Critical Congenital Heart Disease Screening Using Pulse Oximetry

Lowell H. Frank, MD1, Elizabeth Bradshaw, MSN, RN, CPN1, Robert Beekman, MD2, William T. Mahle, MD3, and Gerard R. Martin, MD1

Congenital heart disease (CHD) is the most common congenital malformation, occurring at a frequency of 8-12 per 1000 live births. Critical congenital heart disease (CCHD) occurs at a frequency of 1.2-1.7 per 1000 live births and accounts for 10%-15% of all cases of CHD. Although there is variation in how the term is defined, CCHD is generally accepted as referring to any congenital cardiac lesion that requires intervention or may cause significant morbidity or mortality in the first weeks of life. The public health impact of CHD is considerable, as CHD is responsible for 7.4% of all infant deaths, of which 10% are not diagnosed until autopsy. Chang et al6 reported that 50% of infants with previously undiagnosed CCHD died at home or in emergency departments. Up to 30 infant deaths per year with previously undiagnosed CCHD died at home or in emergency departments. Up to 30 infant deaths per year have been attributed to undiagnosed CHD in California alone. In 2007, Aamir et al7 reviewed the birth records in New Jersey and found 47 patients during a period of 5 years with a delayed diagnosis of CCHD (57% <4 weeks, 66% <2 months). Many of these patients were subject to multiple diagnoses, admissions, and procedures, suggesting an increased financial cost with delayed diagnosis. Delays in diagnosis can also lead to significant morbidity and worse outcomes after interventions. Because of its frequency in the population, potential for serious and life-threatening presentation, and availability of effective interventions, CCHD is an excellent candidate for a screening examination.

Current Detection Methods

The ideal screening test for CCHD should be accurate in recognizing disease in the preclinical state, have an excellent safety profile, be reasonably priced, have a wide availability, and lead to improved outcomes. Many of the existing methods of detecting CCHD have shortcomings in these areas. Obstetric ultrasound, typically performed between 18 and 22 weeks of gestation, is a common way in which structural cardiovascular abnormalities are diagnosed. However, controversy exists as to what images should be included in the “routine” obstetric examination of the fetal heart, which affects the sensitivity of this examination, and detection rates remain low. When abnormalities are detected, referral for comprehensive fetal echocardiography is often indicated; however, access varies widely by geographic region. Furthermore, certain lesions such as transposition of the great arteries (TGA) can be challenging to detect by physicians without expertise in CHD. Last, infants born to mothers who have had limited or no prenatal care do not have the benefit of access to this potential screening.

Fetal echocardiography is another method of detection of CHD, and it may improve preoperative acidosis, postoperative intensive care course, and surgical survival, although data regarding mortality reduction are mixed. It is often performed because of an abnormal cardiac screen on obstetric ultrasound, detection of other congenital malformations, an abnormal nuchal fold thickness or triple screen, a family history of CHD, or maternal medical conditions such as diabetes. However, it has significant cost, and even in urban settings with easy access to fetal echocardiography, fewer than one-half of newborns admitted postnatally for CHD are detected with fetal echocardiography.

The immediate postnatal period provides another opportunity for screening for CHD via the routine newborn physical examination. Unfortunately, many forms of CCHD do not present with obvious heart murmurs. Cyanosis may not be easily apparent until saturations are <80% and may be more difficult to appreciate in individuals with dark skin pigmentation. Mellander et al18 showed that in a population of infants requiring cardiac catheterization or surgery within the first 2 months of life (excluding patients diagnosed prenatally), 57% of infants with CCHD had been discharged home at 72-120 hours of life. Ductal-dependent CCHD was diagnosed after discharge in 20%, and 43% of these infants were in shock at admission. Although a more recent study has placed the missed diagnosis rate at 25%,19 figures vary widely, and it is reasonable to conclude that a more sensitive and uniform newborn screen is needed.

