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Neonatology Today (NT) is a monthly newsletter for BC/BE neonatologists and perinatologists that provides timely news and information regarding the care of newborns and the diagnosis and treatment of premature and/or sick infants.

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Pulse Oximetry Screening for Unrecognized Congenital Heart Disease in Neonates

By John S. Hokanson, MD

Background

Congenital heart disease is the most common serious birth defect in humans. Many newborns with ductal-dependent heart disease will appear to be entirely well at the time of routine hospital discharge only to become critically ill a few days later.

Various estimates suggest that potentially life-threatening congenital heart disease is present in approximately 1:1,000 births[1-5] (Table 1). Unfortunately this heart disease will go unrecognized in some neonates until symptoms develop. These delayed or missed diagnoses can result in both disability and death. The incidence of a missed diagnosis of critical congenital heart disease can be defined in various terms and occurs in anywhere from 1 in 3,500 to one in 25,000 live births.[1-4, 6] The low incidence of missed congenital heart disease in our data from Wisconsin may be related to limiting the definition to death or readmission due to critical congenital heart disease occurring at less than 14 days of age.[6]

A retrospective analysis of patients admitted to the Children's Hospital of Philadelphia (CHOP) with critical congenital heart disease at less than 30 days of age suggested that 6.7% had a "significant physiologic compromise due to a missed diagnosis of critical congenital heart disease."[7] This study could not evaluate the number of babies who died prior to diagnosis of congenital heart disease and transfer to CHOP and may underestimate the consequences of a missed diagnosis of critical congenital heart disease.

Studies of death due to unrecognized congenital heart disease suggest that the incidence of death due to missed congenital heart disease occurs in 1 in 20,000 to 1 in 40,000 births. If extrapolated to the US birth rate of roughly four million per year, somewhere between 100 and 200 deaths due to unrecognized heart disease in newborns would be expected each year.

Table 1. Incidence of Missed Diagnosis of Critical Congenital Heart Disease

Reference	Years	Incidence of Critical Congenital Heart Disease	Missed or Delayed Diagnosis	Death Due to Mixed Dx	Deaths per Live Births	Location
Wren	1985-2004	1:1,032	1:3,486	1:23,007	30/690,215	Northern Heath Region, UK
Mellander*	1993-2001	1:1,135	1:6,899	Not Reported		Sweden
Aamir*	1999-2004	1:971	1:14,261	Not Reported		New Jersey
Ng**	2002-2006	Not Reported	1:24,684	1:38,397	9/345,572	Wisconsin
de-Wahl Granelli	2004-2007	1:853	1:3,878	1:21,721	5/108,604	Sweden

* Does not include those dying before diagnosis
** Limited to missed diagnosis or death under the age of 14 days

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Although not indexed for the birth rate, a study by Chang[8] suggested that there might be as many as 30 deaths per year due to unrecognized critical congenital heart disease in California alone.

Screening for Unrecognized Heart Disease in Other Settings

Significant efforts have been undertaken in recent years to screen for heart diseases that may result in sudden death in children, particularly in athletes and in those taking stimulant medications. The incidence of sudden death due to unrecognized heart disease in a child between 1 and 20 years of age has been reported in the range of 1:100,000 per year.[9] The sudden death of a high school athlete due to unrecognized heart disease occurs in roughly 1:200,000 per year.[10] Overall, the sudden death of a young athlete (up to the age of 39 years) during exercise occurs less than 100 times each year in the United States[11]. Although an association has been suggested between the use of stimulant medications and sudden death in children, the available literature suggests that this occurs less than ten times per year in the United States[12-14] (Table 2). Based in part on a small number of adverse effects reported in Canada, recommendations to consider ECG screening of children taking stimulant medications were made by the AHA and AAP in 2008.[15]

Table 2. Incidence of Death Due to Unrecognized Heart Disease

Cause	Estimated Number of Deaths Per Year in US
Unrecognized Critical Congenital Heart Disease in Neonates	100-200
Sudden Death of a Young Athlete	<100
Sudden Death Associated with Stimulant Medication Use	<10

In de-Wahl Granelli's study[4] there were 5 deaths due to unrecognized congenital heart disease in the 108,604 babies in the control arm and no deaths in the 38,429 babies in the population in which pulse oximetry screening was performed. Although not designed to test the hypothesis, her study suggests that the implementation of pulse oximetry screening decreases the risk of death due to a missed diagnosis of critical congenital heart disease. No such population based data exists for the implementation of screening strategies to decrease the incidence of death in athletes or those taking stimulant medications.

