NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

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IN THIS ISSUE

Upcoming Meetings

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www.pas-meeting.org

The 26th Annual Meeting of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC 2015)
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A Rare Congenital Long QT Syndrome Diagnosed Prenatally with Fetal Magnetocardiography

By Rodrigo Rios, MD; Ronald T. Wakai, PhD; Janette F. Strasburger, MD

Introduction

Historically, the assessment of fetal cardiac electrical activity has been limited due to the difficulty of obtaining adequate and reliable electrograms using traditional electrocardiography. Mechanisms for these limitations have been proposed including limited availability of specialized fetal electrocardiography tools as well as a low signal-to-noise ratio likely related to insulation of the fetus with vernix caseosa later in gestation.[1] Fetal echocardiography allows for the assessment of heart rhythm by evaluation of the structural and mechanical properties of the fetal heart, but does not allow for assessment of fetal cardiac electrophysiology. Important electrocardiographic parameters such as P-wave and QRS morphologies, preexcitation, QT intervals, and T-wave morphology are unable to be evaluated with traditional fetal cardiac screening including fetal echocardiography. Thus, the electrophysiological features of fetal arrhythmias remain largely unknown.

Fetal magnetocardiography is a recently developed noninvasive modality for evaluation of the fetal cardiac electrical activity. This technology allows for the recording of magnetic fields generated by the electrical activity of the fetal heart. The availability of this technology has been limited to a few physics laboratories around the world mostly due to associated cost and technical constraints. Despite this limitation, the usefulness of fetal magnetocardiography for evaluating fetal electrophysiological disease, including long QT Syndrome, has recently been evaluated and described.[2] We present a case in which evaluation using fetal magnetocardiography revealed marked prolongation of the QT interval in a patient who was subsequently confirmed to have Timothy Syndrome, a rare form of congenital Long QT Syndrome.

Case Description

A 34-year-old, Gravida 4, Para 3, woman with an uncomplicated pregnancy was referred to the Fetal Heart Program at the Children's Hospital of Wisconsin Herma Heart Center at 22 and 5/7 weeks gestation due to concerns about pericardial effusion and a small left ventricle seen on routine prenatal ultrasonography. There was no evidence of extracardiac abnormalities. She was taking a routine prenatal vitamin with iron fumarate and denied any other exposure to medications. There was no history of Congenital Heart Disease (CHD) or inherited arrhythmias in first-degree relatives. A fetal echocardiogram was suggestive of borderline biventricular hypertrophy, a small mid-muscular VSD, a 2-3mm anterior pericardial effusion, and a small Patent Ductus Arteriosus (PDA) with intermittent ductal constriction. The fetus remained in normal sinus rhythm throughout the examination. During a follow-up study at 28 and 5/7 weeks, the ductal arch was well visualized with unobstructed flow. The remainder of the study was unchanged from the previous exam, except for an irregular cardiac rhythm with apparent atrial bigeminy. A repeat fetal echocardiogram at 30-weeks

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gestation identified 2:1 atrioventricular conduction with a bradycardic atrial rate of 120-130 bpm and a ventricular rate of 65-68 bpm. However, ventricular function remained normal and the fetus had a normal biophysical profile. Due to concern for antibody mediated fetal heart block, the mother did receive one dose of steroid, and as Vitamin D level was low, she was started on supplemental Vitamin D. Maternal Anti-SSA and Anti-SSB antibodies were negative, and her electorcardiogram was normal (QTc = 430msec). A paternal ECG was not obtained. The fetus continued to have 2:1 atrioventricular conduction during the next fetal echocardiogram performed at 31 and 5/7 weeks gestation, with ventricular rates 63-67 bpm. There continued to be biventricular hypertrophy and normal ventricular function with no signs of hydrops fetalis. Due to the persistent arrhythmia, the mother was referred to the Biomagnetism Laboratory at the University of Wisconsin-Madison for fetal magnetocardiography. Fetal magnetocardiography was performed at 33 weeks gestation, and was significant for sinus bradycardia with intermittent 2:1 atrioventricular conduction, a markedly prolonged fetal QTc interval of 580 – 700 milliseconds, and T wave alternans throughout the study (Figures 1, 2). A fetal echocardiogram was repeated at 33 weeks. The fetus was in sinus rhythm during the entire study with heart rates 109 bpm to 148 bpm. There were no episodes of conduction abnormalities or fetal tachycardia. Spasm of the ductus arteriosis was observed as had been intermittently seen throughout the pregnancy. There continued to be a very small pericardial effusion without further signs of hydrops fetalis. Fetal magnetocardiography was repeated at 34 weeks gestation and continued to show a markedly prolonged QTc of 520 – 600 milliseconds. The T wave alternans was less pronounced and there were no episodes of atrioventricular conduction block. The infant was delivered via uncomplicated elective Caesarian-section at 36 and 2/7 weeks gestation secondary to non-reactive fetal cardiac tracings. Given the risk of life-threatening arrhythmias, an electrophysiologist was present at the delivery. The infant had a normal heart rate in the immediate postnatal period and did not require any neonatal resuscitation. Her Apgar scores were reassuring at 7, 9, and 9 at 1, 5, and 10 minutes respectively. She was noted to have multiple congenital abnormalities including bilateral syndactyly of the 3rd, 4th, and 5th digits of the hands, bilateral syndactyly of the 2nd and 3rd digits of the feet, micrognathia