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How Pulse Oximetry Works

Oxygenated blood absorbs red light at a wavelength of 640 nm and deoxygenated blood absorbs light in the infrared spectrum at 940 nm. Pulse oximeters contain 2 light-emitting diodes at different wavelengths and sensors that measure the amount of red and infrared light emerging from the tissue. The ratio of oxygenated to deoxygenated hemoglobin can be calculated from this, and an oxygen saturation level displayed. Because most forms of CCHD rely on the ductus arteriosus to supply blood flow to the pulmonary circulation, the systemic circulation, or, preferentially, the lower half of the body, hypoxemia or a saturation difference is often present.

Pulse oximetry has been used in its current form since the early 1980s and has been validated by comparison with arterial blood gases. During the past decade, there have been advances in the technology used in these devices to address their performance in historically challenging settings, including patient movement or poor perfusion. Newer devices have been shown to have improvements with regard to patient motion, false or missed hypoxic or bradycardic alarms, and time needed to obtain a reliable reading. New pulse oximeters are also extremely precise even when the anatomic location of the sensor is varied. Guidance for industry on the premarket notification [for 510(k) clearance] of pulse oximeters is available from the US Food and Drug Administration. Pulse oximeters are extremely accurate—in the range of arterial saturations of 85%-100%, which is the range that would be most important in a newborn screening program for those forms of CHD that are likely to cause early morbidity and mortality.

Clinical Studies

One of the earliest studies using pulse oximetry as a screening test for CCHD was performed by Hoke et al from 1993-1995. This study screened 2876 newborns admitted to well-baby nurseries and 32 newborns with known CCHD. The primary target was the early detection of ductal-dependent left-sided heart obstructive disease, and although this was a relatively small study, it laid the groundwork for more comprehensive investigations that followed.

In 2009, the American Heart Association (AHA) and the American Academy of Pediatrics (AAP) released a scientific statement on the role of pulse oximetry in screening for CCHD. The writing group reviewed the existing published evidence and rated screening for CCHD with pulse oximetry as class IIb, level of evidence C, suggesting that there were no adequate large studies and that expert opinion was mixed. The writing group also called for additional population-based studies to evaluate the false-positive and false-negative rates and the detection rate of pulse oximetry as a screen for CCHD. It also highlighted the need to consider the effect of early detection on hospital costs. Importantly, the group wrote that prenatal ultrasound alone is insufficient for detection based on population data and that delayed or missed diagnoses are associated with significant brain injury and higher mortality. The AHA/AAP scientific statement concluded that “methods to improve the early detection of CCHD appear warranted” and called for larger population-based studies on implementation.

Recently, several studies have contributed data that address the concerns raised in the AHA/AAP statement (Table I). The data have been substantially larger than previously published data. In 2009, de-Wahl Granelli et al published a cohort study of 39,821 neonates screened with upper and lower extremity oxygen saturation measurements to evaluate for CCHD as defined by ductal-dependent lesions. The main outcomes were the sensitivity, specificity, positive and negative predictive values, and likelihood ratios for screening with physical examination and pulse oximetry versus physical examination alone. A screen was considered positive if both extremity measurements were <95% or if there was a >3% difference between the measurements. Screens were repeated 2 or 3 times depending on discharge planning; if the results remained within the classification of a positive screen, an echocardiogram was performed. A saturation of <90% immediately resulted in an echocardiogram. The sensitivity, specificity, positive predictive value, and negative predictive value of pulse oximetry alone are shown in Table I. The false-positive rate with pulse oximetry of 0.17% (69 patients) compared favorably with 1.9% with physical examination alone. This study also addressed the important question of differential outcomes, a key issue in evaluating screening for CCHD, as worse acidosis and mortality rates were present in the control (physical examination alone) cohort. Furthermore, 8% of infants with ductal-dependent disease left the hospital in the study cohort versus 28% in the control cohort. The authors addressed cost and feasibility, estimating that 2.3 normal echocardiograms per true-positive test were performed, and an estimated 5 minutes of nursing time per child was required. Importantly, 31 of the 69 infants with false-positive results had other significant (noncardiac) diseases that required treatment. The authors concluded that CCHD