Detection of Congenital Heart Disease and the Cyanotic Blind Spot

Traditionally, congenital heart disease is detected prenatally with obstetric ultrasound or postnatally by physical examination or the development of symptoms. The prenatal diagnosis of congenital heart disease is the preferred mechanism, but data from both the US and UK suggests that most children with critical congenital heart disease are not detected prior to birth.[16-17]

Physical examination of the newborn is the oldest method for detecting congenital heart disease prior to symptoms and remains invaluable, but has significant limitations. Certain types of critical ductal-dependent congenital heart disease will not be detected, even by experienced clinicians in the first days after birth. In the setting of valvar atresia or single ventricle physiology with systemic pulmonary pressures, there may not be a heart murmur to alert the clinician to the presence of heart disease. With a large PDA supporting the systemic circulation the femoral pulses may well be normal.

A major limitation of the newborn physical examination is the inability for the human eye to detect important degrees of cyanosis. The limits of visual recognition of cyanosis are well documented, but are frequently underappreciated. Nearly a century ago, it was suggested that between 4 and 6 grams of deoxygenated hemoglobin per deciliter of blood would be necessary for central cyanosis to be visible[18] (Lundsgaard & Van Slyke 1923). Later reports suggested that only 3 grams of deoxygenated hemoglobin would be necessary to manifest central cyanosis[19] (Lees 1970). Even if only three grams of deoxygenated hemoglobin need be present for the observation of central cyanosis, this still leaves a wide gap between normal saturation and visible cyanosis, the cyanotic blind spot (Figure 1). In a one day old term baby with a hemoglobin at the 50th percentile (17.5 g/dL),[20] cyanosis would be visible at or below approximately 83%. The cyanotic blind spot widens with anemia and in a one day old term baby with a hemoglobin at the 5th percentile (13.5 g/dL),[20] cyanosis would not be visible until the saturation had dropped to 78% or below.

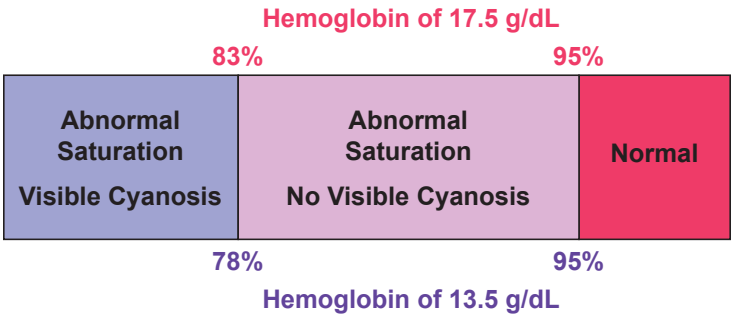

Figure 1: The Cyanotic Blind Spot

More recent work by O'Donnell[21] suggests that both the ability to visually detect cyanosis and the inter-observer reliability of visual observations of cyanosis are poor even among neonatal intensive care personnel. This study was performed in the delivery room where a rapid increase in oxygen saturation is expected. The threshold for the resolution of cyanosis varied from 10% to 100% between the observers. Although the infants' hemoglobin concentrations were not reported in this study, the mean threshold saturation for the visible resolution of cyanosis was 69%.

Pulse Oximetry Screening to Detect Unrecognized Ductal Dependent Heart Defects

The use of pulse oximetry to detect cyanosis in asymptomatic term neonates as a screening for critical congenital heart disease has been studied for several years. The use of pulse oximetry for this purpose has been viewed with scrutiny, as any intervention applied on a large scale should be. Although pulse oximetry could be con-

sidered an additional vital sign, the presence of a fixed cut-off value between normal and abnormal is not how other vital signs are usually considered. Pulse oximetry measurements differ from other vital signs in that there is data to suggest a relatively rigid differentiation between normal and abnormal in the baby greater than 24 hours old. Curiously, in many facilities the only inpatient population in which pulse oximetry is not routinely performed is the normal neonate.