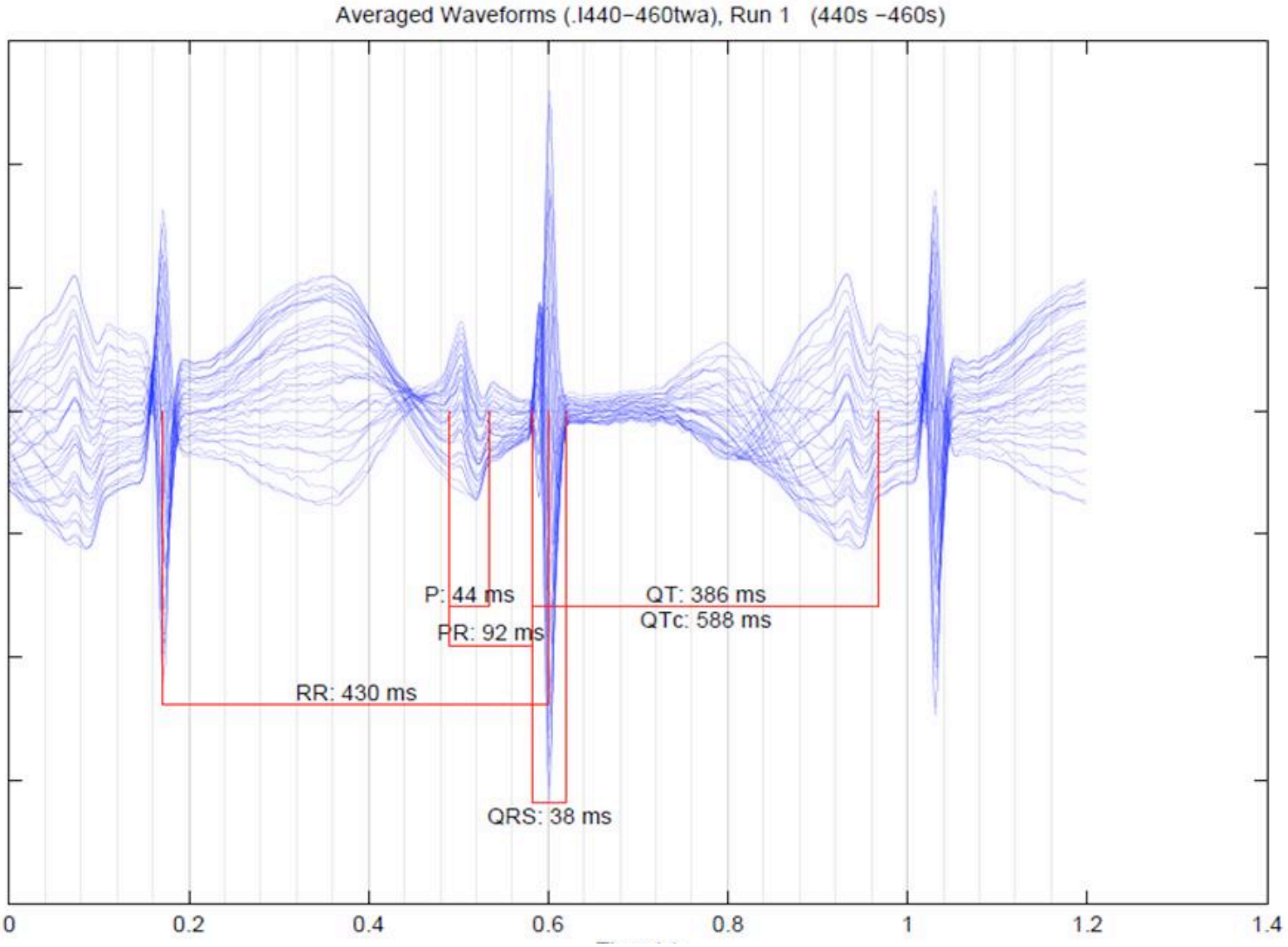

Figure 1. Overlay of Averaged waveforms during fMCG study. The QTc is markedly prolonged at 588 msec.

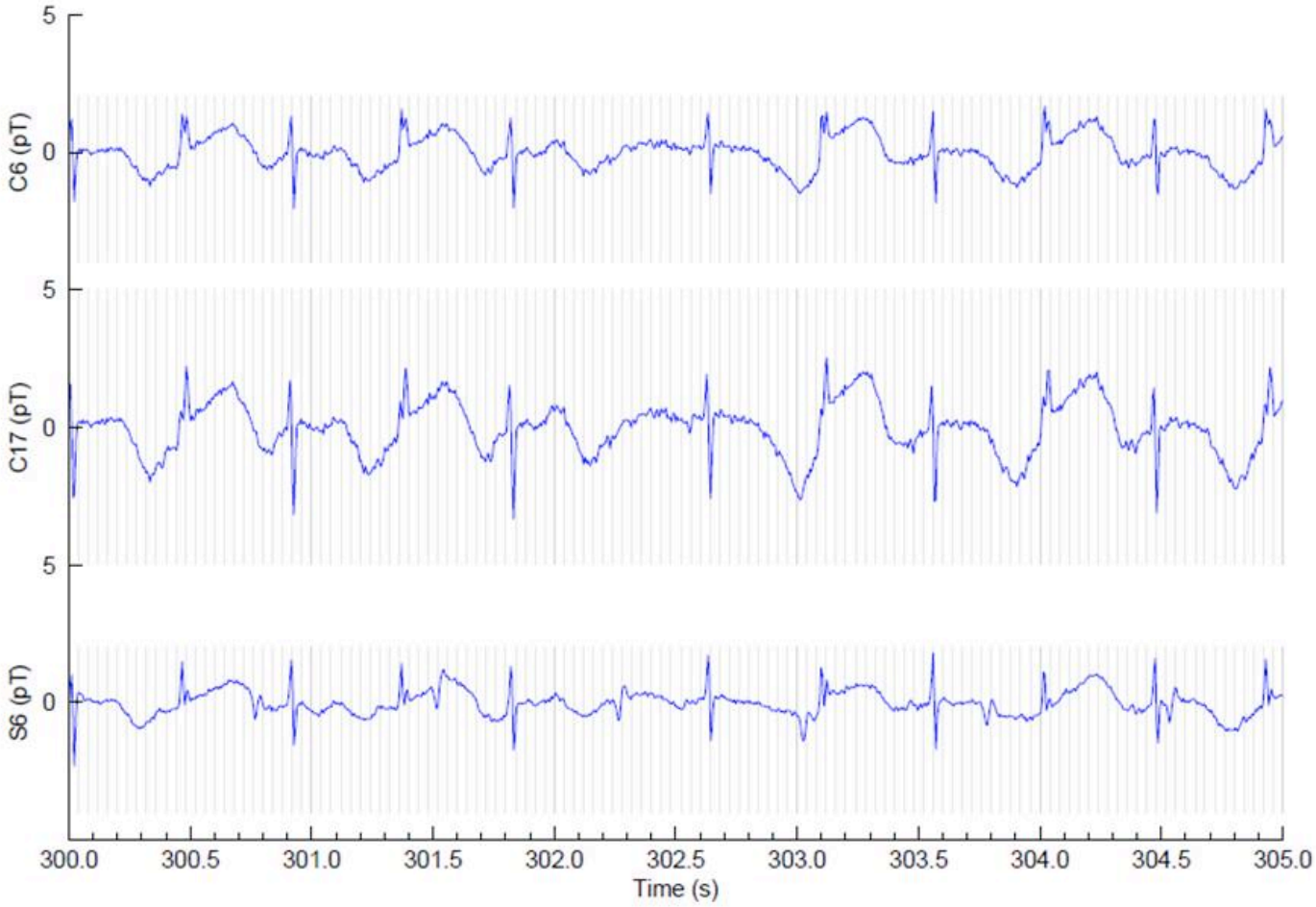

Figure 2. fMCG tracing shows QRS and T wave alterns.