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of births screened</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>False-positive rate</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>de-Wahl Granelli (2009)</td>
<td>39,821</td>
<td>62%</td>
<td>99.8%</td>
<td>0.17%</td>
<td>20.7%</td>
<td>99.97%</td>
</tr>
<tr>
<td>Riede (2010)</td>
<td>41,445</td>
<td>77.8%</td>
<td>99.9%</td>
<td>0.10%</td>
<td>25.9%</td>
<td>99.99%</td>
</tr>
<tr>
<td>Ewer et al (2011)</td>
<td>20,053</td>
<td>75%</td>
<td>99.1%</td>
<td>0.84%</td>
<td>9.23%</td>
<td>99.99%</td>
</tr>
</tbody>
</table>
screening of all well infants in a delivery unit is feasible with a minimum of nursing time, improves detection, and results in a low percentage of false-positive results. They highlight that aortic arch obstruction—which was the diagnosis in all 5 cases of missed disease—should be a target for further screening research.

In 2011, Ewer et al.30 reported the results of a prospective assessment of the accuracy of pulse oximetry as a tool for screening for CCHD in 20,055 newborns of >34 weeks’ gestational age. The primary outcomes measured were sensitivity and specificity for CCHD (as defined by those resulting in death or requiring intervention within 28 days of life) and other “major” forms of CHD (death or intervention with 12 months of life). Importantly, “critical” CHD is defined as ductal-dependent disease as well as only the most severe forms of coarctation of the aorta, tetralogy of Fallot, pulmonary atresia with ventricular septal defect, and total anomalous pulmonary venous return (TAPVR). This is an important inclusion and exclusion, as certain forms of these lesions may confer significant morbidity or mortality in the first month of life, and others may be only mildly symptomatic. Infants were considered to have failed a screen if they had an upper or lower extremity saturation of <95% or if there was a >2% difference between the 2 extremities. All infants who had a failed screen and an abnormal clinical examination or 2 failed screens underwent echocardiography. Major CHD was found in 53 neonates and CCHD in 24. Of these, 35 were suspected antenatally. Sensitivity was lower when considering major CHD and when excluding antenatally diagnosed infants. There were 169 false-positive results, of which 6 had less severe forms of CHD and 40 had other urgent illnesses. False-positive results were associated with earlier time of screening, many of which were before 24 hours of life. In this study, 6 instances of CCHD were missed. One was suspected on prenatal ultrasound, 3 were revealed on physical examination, and 2 infants presented clinically (1 infant was in shock). The authors conclude that pulse oximetry has a better sensitivity than prenatal ultrasound or physical examination and that the detection of noncardiac disease in the false-positive group is an advantage.

Other studies have investigated using pulse oximetry in a single extremity. In 2010, Riede et al.31 published their experience screening 41,445 newborns with a single lower extremity measurement. The lesions targeted were similar to those described in the study of Ewer et al, including all forms of ductal-dependent CHD as well as TGA and TAPVR; this study did not differentiate forms of the latter requiring early intervention. The authors excluded newborns with either a prenatal or a clinical diagnosis of CCHD. Their results are shown in Table I. Similar to previous studies, 40 of the 56 positive screens were false-positives, but 28 of the 40 had sepsis or persistent pulmonary hypertension. There were 4 false-negative results, including 3 infants with arch obstruction and 1 infant with TGA with a ventricular septal defect. No missed cases of CCHD were reported, although the region in which this study was conducted did not have mandatory autopsy screening.

Meberg et al. used a similar protocol of a single lower extremity measurement in a population of almost 58,000 newborns, with <95% as an abnormal value requiring repeat testing and subsequent evaluation32 with comparison with a similarly sized population without CCHD screening with a similar sensitivity, specificity, and detection of other important noncardiac diseases in the false-positive group. Time to in-hospital diagnosis was decreased in the screening group, and there was a trend toward an increased percentage of CCHD detected before hospital discharge in the screening group.

Limitations

One problem in reviewing CCHD screening is the definition of the term “critical.” In pediatric cardiology, this term is often used to refer to a form of CHD that would be lethal without patency of the ductus arteriosus for systemic or pulmonary blood flow. Other forms of CHD, such as the obstructed type of TAPVR or certain forms of TGA, can similarly be classified as having the same clinical urgency. However, a precise definition is most important for research studies, postimplementation monitoring, and counseling of families and care providers because the actual method of screening is not dependent on the definition of CCHD.