Studies of Pulse Oximetry Screening

Although the concept supporting the use of pulse oximetry as a screening tool is elegant in its physiologic simplicity, implementation of pulse oximetry screening is another matter. The available data on the subject suffers from a wide variety of study designs, study populations, and measures of outcome.[2, 4-5, 22-31]

The sensitivity and specificity of pulse oximetry as a screening tool in these studies is highly variable and is influenced by the prenatal detection rate, the timing of screening, and the use of both pre- and post-ductal measurement, or of post-ductal measurements alone. In general, the earlier the screening is performed, the greater the sensitivity and the lower the specificity. In most studies, a post-ductal saturation between 94% and 96% has been used as the cut-off point, as the mean saturation in term neonates at 24 hours of age has been reported to be 97.2% +/- 1.6%.[32] Other protocols have used a difference between pre-ductal and post-ductal saturations as an additional indicator of critical ductal-dependent heart disease,[4,23] although there is only one large scale study of such an approach.[4]

The false positive and positive predictive values are dependent on both the timing of the oximetry and whether or not a repeat measurement of abnormal values was performed. It appears that screening performed either primarily after 24 hours, or repeated after 24 hours will provide the lowest false positive rate and the highest positive predictive value. In comparing the two large studies of pulse oximetry after 24 hours of age,[4, 30] the value of pre-ductal oximetry is difficult to assess. One patient with interrupted aortic arch and aortopulmonary window had pre- and post-ductal saturations of 99% and 95%[4] and would have been missed by post-ductal oximetry alone. The authors of this study report no additional false positives based on the addition of the pre-ductal oximetry.[4]

Although a detailed discussion of individual study design is beyond the scope of this article, the false positive rates and positive predictive values of the more recent studies are presented in Table 3.

Public Policy Initiatives

In 2005, routine pulse oximetry was recommended by the Swiss Society of Neonatology and the Swiss Society of Pediatric Cardiology. By 2007, 85% of Swiss newborns were screened for congenital heart disease with pulse oximetry using a standardized protocol.[33] This protocol utilized post-ductal saturations measured on the first day with abnormal considered to <95%. Echocardiography was performed if repeat measurements remained less than 95%.

In 2005, mandated pulse oximetry screening was proposed in the State of Tennessee. A task force was assembled to determine the utility of such legislation. The available literature at the time comprised four studies of a total of less than 22,000 patients with wide variability in screening protocol and study design.[22-25] Based on this limited data, the task force did not recommend pulse oximetry screening.[34]

A probabilistic cost-effectiveness model reported from the UK in 2007 suggested that addition of pulse oximetry to the routine evaluation of newborns was likely to be cost effective.[35]

In 2009, the American Heart Association and American Academy of Pediatrics published their scientific statement on the use of pulse oximetry in screening for congenital heart disease.[36] This review was completed prior to the publication of Riede's study of 41,445 neonates,[30] and concluded that further study was required prior to large scale implementation of routine pulse oximetry.

On September 17th, 2010, the Secretary's Advisory Committee for Hereditable Disorders in Newborns and Children recommended that pulse oximetry screening be added to the core panel for universal screening of newborns (www.hrsa.gov/heritabledisorderscommittee/default.htm). The US Secretary of Health and Human Services, Kathleen Sebelius, will respond to these recommendations within 180 days. If approved, this recommendation will be forwarded to the individual states for implementation.

Implications of Population-Based Screening

Several factors must be considered regarding the population based implementation of pulse oximetry screening. The published data on this topic is gathered from different health care delivery systems with varying prenatal and postnatal detection rates. Much of the concern regarding pulse oximetry regards the impact of the false positive study. Except in Walsh's study,[31] those children failing oximetry screening proceeded to echocardiography, which may not be immediately available in all settings.

Table 3. Studies of Oximetry Screening

Author	Year	Patients	Timing	Sites	Normal	False Positive Rate	Positive Predictive Value
Sendelbach	2008	15299	4 hours repeat before d/c	foot	≥ 96%	1:15,233 for CHD	(0/1) 0% for CHD
de-Wahl Granelli	2009	39821	38 hours repeated up to three times	hand and foot	≥ 95% OR ≤ 3% difference	1:557 for CHD 1:1601 for any disease	21% for CHD 72% for any disease
Merberg	2009	50008	5 hours repeat in 2-3 hours if abnormal	foot	≥ 95%	1:178 for CHD 1:373 excluding transitional circulation	13% for CHD 56% for CHD or transitional circulation
Walsh	2009	14564	>24 hours no repeat if abnormal	foot	≥ 94%	1:311 for CHD	1%
Riede	2010	44240	>24 hours repeat in 1 hour if abnormal	foot	≥ 96%	1:1036 for CHD 1:3454 for any disease	26% for CHD 78% for any disease