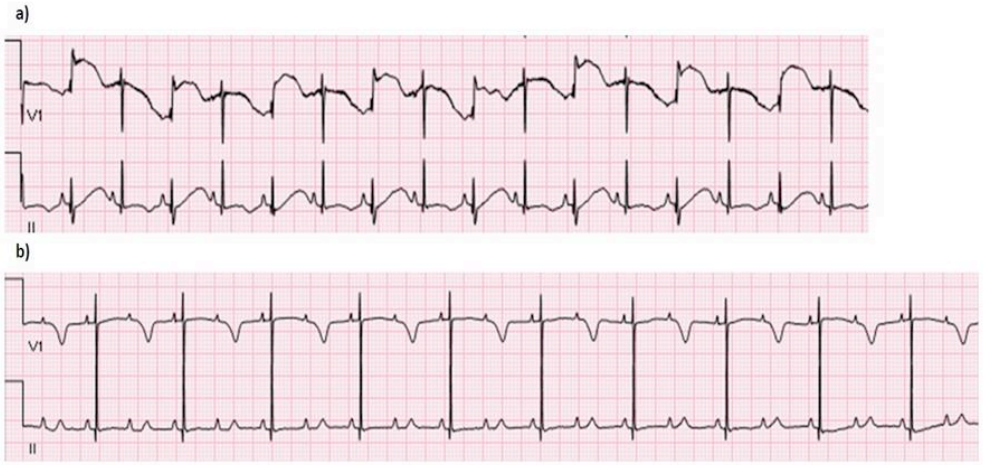

Figure 3. Leads V1 and II of serial ECGs. (a) Obtained shortly after birth consistent with markedly prolonged QTc with T wave alterns. (b) Obtained at about 4 hours of life shows markedly prolonged QTc with 2:1 atrioventricular conduction.

and retrognathia. She was admitted to the Children's Hospital of Wisconsin Neonatal Intensive Care Unit for further management, including cardiorespiratory monitoring. An ECG was obtained and showed a normal sinus rhythm, a markedly prolonged QTc at 580 milliseconds, and T wave alternans (Figure 3a). At about four hours of life, the patient developed 2:1 atrioventricular conduction with a ventricular rate of about 60 bpm (Figure 3b). At that time she was started on orally-administered propranolol at 1.4mg/kg/day divided every 8 hours. She subsequently had decreasing renal saturations per Near-Infrared Spectroscopy monitoring suggesting decreased systemic oxygen delivery consistent with worsening cardiac output. Following this episode she was started on orally-administered mexiletine at 7mg/kg/day divided every 8 hours. Her indices of perfusion improved and she subsequently had return of 1:1 antrioventricular conduction which she had for the remainder of her neonatal intensive care unit course. A postnatal echocardiogram was obtained on the sixth day of life and showed a small PDA with left-to-right shunting, moderate right ventricular hypertrophy, a mildly dilated and hypertrophied left ventricle, and normal biventricular function. She was discharged on Day of Life Seven, has remained on propranolol and mexiletine, and has remained in normal sinus rhythm, with prolonged QTc, and 1:1 atrioventricular conduction with no

evidence of ventricular tachyarrhythmias clinically or per serial Holter monitors. Her constellation of symptoms including prolonged QTc and upper and lower extremity syndactyly was felt to be consistent with the rare, previously described, Timothy Syndrome. Genetic testing for the associated autosomal dominant mutation of the L-type calcium channel gene, CACNA1C, was obtained and revealed heterozygosity for the Gly406Arg missense mutation which has been associated with Timothy Syndrome.

Discussion

This case illustrates the important potential role of a new experimental modality, fetal magnetocardiography, in diagnosing arrhythmias in the prenatal period. This is especially important considering the recently proposed role of fetal arrhythmias in fetal demise.[3] Although abnormal conduction was demonstrated by fetal echocardiography, fetal magnetocardiography allowed for the evaluation of more specific electrophysiological information important in this case such as QTc and T wave alternans. The severe manifestations of Long QT Syndrome, including Torsades de Pointes and heart block, can be life threatening and prenatal diagnosis allows for anticipation of these challenges to clinical management both pre- and postnatally. Specifically in this case, prenatally, the mother was screened for Vitamin D and electrolyte deficiencies, and was treated. She was also studied by fetal magnetocardiography on more than one occasion to rule out Torsades de Pointes ventricular tachycardia, during which the non-reactive heart rate tracing was observed on the day of delivery. Furthermore, an electrophysiologist was present at the delivery and the capability to provide expert medical management in the immediate postnatal period was ensured. In addition, the diagnostic findings were confirmed quickly after birth with electrocardiographic studies and cardiac rhythm monitoring. The concordance of the prenatal electrophysiological findings obtained by fetal magnetocardiography and postnatal findings obtained by standard electrocardiograms is easily appreciated. Both the fetal magnetocardiography tracings and the electrocardiogram tracings show a markedly prolonged QTc with episodes of 2:1 AV conduction as well as abnormal repolarization characteristics including T wave alternans.