In addition, the idea of routine newborn CCHD screening has historically not been universally accepted. A 2009 survey of pediatric cardiologists revealed that even though 58% believed that current practice was adequate for detecting CCHD, only 55% supported mandatory screening with pulse oximetry.35 A task force in Tennessee in 2005 recommended not implement mandatory screening at that time.3 Furthermore, interpretation and generalization of the studies listed here are limited by the differences in the screening protocol used. The wide variety of times (ages) at which screening was performed, the different cutoffs used, and the inclusion population contribute to a variety of outcomes with regard to sensitivity, specificity, and positive and negative predictive values. The details of implementation are also an important consideration. A recent study examining CCHD screening in a nonresearch setting highlighted the importance of establishing strict testing and follow-up procedures, as a positive screen was not acted on.36 In addition, it is not clear that the benefits of CCHD screening demonstrated in numerous European studies will translate into similar success in the US.

Even under optimal circumstances, pulse oximetry has certain limitations as a screening tool for CCHD. Lesions with ductal-dependent systemic blood flow tend to be diagnosed later than those with ductal-dependent pulmonary blood flow.18 Critical aortic arch obstruction may be less amenable to detection with CCHD screening using pulse oximetry and often may not present until days after neonatal discharge.37 In the study of de-Wahl Granelli et al, all 5 newborns with missed CCHD had aortic arch obstructions,30 and coarctation has been missed in other studies using pulse oximetry as well.7,30-32 Less severe cases of coarctation are frequently not diagnosed until late childhood38 and are often
Evaluation of peripheral perfusion by using the plethysmographic signal from a pulse oximeter can allow for noninvasive measurement of flow and may prove to be a useful adjunct technique to common CCHD screening protocols with minimal additional time or training for the detection of left-sided heart obstruction. Another recognized limitation of pulse oximetry screening is the lack of adequate screening cutoffs in high-altitude settings. Different standards for pulse oximetry measurements may be required due to lower environmental oxygen tension.

Beyond the question of the efficacy of pulse oximetry as a screening tool is the challenge of obtaining confirmatory testing if a screen is positive. Echocardiography, with or without clinical evaluation by a pediatric cardiologist, is the gold standard in diagnosing CHD. However, the availability of echocardiography varies greatly from region to region and may require costly medical transport. Furthermore, interpretation in a timely manner by a physician with expertise in CHD may be a limiting factor even if the equipment and technical staff are available. Potential solutions include the use of telemedicine for transmission and interpretation of newborn echocardiograms, although this also requires resources that have varying availability. As the goal of screening for CCHD is largely based on the value of a presymptomatic time period, timely access to these resources is critical before the implementation of any screening program.

Cost-Effectiveness

There have been no published formal cost-effectiveness studies of newborn CCHD screening using pulse oximetry in the US. Nevertheless, as with any screening examination, careful consideration must be given to this issue. In addition to the direct equipment costs of the monitors and sensors, consideration must be given to the time necessary to train staff, the time spent on the examination, the direct cost of the follow-up evaluations, and potentially the cost of medical transport if on-site pediatric echocardiography is not available. Furthermore, if universal screening for CCHD were implemented, there would be additional infrastructure costs involved, including centralized assistance in program implementation, communication to primary care providers, and monitoring of quality and outcomes. Of course, these costs are potentially offset by savings from avoiding unnecessary medical care, including other tests and procedures and hospital admissions while a diagnosis is delayed. Also, because delayed diagnosis is associated with increased severity of illness at presentation, the cost of screening may be also partially balanced by potential lower per-patient costs. Avoiding one case of circulatory collapse can potentially pay for many screening evaluations. Even in a cost-neutral scenario, however, it is likely that certain costs will shift from tertiary care centers caring for critically ill infants to community hospitals charged with screening many patients to detect the presymptomatic newborn with CCHD. As part of implementation planning, reimbursement for these costs would need to be negotiated with payers. Professional societies such as the AAP, AHA, and the American College of Cardiology can play a role in creating or revising Current Procedural Terminology codes to facilitate this.