"When performed after 24 hours and repeated if abnormal, the use of pulse oximetry is a viable method of screening asymptomatic neonates for critical congenital heart disease. Based on the morbidity and mortality related to the missed diagnosis of congenital heart disease in the newborn and the growing body of evidence demonstrating the benefits pulse oximetry screening, the use of pulse oximetry is likely to become more widespread in the near future."

No matter how screening is performed, false positive results will result in increased cost, delay in discharge, and anxiety. However, when echocardiography cannot be performed without transfer to another center the costs, delays, and anxieties associated with false positive studies will increase considerably. The application of pulse oximetry screening to rural settings with limited access to echocardiography may be challenging. In Wisconsin alone, half of the state's children were born in one of the 98 hospitals delivering less than 1250 babies per year and a quarter were born in one of the 80 hospitals delivering less than 675 babies per year.[6]

However, when performed after 24 hours and with repeat screening performed after an initial screening failure, the positive predictive value of pulse oximetry for potentially life-threatening heart disease is between 21% and 26%.[4, 30] This data suggests that in settings where echocardiography is not available, it may be reasonable to extend the hospitalization of an asymptomatic newborn to allow for additional evaluation and to allow transitional circulation to resolve or to transfer the baby to a facility where echocardiography can be performed.

Conclusion

When performed after 24 hours and repeated if abnormal, the use of pulse oximetry is a viable method of screening asymptomatic neonates for critical congenital heart disease. Based on the morbidity and mortality related to the missed diagnosis of congenital heart disease in the newborn and the growing body of evidence demonstrating the benefits pulse oximetry screening, the use of pulse oximetry is likely to become more widespread in the near future.

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Global Neonatology Today: A Monthly Column

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

MILLENNIUM DEVELOPMENT GOAL #7 (MDG #7)

The goal of MDG #7 is to ensure environmental sustainability This goal aims at the way we manage our environment to ensure that natural resources are sustainable for generations to come.

The Problem

Environment affects our life every day. Availability of clean water and sanitation are critical to good health. There is a strong link between poverty and the environment. The poor are particularly affected by changes in the environment that impact sustainability, e.g. the disappearance of forests results in significant soil erosion, which has a negative impact on the production of food; contaminated water results not only in poor agricultural output and destruction of fisheries, but in ill health for humans as well. In fact, 1.2 billion people lack access to safe clean drinking water contributing to infections and diseases. Each day, an average of 5,000 children die due to water and sanitation-related diseases, many easily preventable.

Selected Facts

According to The United Nations Development Programme (UNDP):

- Water and sanitation are essential to achieving all of the MDGs.
- Investment in water supply yields an average economic return of $4.4 to $1.
- Investment in sanitation yields an average economic return of $9.1 to $1.
- Human development is more closely linked to access to water and sanitation than other development drivers, including: spending on health or education, and access to energy services.

Targets Include

- To integrate the principles of sustainable development into country policies and programs and reverse the loss of environmental resources.
- To halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation.
- To have achieved a significant improvement in the lives of at least 100 million slum dwellers by 2020.

Indicators

Although several indicators are used to measure the progress of MDG #7, the indicator of access to safe drinking water and availability of sanitary conditions in rural and urban countries is the major thrust. Other indicators include: proportion of land area covered by forest, to maintain biological diversity, efficient energy use, and low per capita carbon dioxide emission.

> ***"As far as current trends go, the world will miss the sanitation target by a staggering 700 million people, mostly in poor countries and poor communities."***

Progress Made

Most countries have adopted principles of sustainable development, and have agreed to international accords on protecting the environment. However, the land is still being degraded, forests are being lost, fisheries are being overused. Plant and animal species are becoming extinct. And carbon dioxide emissions are driving changes in global climate. As stated above, access to clean water is scarce.

According to UNDP, overall, the world is on track to meet the water MDG, but there are major gaps in many regions and countries, particularly in Sub-Saharan Africa. As far as current trends go, the world will miss the sanitation target by a staggering 700 million people, mostly in poor countries and poor communities. While rich countries have better access to water and sanitary conditions, these same countries are the major consumers of products and services from the environment.

