensive and impractical in many cases.

The cost of routine pulse oximetry performed on asymptomatic newborns after 24 hours of age includes both the direct cost of the pulse oximetry and the follow-up costs of any additional examinations and transfers. The largest direct cost component is staff time. At experienced centers, it may take a technician only 45 seconds on average to perform pulse oximetry on a newborn infant. The cost of diagnostic evaluation of infants who are referred for further examination after pulse oximetry depends on the frequency of referral, the duration of the diagnostic evaluation, and the ability for the evaluation to be performed without transfer to another center. A detailed cost accounting, to be reported elsewhere, indicates an average cost of approximately \$1 per asymptomatic newborn infant, which includes the cost of diagnostic evaluations, in hospitals with moderate obstetric volume and ready access to pediatric echocardiography. Further work is needed to assess the cost and yield of routine pulse oximetry examination of newborns in a wider range of settings.

Oximetry to enhance the detection of CCHD has been considered previously in an evidence review sponsored by

the United Kingdom's National Health Service Health Technology Assessment program.¹⁰⁰ The investigators observed that pulse oximetry is much more effective than current clinical practice in identifying infants with CCHD and more accurate and much less expensive than screening all newborns with echocardiography. The incremental cost per timely diagnosis of life-threatening congenital heart defects was calculated to be approximately \$10 000 for pulse oximetry and \$10 million for screening echocardiography. Although pulse oximetry was regarded as more promising than either the current practice or other options, the report called for further research to improve estimates of test performance and to inform timing, diagnostic, and management strategies and to "investigate the psychosocial effects of newborn screening for congenital heart disease" (p 127).¹⁰⁰ Another report has suggested families were quite receptive to newborn screening with pulse oximetry, with 99.8% of a sample of parents in Poland reported to approve of the screening technique.⁷⁰

SUMMARY

The association of delayed diagnosis of CCHD with mortality, morbidity, and disability provides a rationale for strategies such as pulse oximetry assessment to improve early detection. Some studies have reported a reasonable detection rate with pulse oximetry; however, the usefulness of oximetry in clinical practice is not well established (Class IIb, Level of Evidence C; Level of Evidence C corresponds to observational studies [case-control and cohort design]). Additional studies in larger populations and

across a broad range of newborn delivery systems are needed to determine whether this practice should become the standard of care in the routine assessment of the neonate.

Currently, pulse oximetry is being performed routinely in some delivery centers in the United States and elsewhere.¹⁰¹ Because pulse oximetry cannot detect all cases of CCHD, the diagnoses in some infants will be missed until after discharge from the newborn nursery. Such cases will provoke the question of whether the newborn oximetry screen was performed accurately. Therefore, it is reasonable for centers that routinely use pulse oximetry to ensure the fidelity of oximetry measurements through periodic quality assessment. Parents and caretakers should also be informed that pulse oximetry cannot detect all cases of CCHD, and hence, a negative test result does not exclude the possibility of heart disease.

Call for Future Studies

Collaborative studies among hospitals conducting routine pulse oximetry should analyze pooled data and report detection, false-positive rates, and false-negative rates of CCHD. A pilot study of pulse oximetry screening has recently completed enrollment at 6 English hospitals by the National Institute for Health Research.¹⁰² In addition, a comprehensive assessment of the impact of pulse oximetry assessment and early detection of CCHD on morbidity, postoperative survival, and hospital costs will allow a more critical evaluation of the economic impact of efforts to improve timely diagnosis of CCHD.

DISCLOSURES

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
William T. Mahle	Emory University School of Medicine	None	None	None	None	None	None	None
Robert H. Beekman III	Cincinnati Children's Hospital Medical Center	None	None	None	None	None	AGA Medical Inc (Device Proctor) ^a ; The Medicines Co (DSMC) ^a	None
Samuel S. Gidding	Nemours Children's Clinic	None	None	None	None	None	None	None
Scott D. Grosse	Centers for Disease Control and Prevention	None	None	None	None	None	None	None
Tracey R. Hoke	University of Virginia	None	None	None	None	None	None	None
Robert Koppel	Schneider Children's Hospital	None	None	None	None	None	None	None
G. Paul Matherne	University of Virginia	None	None	None	None	None	None	None
Jane W. Newburger	Boston Children's Heart Foundation	None	None	None	None	None	None	None
Frank C. Smith	Pediatric Cardiology Associates of Central New York	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