The cost of medical care is only one of many considerations; there is also the cost per quality-adjusted life year saved. Hoffman highlights the complexity of the cost issue, including consideration of the cost of raising a child with brain injury or the cost of potential malpractice cases due to delayed detection. He reports an estimated direct cost of $9000 per asymptomatic CCHD case detected, which compares favorably to $68 000 per patient diagnosed with the newborn metabolic screen. This cost could drop further if reusable sensors become commonplace. In another simple analysis, the cost is $5 per infant screened, which compares favorably with other tests.

A recently published economic analysis of the study of Ewer et al of 6 maternal units in the United Kingdom calculated a cost of $38 000 (US) per case of timely diagnosis in which >50% of the cases were suspected prenatally. The authors concluded that using a willingness-to-pay threshold of $157 000, pulse oximetry is 90% likely to be cost-effective. That willingness-to-pay threshold was deemed reasonable if a timely diagnosis resulted in 5 quality-adjusted life years. The per-case cost compares favorably with that of universal hearing screening, a useful comparison in that CCHD and congenital hearing impairment have a similar frequency in newborns and that pulse oximetry and hearing screens are rare nonсмерtnl newborn screening examinations. de-Wahl Granelli et al applied their positive predictive value and false-positive rate to an existing economic model and concluded that CCHD screening is cost neutral before accounting for long-term neurologic morbidity.

Knowles et al performed an extensive systematic review and cost-effectiveness analysis in the United Kingdom before the publication of the large studies just mentioned. They classified 6 lesions as “life-threatening CHD” (coarctation of the aorta/interrupted aortic arch, TGA, aortic stenosis, hypoplastic left heart syndrome, TAPVR, and pulmonary atresia) in which prevention of circulatory collapse before definitive management is thought to decrease the risk of mortality and long-term morbidity. They developed a decision model based on a primary outcome of diagnosis of life-threatening CHD before circulatory collapse or death and a secondary outcome of “clinically significant CHD,” such as tetralogy of Fallot, complete atrioventricular septal defect, ventricular septal defect, atrial septal defect, and patent ductus arteriosus. Probabilities were based on published literature, including prenatal detection rates. The 3 screening pathways considered were clinical examination alone, pulse oximetry plus clinical examination, and screening echocardiography plus clinical examination. The economic model included the costs of staff, equipment, and follow-up evaluations, as well as the cost of caring for an infant in circulatory collapse from a false-negative screen. Multiple
scenarios were tested. Their model showed that 68%, 69%, and 32% of infants with life-threatening heart disease would be detected by pulse oximetry plus examination, echocardiography plus examination, and examination alone, respectively. The total additional cost per timely diagnosis was estimated to be $7800 for pulse oximetry and $7.2 million for screening echocardiography. The authors conclude that pulse oximetry would likely be cost-effective even with significantly higher prenatal detection rates if the societal value for a timely diagnosis is up to $16 000.

Although estimates vary, most analyses focusing on cost conclude that pulse oximetry as a screening test for CCHD is cost-effective. Comparison with mass spectrometry for expanded screening for inborn errors of metabolism supports this conclusion; the prevalence of these disorders is less frequent at 1 in 4100, and the cost of screen is estimated at $7.50 per test and $31 000 per affected infant. Screening for CCHD also compares favorably with the newborn hearing screen, with cost estimates of $58 000 per case detected.

**Present Activity and Future Directions**

CCHD screening has been the focus of much attention by national committees and legislative activities. In January 2010, CCHD was unanimously nominated by the Department of Health and Human Services (HHS) Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) for screening consideration. In October 2010, SACHDNC recommended to HHS Secretary