In addition, this case describes the prenatal presentation and postnatal course of a patient with Timothy Syndrome, a rare congenital syndrome caused by dysfunction of the Cav1.2 calcium channel encoded by the CACNA1C gene. Its clinical manifestations include prolonged QT interval, CHD, abnormalities of the hands and feet, dysmorphic facial features, intermittent hypoglycemia, and neurologic sequelae including neurodevelopment delay, autism, and seizures.[4] The Cav1.2 calcium channel is impaired causing sustained influx of calcium into the cardiac myocytes resulting in a prolongation of the action potential and thus a prolonged QT interval.[5] This is among the most malignant congenital Long QT Syndromes, with an average age of death of 2.5 years and with ventricular arrhythmias being the major cause of death. Timothy Syndrome was first described by Splawski et al. in 2004 and others have subsequently further described genotypic and phenotypic aspects of the syndrome. [6]

The associated congenital defects of Timothy Syndrome, including syndactaly, are difficult to visualize with routine prenatal ultrasound and were not identified until birth in this case.[7] The electrophysiological findings, however, were discovered prenatally. Interestingly, the 2:1 conduction was apparently well tolerated by the fetus with normal serial bio-

"In conclusion, this case illustrates that a new diagnostic modality, fetal magnetocardiography, can be used in conjunction with fetal echocardiography to evaluate fetal electrophysiology and diagnose potentially life-threatening arrhythmias prenatally. Once this technology is more readily available in the clinical setting, obstetricians and cardiologists will be able to refer pregnant mothers carrying a fetus with a suspected arrhythmia to obtain accurate fetal electrophysiological data."

physical profiles but in the immediate postnatal period was associated with signs of decreased cardiac output including decreased renal oxygen saturations measured by Near-Infrared Spectroscopy. Indices of cardiac output returned to normal once 1:1 conduction was attained with shortening of the QTc with propranolol and mexiletine. In previous case reports, mexelitine has been reported to abolish 2:1 atrioventricular block and T wave alterans by inhibition of the cardiac sodium ion channel, INa,L. This channel contributes to QT prolongation in Long QT Syndrome regardless of the underlying mechanism.[8]

In conclusion, this case illustrates that a new diagnostic modality, fetal magnetocardiography, can be used in conjunction with fetal echocardiography to evaluate fetal electrophysiology and diagnose potentially life-threatening arrhythmias prenatally. Once this technology is more readily available in the clinical setting, obstetricians and cardiologists will be able to refer pregnant mothers carrying a fetus with a suspected arrhythmia to obtain accurate fetal electrophysiological data.

Acknowledgments

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Conflicts of Interest

None

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NT Column: Applications for a Mobile Life In the Unit, Part 1 of 3 - *Social and Mobile Media for the Neonatologist*

By Clara H. Song, MD

"Social & Mobile Media for the Neonatologist" by Dr. Song, is a quarterly column in *Neonatology Today*. Dr. Song created and moderates the social media outlets for the American Academy of Pediatrics, Section on Perinatal Pediatrics, as well as the NICU at the Children's Hospital at OU Medical Center. She holds workshops and speaks regionally and nationally on the topic of social communication for the healthcare professional, including: the AAP Perinatal Section Spring meeting, yearly, and the 2011 *NEO: The Conference for Neonatology.*

"Action in the Neonatal Intensive Care Units (NICU) can sometimes move like the far left fast lane on an interstate highway. The right apps can help us stay productive and efficient. Here are some particularly helpful ones that help us stay on the go and at the bedside."

My 2-year-old nephew is pretty savvy with his "big phone," a.k.a. iPad. Apps seem to be a routine part of his life. On-the-go access to information helps him stay entertained and educated in so many ways... at 2 years old! We health professionals are slowly jumping on this band wagon. In a 2013 survey of over 1000 clinicians, 86% and 53% stated that they used smartphones and tablets, respectively, for professional reasons.[1] Action in the Neonatal Intensive Care Units (NICU) can sometimes move like the far left fast lane on an interstate highway. The right apps can help us stay productive and efficient. Here are some particularly useful ones that help us stay on-the-go and at the bedside:

- **TnECHO:** This application comes from The Hospital for Sick Kids in Toronto at no cost. Short video clips and labeled images walk us through the basic technique and the ultrasound views for bedside targeted-neonatal echocardiography (TnECHO). This app was created as a reference tool for the neonatologist who is committed to performing TnECHO. However, the ultrasound and color Doppler images are a great resource in helping understand exactly what we see on the monitor when looking over the ECHO tech's shoulder. *Available at the iTunes Apple Store for your iPhone and iPad. Corresponding website, TnECHO.com.*[2]
- **iNO MAX NICU PRO:** This app includes five medical calculators specifically for use in the NICU. The app includes calculators for the following: Oxygen Index, AaDO2, Pregnancy/Gestational Age, Fractional Excretion of Sodium, and SNAP-II & SNAPPE-II. It was created by Ikaria. The company uses this app to disseminate safety information on their product, INOMAX. *Available at the iTunes Apple Store for your iPhone and iPad without cost.*[3]
- **NEONATAL GROWTH CHART 2013:** Based on the 2013 paper by Dr. Tanis Fenton and Dr. Jae Kim, this is a simple, useful app for tracking the growth of preterm infants until 50 weeks gestational age corrected by percentages and Z-scores. *Available at the iTunes Apple Store for your iPhone and iPad without cost.*[4]
- **NICU NUTRITION CALCULATOR:** This neonatologist-created app calculates nutritional intake from TPN, IL and enteral feeds. The app calculates total caloric intake, the percentage of calories from carbohydrates, protein and fat, as well as intake of calcium, phosphorus and Vitamin D from one or all of these nutritional sources. A variety of human milk variations and formulas are included as feeding options. Due to growing popularity, this app now comes with a cost. *Available at the iTunes Apple Store for your iPhone and iPad and the Google Play Store for your Android device.*[5]
- **iNRP:** The Neonatal Resuscitation Program (NRP) designed this straight-forward app to provide quick access to the 2010 algorithm for neonatal resuscitation and a metronome for teaching and practicing delivering ventilation at the proper rate with and without compressions. *Available at the iTunes Apple Store for your iPhone and iPad without cost*.
- **PEDIAGENE:** This app is currently free to all members of the American Academy of Pediatrics. For non-members, the cost is significant ($49.99), in terms of app-world.[6] However, this speaks to the volume and extent of information that is packed into this app. PediaGene allows for handy access to a patient tracker, screening tools, references of tables and images for a variety of genetic conditions and quick links to ACT sheets from the American College of Medical Genetics. *Available at the iTunes Apple Store for your iPhone and iPad*[7] *and the Google Play Store for your Android device.*[8]
- **NEOFAX:** In 2012, the NeoFax Manual of Drugs Used in Neonatal Care was transformed from print to electronic mobile form.[9, 10] Its usefulness and

immediate access to up-to-date neonatal-specific drug and enteral nutrition information is undeniable, but it comes at a price. This app requires a subscription fee of $29.99 per year for an up-to-date neonatal-specific drug and enteral nutrition information. *Available at the iTunes Apple Store for your iPhone and iPad.*[11]

