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Prenatal Diagnosis of Absent Sternum and Thoracic Ectopia Cordis

By Pascale Aouad, MD; Ali Serhal, MD; Samar Bitar, MD; Nabil El Helou, MD

A 20-year-old primigravida was referred to our department at a gestational age of 29 weeks for evaluation of a fetal cardiac abnormality. The parents were second-degree relatives. There was no family history of congenital abnormalities or any exposure to teratogens.

Prenatal ultrasound demonstrated a cardiac silhouette protruding outside the thoracic cavity and deforming the chest contours. The overlying chest wall appeared intact, and the sternum couldn't be visualized (Figure 1A). Fetal cardiac assessment revealed a large Ventricular Septal Defect and discrepancy in the ventricular size with a hypoplastic right ventricle and a hypoplastic pulmonary artery (Figure 1B). A large amount of ascites was also seen and was supposed to result from the cardiac disease. There were no other detectable defects, and the umbilical cord contained three vessels.

The dismal prognosis was discussed with the parents and they elected termination of pregnancy.

Upon termination, the fetus was a live-born male, weighing 1400 grams. At birth, the fetus had a central depression of the chest wall during inspiration (Figure 1C). The

Figure 1A. Thoracic Ectopia Cordis with cardiac anomalies - Prenatal ultrasound at 29 weeks gestation showed the heart bulging through an intact chest wall (arrows).

heart was bulging through the intact chest wall. The fetus died within few minutes of delivery. Postnatal radiographs confirmed the absence of the sternum with evidence of

"Prenatal ultrasound demonstrated a cardiac silhouette protruding outside the thoracic cavity and deforming the chest contours. The overlying chest wall appeared intact and the sternum couldn't be visualized (Figure 1A). Fetal cardiac assessment revealed a large ventricular septal defect and discrepancy in the ventricular size with a hypoplastic right ventricle and a hypoplastic pulmonary artery (Figure 1B)."



Figure 1B. Thoracic Ectopia Cordis with cardiac anomalies - Ventricular disproportion with a hypoplastic right ventricle (star). Note the large Ventricular Septal Defect (arrow).

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References: 1. Agency for Healthcare Research and Quality. National Guideline Clearinghouse website. http://www.guideline.gov/search/search.aspx?term=hyperoxia. Accessed August 18, 2015. **2.** Kulkarni AC, Kuppusamy P, Parinandi N. Oxygen, the lead actor in the pathophysiologic drama: enactment of the trinity of normoxia, hypoxia, and hyperoxia in disease and therapy. *Antioxid Redox Signal.* 2007;9(10):1717-1730.

widened interclavicular space and vertically-oriented clavicles (Figure 1D).

The final diagnosis was absent sternum and partial thoracic Ectopia Cordis (EC) associated with congenital cardiac abnormalities.

Ectopia Cordis is defined by a malposition of the heart outside the thoracic cavity.¹ It is a rare congenital disease that is usually associated with other congenital malformations and cardiac defects.¹ EC can be classified into four groups: cervical, thoracic, thoracoabdominal and abdominal.²

Thoracoabdominal EC has a better prognosis, and is usually associated with pericardial, diaphragmatic and abdominal wall defects in the setting of Pentalogy of Cantrell.^{2, 3}

Thoracic EC is a unique abnormality with a reported prevalence of 5.5 to 7.9 per million live births.⁴ It can be complete with absent skin and parietal pericardium or partial when the heart is covered by pericardium or skin.

The sternum is usually abnormal in EC. This abnormality can range from a sternal defect to a complete sternal absence.²



Figure 1C. Thoracic Ectopia Cordis with cardiac anomalies - Postnatal image at 30 weeks gestation demonstrated central depression of the chest wall during inspiration (arrow).

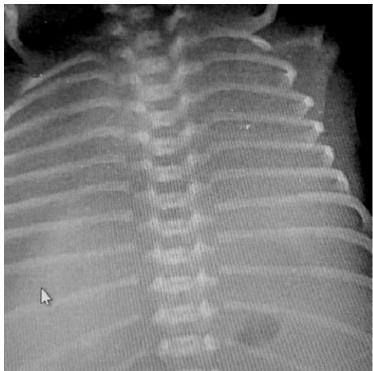


Figure 1D. Thoracic Ectopia Cordis with cardiac anomalies -Postnatal chest radiograph, anteroposterior view, revealing complete absence of the sternum associated with vertically oriented clavicles and widened interclavicular space.