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**Figure 1.** Proposed algorithm for newborn pulse oximetry screening for CCHD. Reproduced with permission from *Pediatrics* Vol. 128, pages(s) e1259-e1267. Copyright 2011 by the American Academy of Pediatrics. RH, right hand; F, foot.
Kathleen Sebelius that screening for CCHD using pulse oximetry be added to the committee’s Recommended Uniform Screening Panel (RUSP). In January 2011, a working group including members of SACHDNC, the AAP, the American College of Cardiology, and the AHA convened and made recommendations for a standardized approach to screening and diagnostic follow-up (Figure 1) while also defining seven types of CCHD (Table II). Importantly, although there is considerable overlap, these lesions differ somewhat from those evaluated in the studies of Granelli, Ewer, and Riede et al. Notably, the list excludes coarctation of the aorta and isolated “critical” aortic and pulmonic valve stenosis and includes all forms of TOF, TAPVR, tricuspid atresia, and truncus arteriosus. The working group highlighted the need for further research into screening special populations, such as those at high altitude, and further recommended evaluation of service infrastructure needs and delivery strategies for hospitals without readily available follow-up testing (eg, echocardiography or telemedicine). The working group did not focus on out-of-hospital births, which have different infrastructure needs, or neonatal intensive care unit patients, who usually undergo frequent monitoring that includes pulse oximetry. These recommendations are summarized in Table II. Subsequently, the Interagency Coordinating Committee on Newborn and Child Screening, a group comprising representatives from the National Institutes of Health, Centers for Disease Control and Prevention, Health Resources and Services Administration, Agency for Healthcare Research and Quality, and the Food and Drug Administration, was tasked with examining the identified evidence gaps and proposing a plan of action “to address identification of effective screening technologies, development of diagnostic processes and protocols, education of providers and the public, and strengthening service infrastructure needs for follow-up and surveillance.”

In September 2011, Secretary Sebelius formally adopted the SACHDNC’s recommendation to add CCHD to the RUSP. The SACHDNC was further tasked with providing information on the impact on state health departments including staffing needs, comprehensiveness of screening, and communication of results to providers. Even though logistical issues remain, implementation has been successful on the regional level with minimal additional staff time for screening.

Because HHS Secretary Sebelius endorsed (not mandated) the recommendation to add CCHD screening to the RUSP, many states have begun efforts to determine best practice for implementing programs in their state. Legislative efforts ensure statewide access and surveillance, and some states have addressed the HHS endorsement through legislative efforts to mandate screening of newborns. Other states, concerned with the possible lack of resources to adequately fund surveillance efforts, have pursued the development of recommendations for standard of care and/or the development of pilot programs and multicenter studies. In May 2011, Indiana and Maryland were the first states to pass legislation surrounding CCHD screening. In June 2011, New Jersey became the first state to implement universal screening in all infants born in licensed birthing facilities; mandatory screening began on August 31, 2011. The status of other state screening programs and legislation is shown in Figure 2. Most recently, the Health Resources and Services Administration awarded grants to Wisconsin, Michigan, New Jersey, New Hampshire (the New England Collaborative), Utah, and Virginia to support the development, dissemination, and validation of screening protocols and newborn screening infrastructure for point-of-care screening specific to CCHD, including the implementation of an electronic health information exchange for reporting and collecting pertinent information from hospitals, as well as the education and

### Table II. Details of proposed pulse oximetry screening and items for further development if universal screening were to be implemented

<table>
<thead>
<tr>
<th>Screening populations</th>
<th>Specific recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-baby nurseries</td>
<td>• Screening should be conducted by using motion-tolerant pulse oximeters approved for use in newborns.</td>
</tr>
<tr>
<td>Intermediate-care nurseries</td>
<td>• Screening should be based on the recommended screening algorithm and be performed by qualified, trained personnel.</td>
</tr>
<tr>
<td>Screening targets</td>
<td>• The algorithm cutoffs may need to be adjusted in high-altitude nurseries.</td>
</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>• Any abnormal pattern of low oxygen saturation requires a complete clinical evaluation, and in the absence of other findings to explain hypoxemia, CCHD needs to be excluded on the basis of a comprehensive echocardiogram interpreted by a pediatric cardiologist before discharge from the hospital. If an echocardiogram or telemedicine is not available, strong consideration should be made for transfer to another center for diagnosis. Before implementing screening, protocols for arranging diagnostic follow-up should be established.</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>• Hospitals and birthing centers should establish partnerships with local and state public health agencies to develop strategies for quality assurance and to monitor the impact of screening.</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>• Primary care providers should ensure that newborns in their practice were appropriately screened and should work to ensure follow-up for those diagnosed with CCHD.</td>
</tr>
<tr>
<td>TAPVR</td>
<td>• Standards should be developed for electronic reporting of pulse oximetry monitoring and diagnostic outcomes.</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td></td>
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<tr>
<td>Truncus arteriosus</td>
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<tr>
<td>Persistent pulmonary hypertension (secondary target)</td>
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<tr>
<td>Screening criteria</td>
<td></td>
</tr>
<tr>
<td>Begin after 24 hours of life</td>
<td></td>
</tr>
<tr>
<td>Completed on the second day of life</td>
<td></td>
</tr>
<tr>
<td>Right hand and one foot either in parallel or in sequence</td>
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Adapted from Kemper et al.43
training of various stakeholders on testing methodology and follow-up protocols.53