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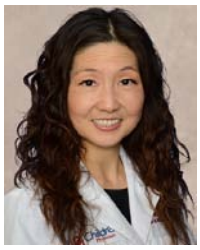

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- No abstract should be submitted.
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Fifth Annual Congenital/Fetal Imaging Conference at University of Utah/Primary Children's Hospital

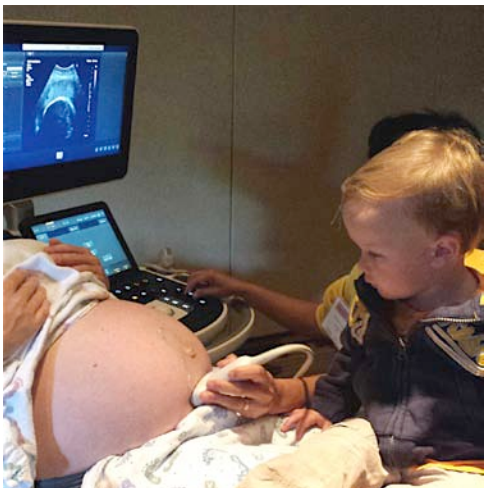
By Nelangi Pinto, MD

Left-to-Right: Drs. Thomas Miller, Nelangi Pinto, Jan Byrne, Mike Puchalski and Jason Su.

The *Fifth Annual Congenital/Fetal Imaging Conference* was held in Park City, Utah in the Fall of 2014 with about 100 attendees from 5 states. Attendees included: obstetrical and postnatal sonographers, obstetricians and pediatric cardiologists. The first conference of its kind in the Western U.S., it was jointly sponsored by Primary Children's Hospital (www.primarychildrens.org), the Department of Pediatrics, the Department of Obstetrics and Gynecology, and the Department of Radiology at the University of Utah.

The 2-day symposium is directed at practitioners who are interested in learning more about imaging fetal and postnatal heart defects. The conference also provides invaluable information on additional fetal screening and prenatal care of affected pregnancies. Each conference has focused on a particular cardiac problem, and 2014's focus was on single ventricle lesions.

The first afternoon of the conference was kicked off by a presentation on fetal cardiac embryology and the origin of single ventricle lesions by Dr. Thomas Sadler. Dr. Sadler taught Embryology and Anatomy at the University of North Carolina for 25 years and gives one of the most approachable and understandable lectures on the development of the human heart. His lecture laid the groundwork for the rest of the session which followed with an overview of fetal heart scanning, specifically reviewing the pearls of actual imaging and interpretation of four chamber and outflow tract views. This was followed by a live scanning session to review the methods of obtaining screening views.



Our youngest participant trying to see his little brother.

The remainder of the first day focused on diagnosing and following genetic syndromes associated with cardiac defect, the nuances of first trimester screening and non-cardiac causes of an abnormal four chamber view.

The second day of the conference provided two simultaneous break out sessions on fetal and postnatal imaging and care. After a general overview on recognizing chamber asymmetry, the fetal session drilled down on how to assess small left and right hearts, which included providing an overview of the differential diagnosis's and reviewing imaging techniques to predict postnatal outcome. The sessions dovetailed into using this imaging information to develop perinatal and postnatal care plans. The parallel session sought to review important technical aspects of postnatal imaging in diagnosing and following single ventricle defects. These talks were framed on assessment of small ventricles and evidenced based knowledge used to determine timing and type of intervention for specific defects.

The most lauded sessions in the conference and mainstays since it began are the hands-on screening and viewing of pathology specimens. These give participants the chance to perform scanning on volunteer mothers with real-time feedback from fetal sonographers and cardiologists. In addition, this year participants were able to review a number of single ventricle pathology specimens with pathologist Lance Erickson.

Next year the conference will be delayed so that it can be held in conjunction with the *Conference for the Western Society of Pediatric Cardiology* in May of 2016. This will provide an opportunity to interface with faculty experts from both conferences so prospective attendees should definitely plan ahead and register early for what promises to be a great event.

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Clinical Trials - Selected & Edited from ClinicalTrials.gov

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Osteopathic Approach Into Neonatology Ward: the NE-O Model

Expanded access is currently available for this treatment.*
Verified May 2014 by European Institute for Evidence Based Osteopathic Medicine

Sponsor: European Institute for Evidence Based Osteopathic Medicine

Purpose: Background Several studies have shown the effect of osteopathic manipulative treatment on neonatal care in reducing length of stay, gastrointestinal problems, clubfoot complications and improving craial asymmetry of infants affected by plagiocephaly. Despite several results obtained, there is still lack of standardized osteopathic evaluation and treatment procedures for newborns recovered in Neonatal Intensive Care Unit (NICU).

The aim of this research is to provide a guideline on osteopathic approach in treating hospitalized newborns. Specific evaluation tests and treatments have been developed to tailor osteopathic method according to preterm and term infants' needs, NICU environment, medical and paramedical assistance.

Condition: The Focus of the Study is to Provide a Guideline on Osteopathic Approach in Treating Hospitalized Newborns.

Intervention - Other: Osteopathic Manipulative Treatment

Study Type: Expanded Access

Ages Eligible for Study: 29 Weeks - 40 Weeks

Genders Eligible for Study: Both

Inclusion Criteria: Newborn admitted to the NICU; informed consent signed from parent or legal guardian

Exclusion Criteria: Post surgery patients

Contact: Francesco Cerritelli, MS, DO
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*Expanded access: A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial.

ClinicalTrials.gov Identifier:
NCT01902563
Other Study ID Numbers: NE-O-prot
Study First Received: July 10, 2013
Last Updated: May 16, 2014

Vermont Oxford Network Very Low Birth Weight Database (VON VLBW)

This study is currently recruiting participants.
Verified April 2013 by Vermont Oxford Network

Sponsor: Vermont Oxford Network (VON)
Information provided by (Responsible Party): VON

Purpose: VON maintains a database for live born infants 401 to 1500 grams or 22 to 29 weeks gestational age who are born at participating hospitals or admitted to them within 28 days of birth, regardless of where the infant receives care.