^a Modest.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Constance Cephus	Texas Children's Hospital	None	None	None	None	None	None	None
Steven D. Colan	Children's Hospital Boston	None	None	None	None	None	None	None
Rodney Howell	University of Miami	None	None	None	None	None	None	None
Alex Kemper	Duke University	None	None	None	None	None	None	None
LuAnn Minich	Intermountain Healthcare	None	None	None	None	None	None	None
Catherine L. Webb	Northwestern University	None	None	None	None	Johnson & Johnson ^a	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

^a Significant.

References

1. Botto LD, Correa A, Erickson JD. Racial and temporal variations in the prevalence of heart defects. *Pediatrics*. 2001;107:E32
2. Talner CN. Report of the New England Regional Infant Cardiac Program, by Donald C. Fyler, MD, *Pediatrics*, 1980;65(suppl):375–461. *Pediatrics*. 1998;102(pt 2):258–259
3. Heron MP, Smith BL. Deaths: leading causes for 2003. *Natl Vital Stat Rep*. 2007;55:1–92
4. Rosano A, Botto LD, Botting B, Mastroiacovo P. Infant mortality and congenital anomalies from 1950 to 1994: an international perspective. *J Epidemiol Community Health*. 2000;54:660–666
5. Boneva RS, Botto LD, Moore CA, Yang Q, Correa A, Erickson JD. Mortality associated with congenital heart defects in the United States: trends and racial disparities, 1979–1997. *Circulation*. 2001;103:2376–2381
6. Mississippi 2005 Regular Session, House Bill 1052. 2005
7. Brown KL, Ridout DA, Hoskote A, Verhulst L, Ricci M, Bull C. Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates. *Heart*. 2006;92:1298–1302