Most cases are associated with cardiac malformations. Ventricular Septal Defect is the most common anomaly, although Atrial Septal Defect, Tetralogy of Fallot, double outlet right ventricle, diverticulum of the left ventricle and pulmonary hypoplasia were also described.^{2, 4}

Associations with non-cardiac abnormalities are uncommon and include oral clefting and neural tube defects. $\!\!^2$

The etiology of EC is heterogeneous and complex. The defects result from altered mesodermal development during early embryogenesis. Some forms of EC may be related to Amniotic Band Syndrome or chromosomal aneuploidy.^{2, 3}

"Prenatal ultrasound diagnosis is usually made at the beginning of the second trimester. The use of three-dimensional ultrasound and Doppler are helpful in establishing the diagnosis early. Prenatal magnetic resonance imaging also has a role in the diagnosis and management.3"



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Prenatal ultrasound diagnosis is usually made at the beginning of the second trimester. The use of three-dimensional ultrasound and Doppler are helpful in establishing the diagnosis early. Prenatal magnetic resonance imaging also has a role in the diagnosis and management.³

Surgical management of Ectopia Cordis is a complex, staged repair. Prognosis of EC is usually poor, and surgical results depend mainly on the severity of associated cardiac defects.^{1, 5}

In conclusion, we present an extremely rare case of partial thoracic Ectopia Cordis with cardiac defects in the setting of an absent sternum.

"Surgical management of Ectopia Cordis is a complex staged repair. Prognosis of EC is usually poor, and surgical results depend mainly on the severity of associated cardiac defects.^{1,5}"

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Neonatal Nurse Practitioner, St. Luke's Children's Hospital - Idaho!

Boise, Idaho

St. Luke's Children's Hospital in Boise seeks an NNP to assist with coverage in our NICU's. The Neonatology team is comprised on 10 BC Neonatologists and 10 NNP's. The Children's Hospital provides a full complement of Pediatric Subspecialty services with the exception of ECMO & complex congenital heart surgery. The level IV Boise NICU is a modern 61-bed unit with 900 admissions annually providing advanced technology support (HFV, iNO, therapeutic hypothermia, non-invasive ventilation), semi-private rooms and a priority of family-centered care. The program is supported by a skilled Obstetrical department including 5 full-time MFM specialists. At this facility NNP's provide daily rounding support and in-house night coverage along with a Neonatologist. In addition, the team provides coverage at our 12-bed, Level IIb NICU in Meridian, ID 0 just 10 miles from Boise. NNP's provide weekend coverage and home call at this facility.

Known as the "City of Trees," Boise is Idaho's capital city—both a cultural center and a playground for those who love the outdoors. A vibrant downtown area affords fine dining, theatre, music, and college and semi-professional sports. Whole Foods, Trader Joe's, The Boise Co-op, and seasonal farmers markets are within a mile of the hospital. The Greenbelt follows the beautiful Boise River corridor for more than 30 miles, and the Boise foothills are home to miles of hiking and biking trails.

Twin Falls, Idaho

St. Luke's Children's Hospital seeks an experienced NNP to join the team in our Twin Falls location! This position currently covers nights with opportunity for future daytime coverage. The ideal candidate for this position is an experienced NNP with strong teaching skills and a desire to educate front-line staff to the higher skill set that a Level II NICU demands. Built in 2011, this state-of-the art 18-bed Level IIIa NICU with 250 admissions annually, and excellent growth potential. While based in Twin Falls, this position rotates regularly through the NICU at St. Luke's Children's in Boise. This provides opportunity to maintain a higher acuity skillset and consistency across the Health System NICUs. Additionally, as part of this larger practice group, coverage for time off and conferences is well-supported.

Twin Falls is located in an area of Idaho referred to as the Magic Valley. It has a population of 44,000 and is the fastest growing city in south central Idaho. It is located in the heart of a rich agricultural area of the state along the mighty Snake River. Housing is affordable, and recreational opportunities abound, with rafting, hiking, skiing, and fishing easily accessible in the immediate area. South central Idaho has a mild, 4-season, high-desert climate. Summers are hot with low humidity, great for outdoor activities. In winter, the valley is largely protected from the cold arctic fronts by the mountains to the north, with occasional snow within the city. Sun Valley, Idaho is just an hour away with excellent skiing in the winter and abundant outdoor recreation in the summer.



St Luke'sTo learn more please contact schechir@slhs.org or 208.493.0354 To learn more please contact:

Fifth Annual UCLA Fetal Echocardiography Symposium: Highlights and Preview of Upcoming Sixth Annual Symposium at UCLA

By Mark S. Sklansky, MD

UCLA's annual practice-based fetal echocardiography symposium, consistently attracting physicians and sonographers from throughout California and across the country, sold out again this past year, with over 200 attendees. The annual *UCLA Fetal Echocardiography Symposium*, held for the fifth year in a row at the Tamkin Auditorium at the Ronald Reagan UCLA Medical Center, last October once again provided attendees with a clinically-oriented, full-day of presentations aimed at improving the prenatal detection and evaluation of congenital heart disease.

Registrants represented a diverse community of clinicians—obstetric and cardiac sonographers, obstetricians and Maternal-Fetal medicine subspecialists, pediatric cardiologists, nurses, and trainees at various levels from each of these respective disciplines. Increasingly, this symposium has grown to become nationally recognized for it's clinical focus, outstanding speakers, and convenience, with registrants coming from 10 states across the U.S. for a single, day-long symposium.