Condition: Neonatology

Intervention - Other: Registry

Study Type: Observational [Patient Registry]

Study Design: Observational Model: Cohort

Time Perspective: Prospective

Target Follow-Up Duration: 1 Year

Official Title: Vermont Oxford Network Very Low Birth Weight Database of Infants 401 to 1500 Grams or 22 to 29 Weeks Gestational Age at Birth

Primary Outcome Measures: Registry of baseline and outcome data for Very Low Birth Weight infants (VLBW) with data collected in a uniform manner [Time Frame: up to 1 year]

[Designated as safety issue: No] Data items include infant and maternal characteristics, delivery room interventions, respiratory care and outcomes, surgeries, infections, comorbid conditions, and length of stay. Time frames for data collection include: characteristics of birth; at day 28; and at discharge. Tracking ends at discharge home (including infants transferred out) or at one year.

Study Start Date: January 1990

Estimated Study Completion Date: December 2040

Groups/Cohorts: Very Low Birth Weight infants. Infants 401 to 1500 g or 22 to 29 weeks gestational age admitted to Vermont Oxford Network member centers within 28 days of birth.

Assigned Interventions - Other: Registry

Detailed Description: The Database collects observational baseline data on both mothers and infants, and the therapies used and outcomes of the infants. The information collected

is not specific to a disease or treatment. The data collected includes information on:

- Demographics of mother and infant
- Mother's health, labor and delivery
- Infant's health upon admission, procedures and interventions, and medical outcomes

These data are used to: provide member centers with reporting for use in quality improvement; examine associations between baseline characteristics, treatments, and outcomes; and track trends in incidences of disease and effectiveness of therapies.

Ages Eligible for Study: Up to 28 Days

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

Sampling Method: Non-Probability Sample

Study Population: Infants who are 401 to 1500 grams birth weight or 22 to 29 weeks gestational age, and who are admitted to VON member centers within 28 days of birth without first going home.

Inclusion Criteria: Any infant who is born alive and whose birth weight is 401 to 1500 grams or 22 weeks 0 days and 29 weeks 6 days gestational age (inclusive) who is born at or admitted to a VON member center within 28 Days of Life without having first gone home, regardless of the where the infant receives care.

Exclusion Criteria: Stillborn infants; Infants discharged home prior to admission to a member center; Infants admitted after 28 days.

Contacts and Locations: To learn more about this study, contact the study research staff:

Contacts:
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Sponsors and Collaborators: VON Investigators

Study Chair: Jeffrey D Horbar, MD; Vermont Oxford Network

ClinicalTrials.gov Identifier:
NCT01825499
First received: March 27, 2013
Last updated: April 4, 2013

For detailed information on these and other clinical trials, please visit: www.ClinicalTrials.gov

JUNE MEDICAL MEETING FOCUS

The 26th Annual Meeting of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC 2015)
June 10-13, 2015 Vilnius, Lithuania
espnic.kenes.com

Overview: Covers Pediatric, Neonatal and Perinatal Intensive Care

Meeting Includes: Internationally well-known faculty with workshops, post graduate courses multidisciplinary sessions, nursing sessions, moderated poster sections, physiology lectures, and scientific sessions

Workshop Topics Include:

- Setting Up Ventilator for Neonates and Older Children
- Feeding Practice in PICU – How to Feed
- Forgoing Life Support: Improving Care in the Face of Inevitable Death
- Circulation, Everything You Always Wanted to Know Extracorporeal Therapies in PICU
- Echo for the Intensivist
- and more....

Sessions and Lecture Topics Include:

- Outcomes
- Cardiopulmonary Interactions
- Modulations of the Immune System: The Next Challenge?
- Non-Invasive Support in the Acute and Chronic Setting
- Drugs in the PICU: Off-Label Use or Drug Development
- Nursing Staff in the PICU and the NICU
- End of Life Care
- Ventilator-Induced Lung Injury in Neonates: Infants and Children
- The Heart is not All...
- Managing Post-Transplantation Complications
- Reduce and Prevent Pain
- Supporting Parents and Families
- Best Practices in Paediatric Cardiac Surgery
- Update in Neurologic Syndromes of ICU
- Young Investigator Session
- and more....

Faculty Includes:
Corinne Buysse, Eduardo Da Cruz, Daniele Da Luca, Andy Darbyshire, Akash Deep, Philippe Eggimann, Ricard Ferrer, Odile Frauenfelder, Jan Hazelzet, Erwin Ista, Koos Jansen, Etienne Javouhey, Koen Joosten, Oliver Karam, Jos Latour, Joris Lemson, Duncan Macrae, Paulo Manzoni, Dieter Mesotten, Marek Migdal, Jens Moller, Anneliese Nusmeier, Peter Rimensberger, Robert Tasker, Dick Tibboel, Pierre Tissieres, Frederic Valla, Monique Van Dijk, Sascha Verbruggen, Virinija Zilinskaite and many others....

Medical News, Products & Information

Compiled and Reviewed by Tony Carlson, Senior Editor

UTSW Researchers Identify Key Substance That Protects Against Pre-Term Birth

Newswise - Researchers at UT Southwestern Medical Center have identified Hyaluronon (HA) as a critical substance made by the body that protects against premature births caused by infection. Pre-term birth from infection is the leading cause of infant mortality in many countries according to the World Health Organization. The findings of the study, recently published in the *Journal of Clinical Investigation*, are the first to identify the specific role that HA plays in the reproductive tract.

"We found that HA is required to allow the epithelial lining of the reproductive tract to serve as the first line of defense against bacterial infections," said senior author Dr. Mala Mahendroo, an Associate Professor in the Department of Obstetrics and Gynecology's Cecil H. and Ida Green Center for Reproductive Biology Sciences. "Because of this action, HA offers cervical protection against the bacterial infections that cause 25% to 40% of pre-term births in women."

Hyaluronon is a natural substance found in many tissues, and is both a lubricant and a beneficial component of eyes, joints, and skin. It has long been thought to play an essential role in increasing the cervix's flexibility during the birth process; however, the study, which was conducted using mouse models, showed that HA is not essential for increased cervical pliability during late pregnancy. Rather, the substance plays an important barrier role in epithelial cells of the lower reproductive tract and in so doing protects against infection-related pre-term birth. The World Health Organization estimates that 1.09 million children under age 5 die from direct complications of being born prematurely, meaning before the 37th week of pregnancy.

Previous studies by UT Southwestern reproductive biology researchers showed that HA is present in both the cervix and cervical mucus of pregnant women. Next steps include determining the mechanism by which HA affects cervical protection against infection.