It is to be recognized that rich and poor countries both have a stake in using environmental resources wisely since MDG #7 affects all other Millennium Development Goals.

There is a need for vigorous implementation of MDG #7 across the globe.

For more information:
http://who.int/topics/millennium_development_goals/mdg7/en/

The Clock is Ticking!

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Medical News, Products & Information

Low Birth Weight May Lead to Poor Growth Rate in Children with Kidney Disease

The lower the birth weight, the greater the chance of poor growth rate in children with chronic kidney disease (CKD), according to a new study appearing in an upcoming issue of the *Clinical Journal of the American Society of Nephrology* (CJASN).

In the general population, low birth weight is not an important cause of poor growth and short stature. To determine whether low birth weight is a risk factor for poor growth in children with CKD, Larry Greenbaum, MD, PhD (Emory University and Children's Healthcare of Atlanta, Atlanta, GA) and his colleagues analyzed results from the Chronic Kidney Disease in Children Prospective Cohort (CKiD) study. Study participants included 426 out of the 586 children enrolled in the CKiD study, all of whom had mild to moderate CKD and were in 48 pediatric nephrology centers across North America.

"This is the first study showing an association between low birth weight and poor growth in children with CKD," explains Dr. Greenbaum. "The study also demonstrates that children with CKD are more likely to be born with low birth weight than the general population. This occurs in children who are born with kidney disease and those who acquire kidney disease during childhood. It is possible that low birth weight is a risk factor for the development of kidney disease during childhood."

This study shows an association between low birth weight and poor growth in children with CKD but does not prove that the low birth weight causes poor growth. The study also does not indicate why low birth weight may lead to poor growth in children with CKD.

Additional research is needed to determine if being born small increases the risk of developing kidney disease during childhood. Previous research has shown that adults who were smaller at birth were more likely to have kidney disease.

Study co-authors include: Alvaro Muñoz, Michael F. Schneider (Johns Hopkins Bloomberg School of Public Health, Epidemiology), Frederick J. Kaskel (Montefiore Hospital, Pediatric Nephrology), David J. Askenazi (University of Alabama at Birmingham, Department of Pediatrics, Division of Nephrology), Randall Jenkins (Emanuel Children's Hospital, Pediatrics), Hilary Hotchkiss (Mount Sinai School of Medicine), Marva Moxey-Mims, MD (National Institutes of Health, National Institute of Diabetes and Digestive Kidney Disease), Susan L. Furth (Johns Hopkins Medical Institutions, Pediatric Nephrology), Bradley A. Warady (Childrens Mercy Hospital, Pediatrics). Dr. Munoz, Dr. Furth and Dr. Warady are the lead investigators on the NIH-sponsored CKiD study, an ongoing observational study of children with CKD.

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The article, entitled "The Association between Abnormal Birth History and Growth in Children with CKD," appeared online at http://cjasn.asnjournals.org/ on October 28, 2010, doi 10.2215/CJN.08481109.

Founded in 1966, the American Society of Nephrology (ASN) is the world's largest professional society devoted to the study of kidney disease. Comprised of 11,000 physicians and scientists, ASN continues to promote expert patient care, to advance medical research, and to educate the renal community. ASN also informs policymakers about issues of importance to kidney doctors and their patients. ASN funds research, and through its world-renowned meetings and first-class publications, disseminates information and educational tools that empower physicians.

Independent Panel Discourages Routine Use of Treatment Regimen for Premature Infants

Premature infants often suffer from respiratory problems due to their underdeveloped lungs. Over the past decade, many of these infants have been treated with inhaled nitric oxide — a treatment designed to ease breathing by widening blood vessels in the lungs. This week, an independent panel convened by the National Institutes of Health determined that the scientific data taken as a whole do not support the use of inhaled nitric oxide in the routine clinical care of premature infants born before the 34th week of pregnancy. Additional studies are needed to ascertain the short and long-term benefits and risks of this treatment.

"In recent years, continuing advances in obstetrics and neonatal intensive care have increased survival of preterm infants," said Dr. F. Sessions Cole, conference panel chairperson and director of the Division of Newborn Medicine at Washington University School of Medicine, St. Louis. "However, these babies remain at substantial risk for medical problems that can create lifelong challenges. We need safe and effective treatments, but the current evidence does not point to inhaled nitric oxide as providing a clear benefit to most of these children."