In addition to the symposium's leadership (Drs. Sklansky, DeVore and Satou), faculty at this past year's symposium included special guests: Dolores Pretorius (Radiology), James Huhta, (Perinatal Cardiology), and Tracy Anton (Sonography). The morning began with an overview of guidelines for fetal cardiac imaging (Pretorius), tips on optimizing the image (Anton), and detailed reviews of abnormalities of the four-chamber view and outflow tracts (Huhta, Satou). Dr. Sklansky reviewed the topic of heterotaxy, followed by a live-scanning demonstration by Tracy Anton. Before lunch, presentations and heart-warming testimonials were provided by actual patients and their families, and a short presentation on the importance of prenatal detection was provided, as well, by Adam Chez, co-founder of the Hopeful Hearts Foundation.

The afternoon sessions included a second live-scanning session, focusing on advanced Doppler/3D/4D techniques (Dr. DeVore),

"Registrants represented a diverse community of clinicians—obstetric and cardiac sonographers, obstetricians and Maternal-Fetal medicine subspecialists, pediatric cardiologists, nurses, and trainees at various levels from each of these respective disciplines."

followed by presentations on fetal arrhythmias (Dr. Sklansky) and fetal hydrops/heart failure (Dr Huhta). Drs. Pretorius and Sklansky participated in an interactive, case-base tutorial led by Tracy Anton, which was followed by a discussion of basic and advanced techniques for the evaluation of fetal cardiac function (Dr. DeVore). The day



Live scanning performed by Dr. Greggory DeVore.



Dr. Mark Sklansky at the state-of-the-art Luskin Conference Center.



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Attendees learning tips on prenatal detection of coarctation of the aorta.



Drs. Nancy Halnon and Dianna Drogalis-Kim.

ended with a lively panel discussion of remaining topics of interest to the audience.

Plans are already underway for the *Sixth Annual Fetal Echocardiography Symposium at UCLA*: Practical Essentials of Fetal Cardiac Screening, to be held on Saturday, October 15, 2016. This sixth annual symposium promises to be the best yet, with a renewed focus on screening (reflected in the title), and a relocation--comfortably to accommodate increased demand--to the state-of-the-art Luskin Conference Center on the UCLA campus.

At this upcoming sixth symposium, we are sharpening the focus to provide a full-day dedicated to real-life tips and pearls specifically for those physicians and sonographers who perform or interpret fetal cardiac screening examinations. State-of-the-art presentations will address



Speakers Drs. Jim Huhta and Dolores Pretorius

clinically relevant topics, such as: what are the current guidelines; how to optimize the image, specific details on how to scan and interpret the four-chamber view/outflow tract views/three-vessel trachea view; how to recognize and interpret major forms of heart disease (including special clues for the detection of Ventricular Septal Defects, aortic/pulmonary stenosis, transposition of the great arteries, Tetralogy of Fallot, coarctation of the aorta, Total Anomalous Pulmonary venous return, and others), fetal arrhythmias; how to evaluate subtle findings, such as: pericardial effusion, left ventricular echogenic foci, and right heart disproportion, and much, much more. The full, final program will be available soon. The entire day will be specifically focused and designed for the practitioner, with outstanding presentations by international experts in the field.

The Sixth Annual Fetal Echocardiography Symposium will be among the first to be held at the brand new, state-of-the-art Luskin Conference Center (http://luskinconferencecenter.ucla.edu), opening in August, 2016. Located squarely in the middle of the UCLA campus, directly across from the Pauley Pavilion and the John Wooden Center, the Luskin Conference Center will provide comfortable seating in a beautiful and spacious ballroom, a deluxe luncheon and refreshments throughout the day, and a special area for exhibitors. Specially-priced luxurious hotel rooms (on site within the Luskin Conference Center) will be available for those who wish to spend additional time in the heart of one of the most relaxing and beautiful areas of West Los Angeles.

Questions regarding the Sixth Annual Fetal Echocardiography Symposium at UCLA may be addressed to Dr. Sklansky at msklansky@mednet.ucla.edu. Registration is already filling up at the following link: https://www.cme.ucla.edu/courses/event-description?registration%5fid=124261.

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Perinatal Loss and Bereavement: A Transcultural View - Part 1

By Marylouise Martin, MSN, RNC-NIC

Members of the NPA write a regular column in Neonatology Today.