"This study demonstrates that HA plays a crucial role in the epithelial barrier as well as the cervix's mucus," said Dr. Yucel Akgul, first author of the study and research scientist in the Department of Obstetrics and Gynecology. "Our next step is to identify exactly how HA protects the cervix, which can have important clinical implications in the effort to reduce infection-mediated pre-term labor."

Other UT Southwestern researchers involved in the study include Dr. R. Ann Word, Professor of Obstetrics and Gynecology. Dr. Word holds the Mary Dees McDermott Hicks Chair in Medical Science.

UT Southwestern, one of the premier academic medical centers in the nation, integrates pioneering biomedical research with exceptional clinical care and education. The institution's faculty includes many distinguished members, including six who have been awarded Nobel Prizes since 1985. Numbering approximately 2,800, the faculty is responsible for groundbreaking medical advances and is committed to translating science-driven research quickly to new clinical treatments. UT Southwestern physicians provide medical care in 40 specialties to about 92,000 hospitalized patients and oversee approximately 2.1 million outpatient visits a year.

Rate of Investment in Medical Research Has Declined in US, While Increasing Globally

From 2004 to 2012, the rate of investment in medical research in the U.S. declined, while there has been an increase in research investment globally, particularly in Asia, according to a study in the January 13th issue of *JAMA*.

For the last century, medical research, including public health advances, has been the primary source of and an essential contributor to improvement in the health and longevity of individuals and populations in developed countries. The United States has historically been where research has found the greatest support and has generated more than half the world's funding for many decades. Few previous analyses have compared medical research in the United States with other developed countries, according to background information in the article.

Hamilton Moses III, MD, of the Alerion Institute and Alerion Advisors LLC, North Garden, VA, and Johns Hopkins School of Medicine, Baltimore, and colleagues examined developments over the past two decades in the pattern of who conducts and who supports medical research, as well as resulting patents, publications, and new drug and device approvals. Publicly available data from 1994 to 2012 were compiled showing trends in U.S. and international research funding, productivity, and disease burden by source and industry type. Patents and publications (1981-2011) were evaluated using citation rates and impact factors.

Among the findings of the study:

The largest increase in biomedical and health services research funding in the U.S. occurred between 1994 and 2004, when funding grew at 6% per year. However, from 2004 to 2012, the rate of investment growth declined to 0.8% annually and (in real terms) decreased in 3 of the last 5 years, reaching $117 billion (4.5%) of total health care expenditures. From 1994 to 2004, the medical device, biotechnology, and pharmaceutical industries had annual growth rates greater than 6% per year, with biotechnology demonstrating the largest increases. The share of U.S.

medical research funding from industry accounted for 46% in 1994 and grew to 58% in 2012.

Industry reduced early-stage research, favoring medical devices, bioengineered drugs, and late-stage clinical trials, particularly for cancer and rare diseases. National Institutes of Health (NIH) allocations did not correlate proportionately with disease burden. Cancer and HIV/AIDS were funded well above the predicted levels based on U.S. disability alone, with cancer accounting for 16% of total NIH funding and 25% of all medicines currently in clinical trials.

Underfunding of service-innovation health services research (which examines access to care, the quality and cost of care, and the health and well-being of individuals, communities, and populations), accounted for between 0.2% and 0.3% of national health expenditures between 2003 and 2011, an approximately 20-fold difference in comparison with total medical research funding. Private insurers ranked last (0.04% of revenue) and health systems 19th (0.1% of revenue) among 22 industries in their investment in innovation. An increment of $8 billion to $15 billion yearly would occur if service firms were to reach median research and development funding.

Globalization U.S. government research funding declined from 57% (2004) to 50% (2012) of the global total, as did that of U.S. companies (50% to 41%), with the total U.S. (public plus private) share of global research funding declining from 57% to 44%. Asia, particularly China, tripled investment from $2.6 billion (2004) to $9.7 billion (2012). The U.S. share of life science patents declined from 57% (1981) to 51% (2011), as did those considered most valuable, from 73% (1981) to 59% (2011).

"The analysis underscores the need for the United States to find new sources to support medical research, if the clinical value of its past science investment and opportunities to improve care are to be fully realized. Substantial new private resources are feasible, though public funding can play a greater role. Both will require non-traditional approaches if they are to be politically and economically realistic. Given global trends, the United States will relinquish its historical innovation lead in the next decade unless such measures are undertaken," the authors conclude.

Editorial: Restore the U.S. Lead in Biomedical Research

"To achieve a new strategic vision for research, the United States will need a roadmap that sets priorities, describes needed structural and organizational changes, and creates an environment that enables innovation," write Victor J. Dzau, MD, of the Institute of Medicine, Washington, DC, and Harvey V. Fineberg, MD, PhD, of the University of California, San Francisco, in an accompanying editorial.

"The needed changes include better coordination across funders and research institutions, development of new funding sources, improved grant evaluation processes, changes in education and training, rationalization of capital investments, and improved operational efficiencies. By taking the necessary political and institutional steps to ensure commitment of adequate resources over time, adopting a comprehensive research strategy, and attaining greater coordination and efficiency, the United States can retain its leadership position in biomedical research."

New Research Finds Baby's Genes, Not Mom's, May Trigger Some Preterm Births

Newswise — Some babies may be genetically predisposed to being born too soon, and variants in the DNA of the fetus, not the mother, may be the trigger for some early births.

That is the finding of research conducted by Joseph Biggio, MD, Professor and Director of the University of Alabama at Birmingham Division of Maternal-Fetal Medicine in the Department of Obstetrics and Gynecology, and his colleagues from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Genomics and Proteomics Network for Preterm Birth Research. The March of Dimes will present its award for Best Research in Prematurity to Biggio for this work during the annual Society for Maternal-Fetal Medicine meeting, which was recently held in San Diego, California.

Biggio's research analyzed the number of copies of certain segments of DNA in the blood or saliva from hundreds of babies and their mothers.

"These findings really open a whole different arena for us to look into as we think about preterm birth," said Biggio, who was assisted by William Andrews, PhD, MD, Professor and Chair of UAB's Department of Obstetrics and Gynecology in UAB's School of Medicine, and others. "It causes us to think more critically about the role of the fetus in causing preterm birth. We've always thought about preterm birth as a maternal issue, but these data change the paradigm. It may be the fetus who has the underlying predisposition, not the mother. This still is very preliminary, and more investigation is needed; but the research clearly identified genetic regions associated with an increased risk of preterm birth."