8. Aamir T, Kruse L, Ezeakudo O. Delayed diagnosis of congenital cardiovascular malformations (CCVM) and pulse oximetry screening of newborns. *Acta Paediatr.* 2007;96:1146–1149
9. Pryds O, Greisen G, Lou H, Friis-Hansen B. Vasoparalysis associated with brain damage in asphyxiated term infants. *J Pediatr.* 1990;117(pt 1):119–125
10. Limperopoulos C, Majnemer A, Shevell MI, Rohlicek C, Rosenblatt B, Tchervenkov C, Darwish HZ. Predictors of developmental disabilities after open heart surgery in young children with congenital heart defects. *J Pediatr.* 2002;141:51–58
11. Wu YW, Escobar GJ, Grether JK, Croen LA, Greene JD, Newman TB. Chorioamnionitis and cerebral palsy in term and near-term infants. *JAMA.* 2003;290:2677–2684
12. Mahle WT, Tavani F, Zimmerman RA, Nicolson SC, Galli KK, Gaynor JW, Clancy RR, Montenegro LM, Spray TL, Chiavacci RM, Wernovsky G, Kurth CD. An MRI study of neurological injury before and after congenital heart surgery. *Circulation.* 2002;106(suppl 1):I-109–I-114
13. McQuillen PS, Barkovich AJ, Hamrick SE, Perez M, Ward P, Glidden DV, Azakie A, Karl T, Miller SP. Temporal and anatomic risk profile of brain injury with neonatal repair of congenital heart defects. *Stroke.* 2007;38(suppl):736–741
14. Dent CL, Spaeth JP, Jones BV, Schwartz SM, Glauser TA, Hallinan B, Pearl JM, Khoury PR, Kurth CD. Brain magnetic resonance imaging abnormalities after the Norwood procedure using regional cerebral perfusion. *J Thorac Cardiovasc Surg.* 2005;130:1523–1530
15. Wernovsky G, Stiles KM, Gauvreau K, Gentles TL, duPlessis AJ, Bellinger DC, Walsh AZ, Burnett J, Jonas RA, Mayer JE Jr, Newburger JW. Cognitive development after the Fontan operation. *Circulation.* 2000;102:883–889
16. Bellinger DC, Wypij D, Kuban KC, Rappaport LA, Hickey PR, Wernovsky G, Jonas RA, Newburger JW. Developmental and neurological status of children at 4 years of age after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. *Circulation.* 1999;100:526–532
17. Bellinger DC, Rappaport LA, Wypij D, Wernovsky G, Newburger JW. Patterns of developmental dysfunction after surgery during infancy to correct transposition of the great arteries. *J Dev Behav Pediatr.* 1997;18:75–83
18. Limperopoulos C, Majnemer A, Shevell MI, Rosenblatt B, Rohlicek C, Tchervenkov C, Darwish HZ. Functional limitations in young children with congenital heart defects after cardiac surgery. *Pediatrics.* 2001;108:1325–1331
19. Forbess JM, Visconti KJ, Hancock-Friesen C, Howe RC, Bellinger DC, Jonas RA. Neurodevelopmental outcome after congenital heart surgery: results from an institutional registry. *Circulation.* 2002;106(suppl 1):I-95–I-102
20. Ellerbeck KA, Smith ML, Holden EW, McMenamin SC, Badawi MA, Brenner JI, Kan JS, Hyman SL. Neurodevelopmental outcomes in children surviving d-transposition of the great arteries. *J Dev Behav Pediatr.* 1998;19:335–341
21. Samango-Sprouse C, Suddaby EC. Developmental concerns in children with congenital heart disease. *Curr Opin Cardiol.* 1997;12:91–98
22. Wright M, Nolan T. Impact of cyanotic heart disease on school performance. *Arch Dis Child.* 1994;71:64–70
23. Mahle WT, Visconti KJ, Freier MC, Kanne SM, Hamilton WG, Sharkey AM, Chinnock RE, Jenkins KJ, Isquith PK, Burns TG, Jenkins PC. Relationship of surgical approach to neurodevelopmental outcomes in hypoplastic left heart syndrome. *Pediatrics.* 2006;117:e90–e97
24. Mahle WT, Spray TL, Gaynor JW, Clark BJ III. Unexpected death after reconstructive surgery for hypoplastic left heart syndrome. *Ann Thorac Surg.* 2001;71:61–65
25. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Kachaner J, Sidi D. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. *Circulation.* 1999;99:916–918
26. Soongswang J, Adatia I, Newman C, Smallhorn JF, Williams WG, Freedom RM. Mortality in potential arterial switch candidates with transposition of the great arteries. *J Am Coll Cardiol.* 1998;32:753–757
27. Kuehl KS, Loffredo CA, Ferencz C. Failure to diagnose congenital heart disease in infancy. *Pediatrics.* 1999;103(pt 1):743–747
28. Abu-Harb M, Wyllie J, Hey E, Richmond S, Wren C. Presentation of obstructive left heart malformations in infancy. *Arch Dis Child Fetal Neonatal Ed.* 1994;71:F179–F183
29. Wren C, Reinhardt Z, Khawaja K. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. *Arch Dis Child Fetal Neonatal Ed.* 2008;93:F33–F35
30. Acharya G, Sitras V, Maltau JM, Dahl LB, Kaarensen PI, Hanssen TA, Lunde P. Major congenital heart disease in Northern Norway: shortcomings of pre- and postnatal diagnosis. *Acta Obstet Gynecol Scand.* 2004;83:1124–1129