Premature infants, in general, face increased risk for adverse outcomes including death, lung disease, and neurodevelopmental problems such as cerebral palsy, blindness, and learning disabilities. In 1999, the US Food and Drug Administration (FDA) approved inhaled nitric oxide therapy to treat one of these risks — pulmonary hypertension, or high blood pressure in the blood vessels supplying the lungs — in term and near-term infants. Since that time, some hospitals have extended the use of nitric oxide on an off-label basis for younger babies, less than 34 weeks gestation, in the hope of promising results.

The consensus development panel examined combined evidence from 14 randomized controlled trials of nitric oxide in premature infants ≤34 weeks gestation and concluded that as a whole, the studies did not show a favorable impact on survival or lung function.

The panel concluded that long-term follow-up studies would be necessary to determine the balance of treatment risks and benefits, but also acknowledged difficulties in conducting this research. "Inhaled nitric oxide affects multiple organ systems, and developing premature infants are especially vulnerable to adverse treatment effects, long after they leave the neonatal intensive care unit. If further trials are pursued, children must be followed at least through school age," Dr. Cole explained. "Unfortunately, this research is

not only logistically challenging but in many cases very expensive."

The panel pointed to remaining uncertainties regarding the respective roles of dosing, timing, and delivery method of inhaled nitric oxide that should be addressed to optimize benefits and reduce treatment risks. The panel recommended that future trials examine the relative contributions of different treatment regimens and use larger sample sizes to assess safety and efficacy among different subgroups of premature infants.

Although inhaled nitric oxide is approved for term and near-term infants with pulmonary hypertension, the panel concluded that this treatment should be considered only for certain premature infant subgroups, and only when other clinical options have been exhausted. The panel suggested that clinicians provide families with accurate and understandable information about inhaled nitric oxide, and foster partnership and shared decision-making when considering its use.

An updated version of the panel's draft consensus statement, which incorporates public comments, has been posted at http://consensus.nih.gov.

Women & Infants Receives $2 Million Grant From The NIH To Continue Work On Perinatal Biology

Women & Infants Hospital has recently received a $2.1 million grant from the National Institutes of Health (NIH) to continue work under the Center of Biomedical Research Excellence (COBRE) for Perinatal Biology. Of the 108 COBREs across the country, Women & Infants is the only one specifically focused on developmental research.

Under the leadership of Women & Infants' Pediatrician-in-Chief, James F. Padbury, MD, and Surendra Sharma, MBBS, PhD, the COBRE team of researchers are studying embryo, placenta and heart development, the susceptibility to infection in newborns, and the effects of intrauterine development on later outcomes.

"Our projects are focused on critical windows of development. Environmental disturbance or other influences during these critical windows can have lasting effects," said Dr. Padbury. "Our overarching hypothesis is that understanding these effects during critical developmental periods informs the mechanisms of health and disease throughout life." Carmen Marsit, PhD, from the Department of Pathology at Brown University, is studying epigenetic effects of the intrauterine development, the environment, and alterations in placental DNA. An adverse intrauterine environment, especially in late pregnancy, can be associated with heightened risk of disease in adult life; including hypertension, diabetes and cardiovascular disease. By optimizing both the intrauterine and the postnatal environment, researchers hope to improve outcomes for the most vulnerable children.

Women & Infants' reproductive endocrinologist Jared Robins, MD, and his team are studying how environmental conditions may affect embryonic development. The results will improve outcomes in infertility treatment by examining the optimal conditions for an embryo to develop, thereby increasing the success of many infertility treatment protocols.

Joseph Bliss, MD, PhD, a neonatologist at Women & Infants, is researching infection in extremely low birth weight newborns with the hopes that his discoveries will improve care not only for these infants but also for immune-compromised children and adults whose susceptibility to these infections may be life threatening.

A team led by Yi-Tang Tseng, PhD, a research scientist in Women & Infants' Department of Pediatrics, has identified the unique mechanisms in fetal life that control cell division during heart development. Using translational science, the team is looking at how overexpression of these mechanisms may induce cardiac repair and regeneration following a myocardial infarction during adult life.

The COBRE researchers' laboratories are all located in Providence's "Knowledge District" in the Kilguss Research Institute, the Laboratory for Molecular Medicine and the Coro Research Building.