A famous Japanese Haiku poet was once asked by the Emperor to write a poem which would immortalize his family and dynasty. The master poet went off to work on the project and returned a number of weeks later. Upon his return he recited the following poem for the Emperor: Grandfather dies; Father dies; Child dies. The Emperor was furious

yelling that the poet had cursed his dynasty and ordered the poet to be beheaded. The poet replied to the Emperor, "What better gift could I give you than to wish that the oldest dies first and the youngest dies last" (McCracken and Semel, 2000, p. 2). Children are not supposed to die. The pregnancy, newborn and childhood periods are expected only to be happy times. Children are expected to fulfill both the personal and social needs of their parents. The death of a child is a powerful loss. Children are a link to immortality, security in old age, and lifelong affection and companionship. They can provide a sense of achievement, competence and creativity and can underscore their parent's adult status and social identity depending upon cultural beliefs and practices.

As perinatal providers, we deal with the families who suffer a perinatal loss from an ever-widening variety of ethnic and cultural groups as the face of America changes. Therefore we need to have a better understanding of how to assist these culturally diverse families during their loss.

In the early years of the United States, the loss of young children was common. Families would have many children in the hope that some would survive childhood, work the land and help support/care for the family. Although there are no accurate reports on death rates for the 1600s and 1700s, diaries have recorded the sorrow felt by parents over the death of their children (Chichester, 2005, p 312).

In many cases parents viewed the death as the will of God. Because of this and the belief they would be punished for an outward expression of grief, they would suppress or mute their grief. In the late 1700s, more women learned to write and began to express their grief through the use of diaries and letters. In the late 1800s, the funeral industry began to develop and therefore, a need for more "formal consolation" services, as well as comforting literature and articles to be provided to the family (Gemma and Arnold, 2002, p.18).

By the 1900s, parents could expect to bury at least one of their children and/or help to bury a relative or friend's child (Chichester, 2005). At this time infant mortality was about one in ten births (March of Dimes, 2002). Most of the time, family was nearby and they, along with friends, would help the mother wash her baby's body, and prepare the child for burial in the church cemetery or in the cemetery on the family farm. Dad, family members and neighbors (usually the males) would help dig the burial site (Bowman, 1959, Norfleet, 1993, Chichester, 2005).

A photographer may have been secured to take a postmortem picture of the baby, which in most cases was the only picture the family would have. For many, this brought some comfort. Also, family and friends

were readily available to provide support and caring as they buried a baby (Chichester, 2005, Norfleet, 1993).

According to the March of Dimes (2002), infant mortality dropped to one in fifty births by 1960 and most parents suffering a loss would not know who had (Chichester 2005). At this time, neonatal deaths usually occurred in the hospital setting, and the baby was taken away from the mother so as not to cause her grief. Often times, the mother would not have the opportunity to see the baby or even know the sex of the child. Photographs were not normally taken, and parents were expected to hold back their grief, and "get on with their lives" (Chichester, 2005).

Today, it is common place for facilities to have special bereavement programs to assist families who have suffered a perinatal/neonatal loss, but do they meet the cultural needs of the family? How can we provide more cultural-sensitive bereavement care?

To provide more culturally sensitive bereavement care, we need to become more culturally proficient. According to the National Perinatal Association (NPA, 2016), cultural proficiency is defined as "the accrual of knowledge and skills that enables providers to adapt healthcare in accordance with the ethnocultural, religious heritage of the individual, family and community" (PowerPoint Presentation). In other words, we need to follow the Platinum Rule: "Do unto others as they would like done unto them (O'Connor and Alessandra, 1996, p. 1).

There are five elements to cultural proficiency:

- Awareness of one's own cultural values.
- Development of cultural knowledge
- Awareness and acceptance of the differences between you and the patient/family.
- · Understanding the dynamics of the differences and
- The ability to adapt practice skills to fit the cultural context of the client (NPA, 2016).

In addition to the above elements, we need to tailor our assessments to meet the needs of the bereaved family. A culturally-sensitive assessment of different cultures' response patterns to death can help

"Children are not supposed to die. The pregnancy, newborn and childhood periods are expected only to be happy times. Children are expected to fulfill both the personal and social needs of their parents. The death of a child is a powerful loss. Children are a link to immortality, security in old age, and lifelong affection and companionship. They can provide a sense of achievement, competence and creativity, and can underscore their parent's adult status and social identity depending upon cultural beliefs and practices."

healthcare professionals facilitate the grieving process. It is important to ask some culturally sensitive questions to those who are coping with the loss of their child such as:

- What are the family's cultural traditions and rituals for coping with dying, a deceased body and honoring the dead? Are there special rituals such as: washings, shrines or gender issues in providing this care?
- What are the family's beliefs about what happens after death? Do they believe in an afterlife or reincarnation?
- What does the family feel to be a "normal" expression of grief and acceptance of loss? Are they stoic? Do they wail? Do they slash clothing or shave their heads? Do they grieve for only a few days, or do they openly grieve for many years?
- What does the family consider to be the role for each member of the family in coping with the death? Does the father have to be the "strong" one? Who makes the funeral arrangements?
- Are certain types of death less acceptable, or seen as a real loss (i.e. suicide, murder, euthanasia)?
- Are certain types of death especially difficult to handle for the family's culture (i.e. loss of newborn vs. miscarriage or death of child vs. a fetus or newborn; seen as a "real person" vs. a "nonperson?" (NPA, 2013).