31. Riehle-Colarusso T, Mahle WT, Correa A. Death due to delayed diagnosis of congenital heart disease: a contemporary population-based study. *Congenit Heart Dis*. 2007;2:376. Abstract
32. Chang RK. How many infants with critical congenital heart disease are missed? *Circulation*. 2007;116(suppl II):II-614. Abstract
33. Tworetzky W, McElhinney DB, Reddy VM, Brook MM, Hanley FL, Silverman NH. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. *Circulation*. 2001;103:1269–1273
34. Mahle WT, Clancy RR, McGaurn SP, Goin JE, Clark BJ. Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. *Pediatrics*. 2001;107:1277–1282
35. Tweddell JS, Hoffman GM, Mussatto KA, Fedderly RT, Berger S, Jaquiss RD, Ghanayem NS, Frisbee SJ, Litwin SB. Improved survival of patients undergoing palliation of hypoplastic left heart syndrome: lessons learned from 115 consecutive patients. *Circulation*. 2002;106(suppl I):I-82–I-89
36. Allan LD. A practical approach to fetal heart scanning. *Semin Perinatol*. 2000;24:324–330
37. Hunter S, Heads A, Wyllie J, Robson S. Prenatal diagnosis of congenital heart disease in the northern region of England: benefits of a training programme for obstetric ultrasonographers. *Heart*. 2000;84:294–298
38. Klein SK, Cans C, Robert E, Jouk PS. Efficacy of routine fetal ultrasound screening for congenital heart disease in Isère County, France. *Prenat Diagn*. 1999;19:318–322
39. Randall P, Brealey S, Hahn S, Khan KS, Parsons JM. Accuracy of fetal echocardiography in the routine detection of congenital heart disease among unselected and low risk populations: a systematic review. *BJOG*. 2005;112:24–30
40. Tegnander E, Williams W, Johansen OJ, Blaas HG, Eik-Nes SH. Prenatal detection of heart defects in a non-selected population of 30,149 fetuses: detection rates and outcome. *Ultrasound Obstet Gynecol*. 2006;27:252–265
41. Westin M, Saltvedt S, Bergman G, Kublickas M, Almström H, Grunewald C, Valentin L. Routine ultrasound examination at 12 or 18 gestational weeks for prenatal detection of major congenital heart malformations? A randomised controlled trial comprising 36,299 fetuses. *BJOG*. 2006;113:675–682
42. Gaynor JW, Mahle WT, Cohen MI, Ittenbach RF, DeCampi WM, Steven JM, Nicolson SC, Spray TL. Risk factors for mortality after the Norwood procedure. *Eur J Cardiothorac Surg*. 2002;22:82–89
43. Hancock Friesen CL, Zurakowski D, Thiagarajan RR, Forbess JM, del Nido PJ, Mayer JE, Jonas RA. Total anomalous pulmonary venous connection: an analysis of current management strategies in a single institution. *Ann Thorac Surg*. 2005;79:596–606
44. Brown JW, Park HJ, Turrentine MW. Arterial switch operation: factors impacting survival in the current era. *Ann Thorac Surg*. 2001;71:1978–1984
45. Queisser-Luft A, Stopfkuchen H, Stolz G, Schlaefer K, Merz E. Prenatal diagnosis of major malformations: quality control of routine ultrasound examinations based on a five-year study of 20,248 newborn fetuses and infants. *Prenat Diagn*. 1998;18:567–576
46. Timor-Tritsch IE. As technology evolves, so should its application: shortcomings of the “18-week anatomy scan.” *J Ultrasound Med*. 2006;25:423–428
47. Bofill JA, Sharp GH. Obstetric sonography: who to scan, when to scan, and by whom. *Obstet Gynecol Clin North Am*. 1998;25:465–478
48. Forrester MB, Merz RD. Use of prenatal diagnostic procedures in pregnancies affected with birth defects, Hawaii, 1986–2002. *Birth Defects Res A Clin Mol Teratol*. 2006;76:778–780
49. Gavin NI, Adams EK, Hartmann KE, Benedict MB, Chireau M. Racial and ethnic disparities in the use of pregnancy-related health care among Medicaid pregnant women. *Matern Child Health J*. 2004;8:113–126
50. Danford DA. Sorting through the haystack: decision analysis and the search for heart disease among children with murmur. *J Pediatr*. 2002;141:465–467
51. Ing FF, Starc TJ, Griffiths SP, Gersony WM. Early diagnosis of coarctation of the aorta in children: a continuing dilemma. *Pediatrics*. 1996;98(pt 1):378–382
52. Gidding SS, Anisman P. What pediatric residents should learn (or what pediatricians should know) about congenital heart disease. *Pediatr Cardiol*. 2003;24:418–423
53. Ainsworth S, Wyllie JP, Wren C. Prevalence and clinical significance of cardiac murmurs in neonates. *Arch Dis Child Fetal Neonatal Ed*. 1999;80:F43–F45
54. Patton C, Hey E. How effectively can clinical examination pick up congenital heart disease at birth? *Arch Dis Child Fetal Neonatal Ed*. 2006;91:F263–F267
55. Reich JD, Miller S, Brogdon B, Casatelli J, Gompf TC, Huhta JC, Sullivan K. The use of pulse oximetry to detect congenital heart disease. *J Pediatr*. 2003;142:268–272