Summary

In 2012, evaluation of newborn screening for CCHD using pulse oximetry has the benefit of many large multicenter studies that highlight the favorable sensitivity, specificity, and positive and negative predictive values of this tool. Care must be taken in interpreting these data, as these studies differ somewhat in the inclusion of prenatally detected CCHD, time (age) of screening, screening protocol, and measurement cutoff values. There is also variation in the definition of what constitutes CCHD. Similarly, when discussing screening with pediatric cardiologists, primary care providers, and families, it is important to highlight that it is aimed at detecting only CCHD and not all forms of CHD. However, an increasing body of literature supports the use of pulse oximetry as a newborn screening test for CCHD. Although determining cost-effectiveness is a complex calculation involving equipment costs, training and staff time, follow-up testing, costs associated with a delayed diagnosis, increased morbidity, and potential long-term neurologic and physical disability, preliminary studies in this area offer data calculating effectiveness with various willingness-to-pay thresholds. It appears that CCHD screening compares favorably with other forms of newborn screening currently in practice. Last, preliminary work has been done documenting feasibility of implementation of a universal newborn screening protocol on a regional level, and additional recommendations for refinements in this process are available. Professional societies have been active at the local and national levels and have partnered with government organizations in helping to address potential barriers to universal newborn screening, and legislative actions to this end are gaining momentum throughout the country.

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References


Encephalographic Changes in Celiac Disease

This is a case report of a 2-year-old child with diarrhea and failure to thrive who had neurologic and behavioral symptoms. An abnormal electroencephalographic pattern was noted. Based on tests for malabsorption, a clinical diagnosis of celiac disease was made. Gluten-free diet led to significant improvement in symptoms and normalization of the electroencephalographic abnormalities. The authors concluded that there was evidence of an organic or neurophysiologic basis for the abnormal behavior and neurodevelopmental delay of this patient with celiac disease.

Since 1963, major advances have occurred in celiac disease including a better understanding of its pathogenesis, recognition of the variability in clinical presentations, and an improved ability in making a timely diagnosis especially with the use of screening serologic tests (such as anti-endomysial and anti-tissue transglutaminase antibodies). Once considered to be a rare malabsorptive disorder of infancy and early childhood, celiac disease is now known to be a common, multi-system, autoimmune disorder affecting 1% of the population.1

Patients with celiac disease can present with either intestinal or extra-intestinal manifestations. Some of the neurologic and psychologic disturbances include peripheral neuropathy, ataxia, epilepsy with intracranial calcifications, depression, and migraine headaches. The precise role of gluten in the causation of these symptoms is still under investigation. Interestingly, despite limited understanding of pathophysiological mechanisms, the authors of the case report made the astute observation that neurologic symptoms were present in celiac disease and not cystic fibrosis (although both disorders cause steatorrhea). Gluten was, thus, suspected to be the primary cause of the neurobehavioral dysfunction.

Unfortunately, the final diagnosis of celiac disease in the child described in the case report was established only on autopsy. Today, fiberoptic endoscopy is the primary procedure for obtaining small intestinal biopsies to confirm the diagnosis by histopathology while on a regular (gluten-containing) diet. Glucose tolerance testing and barium roentgen studies are no longer used to investigate malabsorption. Magnetic resonance imaging and positron emission tomography scan can better define the structure and function of the brain. The cause of death in the case report was not mentioned. However, with advances in management, mortality in children with celiac disease these days is most unusual.

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