The loss of a child is profound for any family as they have lost hopes, dreams and family expectations. We, as healthcare providers, need to meet the family's bereavement needs based on their cultural beliefs, values and practices in a sensitive manner. Understanding our own cultural beliefs, practices and values helps us to be sensitive to the needs of others. It is vitally important to remember that everyone has their own culture. We should never assume that because someone speaks our language or comes from our country that they share the same beliefs and values. It is imperative that we gain general knowledge about various cultures, need to assess each culture for individual differences.

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"We should never assume that because someone speaks our language or comes from our country that they share the same beliefs and values. It is imperative that we gain general knowledge about various cultures, but keep in mind that we need to assess each culture for individual differences."

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National Perinatal Association (NPA) Transcultural Committee Chairperson

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MAY MEDICAL MEETING **FOCUS**

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Who Should Attend: Physicians, sonographers and nurses in the fields of Pediatric Cardiology, Fetal Cardiology, Obstetrics, Maternal Fetal Medicine, Neonatology, and Radiology, as well as other paramedical colleagues. The information presented will also benefit those who care for neonates with cardiac disease or those who plan to embark on fetal ultrasonography as their career.

Overview: Meeting will discuss concepts in congenital heart disease, as well as, the most recent advances in imaging, diagnosis and management of fetal cardiac abnormalities. This lecture program will be both thematic and lesion specific focusing on the advanced techniques in the assessment of the fetal circulation and extra-cardiac abnormalities. Lectures, procedure demonstrations and interactive case study formats will focus on expanding evidence-based care management strategies for clinical decision making. The activity will provide up to a maximum of 34 AMA PRA Category 1 CME™ credits.

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A Pinterest is Worth a Thousand Words - Social and Mobile Media for the Neonatologist

By Clara H. Song, MD

"Social & Mobile Media for the Neonatologist" by Dr. Song, is a periodic column in *Neonatology Today*. Dr. Song created and moderates the social media outlets for the American Academy of Pediatrics, Section on Neonatal-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*.

The tagline for "Pinterest," (www.pinterest.com) a social networking site is, "Discover and save creative ideas." The social media platform allows "Pinners" to grab contents from anywhere on the web and organize them onto their very own giant virtual cork board. Pins- websites, photos and video- are catalogued onto mini boards. This visual library of resources makes for an easy go-to for searching through your own collection. "Pinners" can gather articles on a rare skeletal dysplasia, or instructional videos on intubation. As clinicians, we can help our families navigate life in the Neonatal Intensive Care Unit (NICU) by gathering well-vetted and pertinent resources. As educators, Pinterest boards can be used to aggregate web resources, procedural videos, for example, or journal articles categorized by systems or disease. This social site helps create a visual roadmap of your all-time-greatest web souvenirs, so that you can remember where you were and plan where you want to go. This is social bookmarking on a whole different level.

Like Twitter and Facebook, Pinterest has been around long enough to evolve into its own social search engine. You discover the treasured pins of fellow pinners, thereby, mutually enriching the communal knowledge bank by endorsing and overlooking various pins. As individual libraries grow, the information in the Pinterest community continues to expand as well. The internal search options allow us to search by category or typing in text. The National Institute of Child Health & Human Development (NICHD) [www.nichd.nih.gov] and the American Academy of Pediatrics (AAP Neonatal-Perinatal Medicine Section both maintain Pinterest boards, mainly for public outreach.1 As mainstream use filters over into healthcare and research, we will only continue to find more medical information aggregated into Pinterest. Currently, the majority of that information has been gathered by the non-expert on such medical topics like, vaccines. When "Hepatitis B vaccine" is entered in the Pinterest search bar, the first half dozen pins discuss the "dangers of Hepatitis B vaccine" and "Hepatitis B vaccine linked to SIDS," and so forth. Like the web at large, what is desperately needed is evidence-based information curated by experts. This would help combat the misinformation (We don't even have time to get started on home and water births.). For our NICU families at OU Medical Center, we have started a social family called "Tiniest Sooners," which includes

a Pinterest page with reliable information that families can use as an educational resource.²

Previously, the major limitation of Pinterest was that you could only pin images. This meant that only webpages that had pictures, photos or attached video could be pinned. So, articles without visual content could not be saved onto boards. However, that is all in the past. Pinterest has been able to circumvent this minor annoyance, so that you can create an entire collection of images - less PubMed abstracts on VEGF and endothelium - derived retinoid acid or the like. Similarly, we can now search for articles that have already been hoarded by others and grouped in a similar fashion.