56. Griebisch I, Knowles RL, Brown J, Bull C, Wren C, Dezateux CA. Comparing the clinical and economic effects of clinical examination, pulse oximetry, and echocardiography in newborn screening for congenital heart defects: a probabilistic cost-effectiveness model and value of information analysis. *Int J Technol Assess Health Care*. 2007;23:192–204
57. Lundsgaard C, Van Slyke DD. Cyanosis. *Medicine*. 1923;2:1–76
58. Lees MH. Cyanosis of the newborn infant: recognition and clinical evaluation. *J Pediatr*. 1970;77:484–498
59. Hoke TR, Donohue PK, Bawa PK, Mitchell RD, Pathak A, Rowe PC, Byrne BJ. Oxygen saturation as a screening test for critical congenital heart disease: a preliminary study. *Pediatr Cardiol*. 2002;23:403–409
60. Koppel RI, Druschel CM, Carter T, Goldberg BE, Mehta PN, Talwar R, Bierman FZ. Effectiveness of pulse oximetry screening for congenital heart disease in asymptomatic newborns. *Pediatrics*. 2003;111:451–455
61. Aoyagi T. Pulse oximetry: its invention, theory, and future. *J Anesth*. 2003;17:259–266
62. Salyer JW. Neonatal and pediatric pulse oximetry. *Respir Care*. 2003;48:386–396
63. O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ. Clinical assessment of infant colour at delivery. *Arch Dis Child Fetal Neonatal Ed*. 2007;92:F465–F467
64. Katzman GH. The newborn's SpO₂: a routine vital sign whose time has come? *Pediatrics*. 1995;95:161–162
65. O'Brien LM, Stebbens VA, Poets CF, Heycock EG, Southall DP. Oxygen saturation during the first 24 hours of life. *Arch Dis Child Fetal Neonatal Ed*. 2000;83:F35–F38
66. Poets CF. Assessing oxygenation in healthy infants. *J Pediatr*. 1999;135:541–543
67. Poets CF, Stebbens VA, Lang JA, O'Brien LM, Boon AW, Southall DP. Arterial oxygen saturation in healthy term neonates. *Eur J Pediatr*. 1996;155:219–223
68. Levesque BM, Pollack P, Griffin BE, Nielsen HC. Pulse oximetry: what's normal in the newborn nursery? *Pediatr Pulmonol*. 2000;30:406–412
69. Arlettaz R, Bauschatz AS, Mönkhoff M, Essers B, Bauersfeld U. The contribution of pulse oximetry to the early detection of congenital heart disease in newborns. *Eur J Pediatr*. 2006;165:94–98
70. Kawalec W, Blaz W, Turska-Kmiec A, Zuk M, Helwich E, Tobota Z. Pulse oximetry as a population screening test in detection of critical congenital heart disease in presymptomatic newborns: Polish multicentre study. *Cardiol Young*. 2006;16(suppl 2):25. Abstract
71. Richmond S, Reay G, Abu Harb M. Routine pulse oximetry in the asymptomatic newborn. *Arch Dis Child Fetal Neonatal Ed*. 2002;87:F83–F88
72. Bakr AF, Habib HS. Combining pulse oximetry and clinical examination in screening for congenital heart disease. *Pediatr Cardiol*. 2005;26:832–835
73. Rosati E, Chitano G, Dipaola L, De Felice C, Latini G. Indications and limitations for a neonatal pulse oximetry screening of critical congenital heart disease. *J Perinat Med*. 2005;33:455–457
74. Meberg A, Brüggmann-Pieper S, Due R Jr, Eskedal L, Fagerli I, Farstad T, Frøisland DH, Sannes CH, Johansen OJ, Keljalic J, Markestad T, Nygaard EA, Røsvik A, Silberg IE. First day of life pulse oximetry screening to detect congenital heart defects [published correction appears in *J Pediatr*. 2009;154:629]. *J Pediatr*. 2008;152:761–765
75. Sendelbach DM, Lai S, Jackson GJ, Fixler D, Stehel EK, Engle WD. Pulse oximetry (POx) screening of term and late pre-term neonates at 4 hours postnatal (PN) to detect cyanotic congenital heart disease (CCHD). Presented at: Pediatric Academic Societies; Honolulu, Hawaii; May 2–6, 2008. Abstract E-PAS2008:5896.2
76. Thangaratinam S, Daniels J, Ewer AK, Zamora J, Khan KS. Accuracy of pulse oximetry in screening for congenital heart disease in asymptomatic newborns: a systematic review. *Arch Dis Child Fetal Neonatal Ed*. 2007;92:F176–F180
77. Niermeyer S, Shaffer EM, Thilo E, Corbin C, Moore LG. Arterial oxygenation and pulmonary arterial pressure in healthy neonates and infants at high altitude. *J Pediatr*. 1993;123:767–772
78. Bakr AF, Habib HS. Normal values of pulse oximetry in newborns at high altitude. *J Trop Pediatr*. 2005;51:170–173
79. de Wahl Granelli A, Mellander M, Sunnegårdh J, Sandberg K, Ostman-Smith I. Screening for duct-dependant congenital heart disease with pulse oximetry: a critical evaluation of strategies to maximize sensitivity. *Acta Paediatr*. 2005;94:1590–1596
80. Gurian EA, Kinnamon DD, Henry JJ, Waisbren SE. Expanded newborn screening for biochemical disorders: the effect of a false-positive result. *Pediatrics*. 2006;117:1915–1921
81. Liske MR, Greeley CS, Law DJ, Reich JD, Morrow WR, Baldwin HS, Graham TP, Strauss AW, Kavanaugh-McHugh AL, Walsh WF; Tennessee Task Force on Screening Newborn Infants for Critical Congenital Heart Disease. Report of the Tennessee Task Force on Screening Newborn Infants for Critical Congenital Heart Disease. *Pediatrics*. 2006;118:e1250–e1256