No link was established between the number of copies of the mother's genes and the risk of preterm birth; however, there was a two- to 11-fold increase in preterm births before 34 weeks of gestation among infants in whom any of four genes was duplicated or any of seven genes was deleted.

"These findings may help explain what triggers early labor in some women even when they've done everything right during pregnancy and there's no obvious cause for an early birth," explained March of Dimes Chief Medical Officer Edward R.B. McCabe, MD. "The hope is that this finding may one day lead to a screening test to help identify which babies are at a higher risk of an early birth."

The preterm birth rate in the United States dropped more than 10% between 2006 and 2013, with most of the improvement focused in late preterm births (those between 34 and 37 weeks of pregnancy). Today's research findings focused on early preterm births - births before 34 weeks of pregnancy - in which there has been little improvement in recent years.

More than 450,000 babies are born too soon each year in the United States, and Alabama has one of the highest rates of preterm birth in the nation, at 15.1%. Preterm birth is the leading cause of newborn death, and babies who survive an early birth often face an increased risk of a lifetime of health challenges, such as breathing problems, cerebral palsy, intellectual disabilities and more. Even babies born just a few weeks early have higher rates of hospitalization and illness than full-term infants. It is a serious health problem that costs the United States more than $26 billion annually, according to the March of Dimes.

While the differences in the number of copies of the genes or gene regions may not directly cause a preterm birth, they may make a baby more susceptible to infection or reacting to other harmful environmental factors that trigger early labor and delivery, Biggio says.

"We don't know exactly that it's the genes in these areas," Biggio said. "It may be something else; but these changes are in the areas of these genes, and that's certainly the first place to start looking."

It may also help explain why treatment with progesterone, a naturally occurring hormone in pregnancy shown to prevent some preterm births, works for only about one-third of women.

"We think we are treating the mother with progesterone, but perhaps we are actually treating the baby or changing the fetal-immune response," Biggio said.

The Eunice Kennedy Shriver National Institute of Child Health and Human Development funded this research, which Biggio says emphasizes the importance of genetics and informatics to scientific discovery. This also reinforces the importance of UAB's investment in data infrastructure and its hiring of renowned expert James Cimino, MD, as the inaugural Director of the UAB Informatics Institute.

"Genetics and informatics are going to be a key to our understanding of complex disease, and preterm birth is a prime example," Biggio said. "If we can begin to understand the complexity of preterm birth and can work to prevent it, we will be able to avert significant health care expenditures and morbidity."

The Society for Maternal-Fetal Medicine (est. 1977) is the premier membership organization for obstetricians/gynecologists who have additional formal education and training in maternal-fetal medicine. The society is devoted to reducing high-risk pregnancy complications by sharing expertise through continuing education to its 2,000 members on the latest pregnancy assessment and treatment methods. It also serves as an advocate for improving public policy, and expanding research funding and opportunities for maternal-fetal medicine. The group hosts an annual meeting in which groundbreaking new ideas and research in the area of maternal-fetal medicine are shared and discussed. Learn more at: www.smfm.org.

The March of Dimes is a leading nonprofit organization for pregnancy and baby health. For the latest resources and information, visit marchofdimes.org or nacersano.org. Find them on Facebook and Twitter as well.

UAB is an internationally renowned research university and academic medical center and the state of Alabama's largest employer, with some 23,000 employees and an economic impact exceeding $5 billion annually on the state. Learn more at: www.uab.edu.

VIDEO: www.youtube.com/uabnews
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Helping Parents Understand Infant Sleep Patterns

Most parents are not surprised by the irregularity of a newborn infant's sleep patterns, but by six months or so many parents wonder if something is wrong with their baby or their sleeping arrangements if the baby is not sleeping through the night. Healthcare providers, specifically nurse practitioners, can help parents understand what "normal" sleep patterns are for their child, according to researchers.

"Nurse practitioners are at the frontline of healthcare," said Robin Yaure, Senior Instructor of Human Development and Family Studies, Penn State Mont Alto. "They are in an ideal position to help parents understand infant sleep pattern norms. Thus, nurse practitioners can help parents understand that 'sleeping through the night' is not entirely likely in young infants and that infants' sleep patterns change during the first few years of life."

According to the researchers, there are four common areas of concern for both parents and practitioners: what constitutes "normal" infant sleep and waking patterns, whether nightwakings are a problem or not, is a parent's presence disruptive when an infant is falling asleep, and whether sleep training is safe and healthy for infants. Sleep training is one way to establish a sleep routine for a child, although the methods used may not be appealing to parents or in the best interests of the child, the researchers said.

Yaure and colleagues reviewed current research on infant sleep, focusing on the above four areas of concern, and specifically infant safety and the well being of both infant and mother during nighttime care. The researchers suggest how to best integrate parents' preferences for care and best practice information, and include conversation points for nurse practitioners recently online in the *Journal of the American Association of Nurse Practitioners.*

Infants' sleep patterns vary for at least the first three years of life. There are many reasons for this, including changes in infant health and mobility and the development of separation anxiety.

"Sharing this basic information with parents is one way of assuring parents that infants' waking does not necessarily mean that the parents are doing something wrong," the researchers wrote.

Parent presence at bedtime, sleep training and infant self-settling are frequently debated topics about which parents might look to healthcare professionals for advice. Yaure and colleagues again point to sharing information with parents -- for example, recent research suggests that the presence of parents at bedtime, specifically during the transition to sleep, may not trigger nightwakings as previously thought.

The researchers also point out that recent research on the nonresponsiveness of mothers during nighttime care can raise stress for both mom and baby. Elevated stress increases cortisol in the body, which may hurt the baby in the long run. Increased cortisol levels are associated with depression, aggression and attention problems, among other issues, in children and adults.

"I worry about parents who feel like they can't trust their own instincts," said Yaure. "Different parents have different goals and ideas for parenting, and we want parents to figure out how to incorporate best practices into their belief system. We have to be culturally aware and sensitive to different families and beliefs."

By encouraging nurse practitioners to talk about current knowledge on infant nightwakings and parental presence, among other things, Yaure hopes that parents will become more comfortable and confident with their nighttime care choices.

Further research will include how doctors can also help translate research-based knowledge of infant sleep into practice.

Also working on this research were Wendy Middlemiss, Associate Professor of Educational Psychology at the University of North Texas and Erron L. Huey, Assistant Professor of Family Sciences at Texas Woman's University.

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