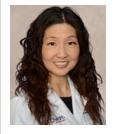
Pinterest started as a site most popular among young mothers who were looking to save recipes, craft DIY projects, find new hairstyles and score the perfect black dress. It has evolved from a simple social aggregation tool to a more functional bookmarking and communication platform. We should use it to our advantage. In our profession, learning and teaching is like walking and talking - it just can't be avoided. It should be transparent, open, honest and shared. Social media tools are inherently designed this way. Pinterest can be an easy way to gather information for sharing articles with colleagues, news with trainees and care tips with families, and all in just a few taps from your smartphone.

"Pinterest can be an easy way to gather information for sharing articles with colleagues, news with trainees and care tips with families...."

References

- Pinterest boards from the AAP, Section on Neonatal-Perinatal Medicine https://www.pinterest.com/aapneonatal/
- Pinterest boards from Tiniest Sooners at the Children's Hospital at OU Medical Center https://www.pinterest.com/tiniestsooners/

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Medical News, Products & Information

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Baby's Breath: A New Way to Study Neonatal Lung Disease

Newswise — Investigators at The Saban Research Institute of Children's Hospital Los Angeles have created a novel model for studying a lung disorder of newborn babies. Their study, published in PLOS ONE on February 10, describes the first model that allows investigators to consider the chronic effects of developmental lung disease.

Neonatal Respiratory Distress Syndrome (RDS) is a restrictive lung disease characterized by insufficient surfactant and lung immaturity. Surfactant plays multiple important roles in the lung, such as facilitating lung expansion, preventing airspaces collapse, and helping fight infection. Babies born with RDS are often given supplemental surfactant and require a ventilator to help them breathe. Additionally, these babies often have other medical issues such as prematurity.

Previous studies have reported that babies with RDS, and adults with other lung diseases, have low levels of vascular endothelial growth factor (VEGF), a signalling protein that promotes the growth of new blood vessels. It is part of the system that restores the oxygen supply to tissues when blood circulation is inadequate. In the lung mesenchyme, it is known to have a central role in formation of the lung's branching structure as well as alveoli and blood vessel development.

To develop an animal model that studies exactly how VEGF affects lung development, it has been necessary to duplicate the comorbidities seen in children, like premature delivery and mechanical ventilation. However, these conditions result in a model that has too many variables, making it difficult to study the effects of abnormal VEGF. Additionally, many studies have evaluated changes only in the first few weeks of life, which does not provide information about long-term changes to the lung and overall health trajectory of the individual.

The model developed at CHLA studied full-term mice with a genetic manipulation to evaluate the long-term effects of abnormal VEGF levels. The investigators were able to observe the mice for three months, until lung development was complete.

"By 'turning down' VEGF signaling, we found that it was enough to 'turn on' lung disease, even in full-term animals who weren't on oxygen and didn't have other problems," said Minna Wieck, MD, an investigator and surgical resident at CHLA and first author on the study. By overproducing – known as "overexpressing" – a decoy receptor that binds VEGF, the team at CHLA was able to replicate the key features of RDS, including low surfactant levels. Ultimately, when mice with this genetic change grew into adults, they demonstrated abnormal restrictive lung function. This may have important implications in the treatment and prognosis of children with Neonatal Lung Disease.

"Babies with respiratory problems often grow up to be adults with respiratory problems," said Tracy Grikscheit, MD, a pediatric surgeon and principal investigator at The Saban Research Institute of CHLA. "Our goal is to be able to find new ways to intervene very early to significantly impact the quality of life for our patients. Now we can investigate the various factors that severely impact the lung development of premature babies and to more specifically target future human therapies. This model mimics the condition and will allow scientists to better determine the mechanism that drives long-term effects that can lead to disabling disease." Grikscheit is senior author

on the study. She is also a tenured Associate Professor of Surgery at the Keck School of Medicine of the University of Southern California.

Additional contributors to the study include: Ryan G. Spurrier, Dan E. Levin, Salvador Garcia Mojica, Michael J. Hiatt, Raghava Reddy, Xiaogang Hou, Sonia Navarro, Jooeun Lee, Amber Lundin and Barbara Driscoll, all of Children's Hospital Los Angeles.

Children's Hospital Los Angeles has been named the best children's hospital in California, and among the top 10 in the nation for clinical excellence with its selection to the prestigious *U.S. News & World Report Honor Roll.* Children's Hospital is home to The Saban Research Institute, one of the largest and most productive pediatric research facilities in the United States. Children's Hospital is also one of America's premier teaching hospitals through its affiliation since 1932 with the Keck School of Medicine of the University of Southern California. For more information, visit CHLA.org. Follow them on Twitter, Facebook, YouTube and LinkedIn, or visit their blog at www.researchlablog.org/.

Big Data and Patient-Powered Research Aim to Solve Complex Diseases - Thousands Enroll in Patient Registry to Solve Lyme Disease

Over the past forty years, little has been learned about how to prevent, diagnose and effectively treat one of the most complex infectious diseases in the country -- Chronic Lyme Disease (CLD). But now, big data tools like patient registries have the potential to change that.