Other investigators include Sunil Shaw, PhD, and Zhongbin Lai, PhD. Senior investigators also participating in the projects are Sandra Carson, MD; Ulrike Mende, PhD; and Karl Kelsey, MD.

For additional information go to: www.womenandinfants.org.

Experts Recommend Universal Screening of Newborns for Congenital Adrenal Hyperplasia

This September The Endocrine Society released a new clinical practice guideline on the diagnosis and treatment of congenital adrenal hyperplasia (CAH). The guideline features a series of evidence-based clinical recommendations developed by an expert task force.

The guideline, published in the September 2010 issue of the *Journal of Clinical Endocrinology & Metabolism* (JCEM), a publication of The Endocrine Society, is endorsed by the American Academy of Pediatrics, Pediatric Endocrine Society, the European Society for Paediatric Endocrinology, the European Society of Endocrinology, the Society for Pediatric Urology, the Androgen Excess and PCOS Society, and the CARES Foundation.

CAH is a genetic disorder of the adrenal glands that affects about one in 10,000 to 20,000 newborns, both male and female. The adrenal glands make the steroid hormones cortisol, aldosterone and androgens. In individuals with CAH, the adrenal glands produce an imbalance of these hormones which can result in ambiguous genitalia in newborn females, infertility and the development of masculine features such as development of pubic hair, rapid growth in both girls and boys before the expected age of puberty.

"If CAH is not recognized and treated, both girls and boys undergo rapid postnatal growth and early sexual development or, in more severe cases, neonatal salt loss and death," said Phyllis Speiser, MD, of Cohen Children's Medical Center of New York and Hofstra University School of Medicine, and chair of the task force that developed the guideline. "We recommend that every newborn be screened for CAH and that positive results be followed up with confirmatory tests."

Other recommendations from the guideline include:

- Prenatal treatment of CAH should continue to be regarded as experimental. Such therapies should be pursued through protocols approved by Institutional Review Boards at centers capable of collecting outcomes data on a large number of patients so that risks and benefits of this treatment can be defined more precisely;
- Diagnosis should rest on clinical and hormone data while genotyping should be reserved for equivocal cases and genetic counseling;
- Regarding treatment, glucocorticoid dosage should be minimized to avoid iatrogenic Cushing's Syndrome. Mineralcorticoids and, in infants, supplemental sodium are recommended in classic CAH patients;
- Clinicians should avoid the routine use of experimental therapies to promote growth and delay puberty, and patients should avoid adrenalectomy;
- Early single-stage genital repair should be considered for severely virilized girls and should be performed only by surgeons experienced in this type of procedure;
- Clinicians should consider patients' quality of life, consulting mental health professionals as appropriate;
- At the transition to adulthood, clinicians should monitor for potential complications of CAH; and
- Clinicians should exercise judicious use of medication during pregnancy and in symptomatic patients with nonclassic CAH.

"People with classic CAH should have a team of health care providers, including specialists in pediatric endocrinology, pediatric urologic surgery (for girls), psychology and genetics," said Speiser. "Other than having to take daily medication, people with classic CAH can have a normal life."

The Hormone Foundation, the patient education affiliate of The Endocrine Society, has published a new bilingual fact sheet about congenital adrenal hyperplasia for patients. It defines CAH and explains how the condition is diagnosed and treated. The fact sheet can be found online at: www.hormone.org/Resources/upload/congenital-adrenal-hyperplasia-bilingual-081310.pdf.

Other members of the task force that developed this guideline include: Ricardo Azziz of Cedars-Sinai Medical Center in Los Angeles, Calif.; Laurence Baskin and Walter Miller of the University of California San Francisco, CA; Lucia Ghizzoni of the University of Turin in Italy; Terry Hensle of Columbia University in New York, NY; Deborah Merke of the National Institutes of Health Clinical Center; Heino Meyer-Bahlburg of New York State Psychiatric Institute in New York, NY; Victor Montori of Mayo Clinic in Rochester, MN.; Sharon Oberfield of Columbia University College of Physicians & Surgeons in New York, NY; Martin Ritzen of Karolinska Institute in Stockholm, Sweden; and Perrin White of the University of Texas Southwestern Medical Center in Dallas, TX.

To learn more about the Society and the field of endocrinology, visit our site at www.endo-society.org.

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