82. Kao BA, Feit LR, Werner JC. Pulse oximetry as a screen for congenital heart disease in newborns. *Pediatr Res*. 1995;37:216A. Abstract
83. Walton JP, Hendricks-Munoz K. Profile and stability of sensorineural hearing loss in persistent pulmonary hypertension of the newborn. *J Speech Hear Res*. 1991;34:1362–1370
84. Toth B, Becker A, Seelbach-Göbel B. Oxygen saturation in healthy newborn infants immediately after birth measured by pulse oximetry. *Arch Gynecol Obstet*. 2002;266:105–107
85. Mok JY, McLaughlin FJ, Pintar M, Hak H, Maro-Galvez R, Levison H. Transcutaneous monitoring of oxygenation: what is normal? *J Pediatr*. 1986;108:365–371
86. Hay WW Jr, Rodden DJ, Collins SM, Melara DL, Hale KA, Fashaw LM. Reliability of conventional and new pulse oximetry in neonatal patients. *J Perinatol*. 2002;22:360–366
87. Hay WW Jr. Physiology of oxygenation and its relation to pulse oximetry in neonates. *J Perinatol*. 1987;7:309–319
88. Severinghaus JW. History and recent developments in pulse oximetry. *Scand J Clin Lab Invest Suppl*. 1993;214:105–111
89. Barker SJ, Shah NK. Effects of motion on the performance of pulse oximeters in volunteers. *Anesthesiology*. 1996;85:774–781
90. Clayton DG, Webb RK, Ralston AC, Duthie D, Runciman WB. Pulse oximeter probes: a comparison between finger, nose, ear and forehead probes under conditions of poor perfusion. *Anaesthesia*. 1991;46:260–265
91. Poets CF, Stebbens VA. Detection of movement artifact in recorded pulse oximeter saturation. *Eur J Pediatr*. 1997;156:808–811
92. Gerstmann D, Berg R, Haskell R, Brower C, Wood K, Yoder B, Greenway L, Lassen G, Ogden R, Stoddard R, Minton S. Operational evaluation of pulse oximetry in NICU patients with arterial access. *J Perinatol*. 2003;23:378–383
93. Bickler PE, Feiner JR, Severinghaus JW. Effects of skin pigmentation on pulse oximeter accuracy at low saturation. *Anesthesiology*. 2005;102:715–719
94. Reich JD, Connolly B, Bradley G, Littman S, Koepfel W, Lewycky P, Liske M. The reliability of a single pulse oximetry reading as a screening test for congenital heart disease in otherwise asymptomatic newborn infants. *Pediatr Cardiol*. 2008;29:885–889
95. Ward CJ, Purdie J. Diagnostic accuracy of paediatric echocardiograms interpreted by individuals other than paediatric cardiologists. *J Paediatr Child Health*. 2001;37:331–336
96. Johnson KM, Lichter DT. Natural increase: a new source of population growth in emerging Hispanic destinations in the United States. *Popul Dev Rev*. 2008;34:327–346
97. Stanger P, Silverman NH, Foster E. Diagnostic accuracy of pediatric echocardiograms performed in adult laboratories. *Am J Cardiol*. 1999;83:908–914
98. Danford DA. Clinical and basic laboratory assessment of children for possible congenital heart disease. *Curr Opin Pediatr*. 2000;12:487–491
99. Sable CA, Cummings SD, Pearson GD, Schratz LM, Cross RC, Quivers ES, Rudra H, Martin GR. Impact of telemedicine on the practice of pediatric cardiology in community hospitals. *Pediatrics*. 2002;109:E3
100. Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, Wren C. Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. 2005; 9:1–152, iii–iv
101. Chang RK, Rodriguez S, Klitzner TS. Screening newborns for congenital heart disease with pulse oximetry: survey of pediatric cardiologists. *Pediatr Cardiol*. 2009;30:20–25
102. Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom. PulseOx Web site. Pulse oximetry as a screening test for congenital heart disease in newborn babies. 2008. Available at: <http://www.pulseox.bham.ac.uk>. Accessed May 22, 2009
103. de-Wahl Granelli A, Wennergren M, Sandberg K, Mellander M, Bejlum C, Inganäs L, Eriksson M, Segerdahl N, Ågren A, Ekman-Joelsson B-M, Sunnegårdh J, Verdicchio M, Östman-Smith I. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39 821 newborns. *BMJ*. 2009;338:a3037. Published January 8, 2009. doi:10.1136/bmj.a3037. Available at: http://www.bmj.com/cgi/reprint/338/jan08_2/a3037. Accessed May 22, 2009