Lorraine Johnson, Chief Executive Officer of LymeDisease.org, will join representatives from the White House Office of Science and Technology and Johns Hopkins Medicine at the annual meeting of the *American Association for the Advancement of Science* (AAAS) on February 13th in Washington, DC. They will discuss the tremendous promise big data holds for solving complex illnesses like Lyme disease. Johnson's talk, Big Data and Patient Powered Research, will explain why patient-centered big data may be a game changer for CLD

LymeDisease.org recently launched MyLymeData, the first national patient-powered registry to accelerate research for Chronic Lyme Disease. The registry has received an overwhelming response --enrolling more than 3,000 patients in three months.

Traditional randomized controlled trials can provide important information. However, only three trials in Chronic Lyme Disease have been funded by the National Institutes of Health (NIH), and they studied too few people (37 to 129) to yield meaningful results. "You need sample sizes in the thousands to perform the subgroup analysis necessary to tell us why some patients respond to treatment, while others don't," says Johnson.

Subgroup analysis can be critical in Lyme Disease, where treatment response may depend on different factors, such as how early the patient was diagnosed or whether the patient also had been infected with other tick-borne pathogens. Patient-powered research networks like MyLymeData are uniquely suited to study this diverse patient population and evaluate complex treatments that are provided in a real-world practice.

Big data tools allow patients to pool their data so that research can be performed quickly and inexpensively. "The last treatment trials of chronic Lyme disease were funded over 15 years ago. We now have

the technology to do this today. Patients no longer need to wait," says Johnson.

The Centers for Disease Control and Prevention (CDC) recently revised its estimate on the number of Lyme Disease cases in the U.S. from 30,000 to 300,000 annually. The disease is six times more prevalent than HIV/AIDS, and almost twice as common as breast cancer.

Many patients who contract Lyme Disease remain seriously ill after treatment. In fact, some studies suggest treatment failure rates may be as high as 35% to 50%. "Nobody knows for sure, but estimates based on treatment failure rates suggest that between 1 and 3 million people may currently be living with Lyme Disease -- a number that grows larger every year," says Johnson.

The financial costs of failing to address this problem are staggering as well. Research indicates that medical expenditures alone for treating Lyme Disease may exceed \$1.3 billion. Other studies suggest the cost to society, in terms of loss of productivity, may be even higher. Forty-three percent of patients report having had to stop work due to the disease, while 24% report that they are receiving disability.

"The only way we are going to increase our understanding of Chronic Lyme Disease and be able to answer the important questions that directly impact patients' lives is through big data projects like MyLymeData," explains Johnson. "It is going to be individual patients coming together and sharing their information that will accelerate research to figure out this disease once and for all."

Bullied Preemies May Develop Mental Illness as Adults - May Develop Depression, Anxiety, Antisocial Behavior or ADHD as Adults

Babies born at an Extremely Low Birth Weight (ELBW) are miracles, but they are more likely to be bullied as children, and this can significantly increase their risk for mental health problems as adults.

Not only that, but the more they were bullied as children, the more likely they are to develop problems such as depression, anxiety, antisocial behavior or Attention-Deficit/Hyperactivity Disorder (ADHD) as adults, says a new study from McMaster University's Michael G. DeGroote School of Medicine.

"Being bullied has a significant and lasting impact for those preemies, even into their 30s," said Kimberly Day, lead author of the study and Lawson Postdoctoral Fellow at the Offord Centre for Child Studies at McMaster.

"This has important implications for parents, teachers, and clinicians who need to be aware of the long-term effects of peer victimization on mental health. They need to watch out for bullying and intervene when possible."

The study was published in the journal *Pediatrics* today. The study included ELBW babies who were 2.2 pounds or less at their birth between 1977 and 1982 in Ontario, who were interviewed at age 8, 22 to 26 and 29 to 36. They were compared to normal birthweight babies of 5.5 pounds or more who were born in the same time span and interviewed at the same intervals.

Bullying is common, with up to one-third of children worldwide facing peer victimization, and ELBW children are even more likely to be victims. ELBW children may be at risk for being bullied because of poor motor abilities, more anxiety and struggles at school, the study said.

And, of those ELBW children who were bullied, they were nearly twice as likely to develop a mental health problem such as: anxiety, depression, or ADHD by the time they were in their 20s. However, the risk was even higher for those who were bullied more often.

By their 30s, the ELBW adults who had been bullied as children were nearly 3 times more likely to have developed anxiety disorders such as: Obsessive-Compulsive Disorder, social phobia, and Panic Disorder. Rates were even higher for those bullied more frequently.

"This is the first study to fully illustrate the profound and long-lasting effects of bullying on the mental health of preterm survivors," said Dr. Ryan Van Lieshout, the senior author of the study and Assistant Professor of Psychiatry and Behavioural Neurosciences at McMaster. "Their risk for anxiety disorders is especially high, particularly among those who are exposed to bullying on a regular basis."