Role of Pulse Oximetry in Examining Newborns for Congenital Heart Disease: A Scientific Statement from the AHA and AAP

William T. Mahle, Jane W. Newburger, G. Paul Matherne, Frank C. Smith, Tracey R. Hoke, Robert Koppel, Samuel S. Gidding, Robert H. Beekman III and Scott D. Grosse
Pediatrics 2009;124;823

DOI: 10.1542/peds.2009-1397 originally published online July 6, 2009;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/124/2/823
References	This article cites 100 articles, 32 of which you can access for free at: http://pediatrics.aappublications.org/content/124/2/823#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Fetus/Newborn Infant http://www.aappublications.org/cgi/collection/fetus:newborn_infant_sub Cardiology http://www.aappublications.org/cgi/collection/cardiology_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://www.aappublications.org/site/misc/reprints.xhtml

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Role of Pulse Oximetry in Examining Newborns for Congenital Heart Disease: A Scientific Statement from the AHA and AAP

William T. Mahle, Jane W. Newburger, G. Paul Matherne, Frank C. Smith, Tracey R. Hoke, Robert Koppel, Samuel S. Gidding, Robert H. Beekman III and Scott D. Grosse
Pediatrics 2009;124;823

DOI: 10.1542/peds.2009-1397 originally published online July 6, 2009;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/124/2/823>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2009 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