Prior Surgical Abortion Linked to Subsequent Preterm Birth

The analysis of more than 1 million women suggests medical methods to clear the uterus in an abortion or after a miscarriage protects against early birth.

Newswise — Surgical methods used in a common form of abortion or to clear the womb after a spontaneous miscarriage appears to significantly increase the risk of a later preterm birth, say researchers at Thomas Jefferson University who analyzed 36 studies that enrolled more than 1 million women.

The additional risk is small — 0.7% — when compared to women who have not had the surgery or who may have used medical means to clear their uterus. "But, when considered in the light of hundreds of thousands of women who have had such surgery, this is an unnecessary risk to take," says the study's senior author, Vincenzo Berghella, MD, Director of Maternal Fetal Medicine at Thomas Jefferson University Hospital, and Professor of Obstetrics and Gynecology at Sidney Kimmel Medical College at Thomas Jefferson University.

"This is not a study that suggests abortions per se are risky and shouldn't be done. What we are saying is that women should be given a choice between a surgical and a medical procedure, and should also be informed about the potential risk to subsequent pregnancy," Dr. Berghella says.

But he added that due to the limitations of some of the studies included in this meta-analysis, "it is difficult to definitively recommend that surgical abortion should be avoided and that medical methods should be preferentially offered."

Their study, published in the *American Journal of Obstetrics & Gynecology*, was a meta-analysis aimed at determining if any link existed between surgical or medical means to clear the uterus and subsequent pregnancies that do not achieve full terms. One reason to conduct the study is that the incidence of preterm births has been rising and falling, in parallel to popularity of abortion; the vast majority of which, until late, have been surgical.

Surgical evacuation of the uterus mechanically stretches the cervix, and does so quickly, Dr. Berghella says. "In normal birth, dilation of the cervix occurs slowly over a period of many hours. Mechanically stretching the cervix, however, may result in permanent physical injury to the cervix." Resulting scar tissue, for example, could increase the probability of faulty placental implantation in the womb, and could increase risk for infectious diseases, he adds.

In contrast, medical abortions involve use of one or two drugs — misoprostol and mifepristone, known as RU-486 — designed to mirror the process of a spontaneous abortion. Mifepristone, which is approved in the U.S. for aborting pregnancies up to 49 weeks, softens the uterus over time and misoprostol induces contractions. The combination is said to be effective in terminating 95% of pregnancies, and in finishing spontaneous abortions where some of the tissue supporting the pregnancy needs to be removed.

Abortions are increasingly being conducted using the medical approach, which requires several days to conduct and likely two visits to a provider, Dr. Berghella says.

Included in the meta-analysis were 31 studies that reported prior abortions in women who later delivered another child, and five studies that focused on women, who later became pregnant, who spontaneously aborted a prior pregnancy but needed either surgery or medicine to complete the miscarriage.

The goal was to look at women who subsequently delivered a child before the 37th week of pregnancy. "The issue is important because preterm birth is the number one cause of perinatal mortality in many countries, including the U.S.," Dr. Berghella says.

Researchers found:

- Considering all 1,047,683 women enrolled in the 36 studies, women with a history of uterine evacuation had a significantly higher risk of preterm birth (5.7%) compared to a control group of women who did not have either a surgical or medical procedure (5%); had babies that were of low birth weight (7.3% versus 5.9%), and infants that were small for their gestational age (10.2%) versus 9.0 %).
- Of the 31 studies that reported prior abortions, 28 included 913,297 women who had surgery, and three included 10,253 women given medical abortions. Women with prior surgical abortion had a significantly higher risk of preterm birth (5.4% versus 4.4% for the control population), low birthweight babies (7.3% versus 5.9%), and small gestational age infants (10.2% versus 9.0%).
- In the three studies that looked at medical abortions, the risk of preterm birth was the same as in the control group.
- In the five studies of 124,133 women that looked at spontaneous miscarriages, those women who had a surgical procedure to clear the uterus had a higher risk of subsequent preterm births compared to the control group (9.4% versus 8.6%).

"These data — the most comprehensive look at the issue to date — find that prior surgical uterine evacuation may be an independent risk factor for preterm birth," says Berghella. "The findings warrant caution in the use of these surgical techniques, and should

encourage the development of safer surgery as well as use of medical methods."

No financial support was received for this study.

Co-authors include: Gabriele Saccone, MD, of the School of Medicine at the University of Naples, Italy, and Lisa Perriera, MD, of Thomas Jefferson's Department of Obstetrics and Gynecology, of the Sidney Kimmel Medical College.

The authors report no conflict of interest.

Article Reference: Saccone G, Perriera L, Berghella V. Prior uterine evacuation of pregnancy as independent risk factor for preterm birth: a systematic review and meta-analysis.

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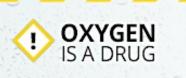
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