NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

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IN THIS ISSUE

Neonate with Hypotrichosis-Lymphedema-Telangiectasia and Fatal Pulmonary Hypertension

By Jane O'Donnell, MD; Casey Cohenmeyer, MD; Crystal Le, MD

Introduction

Hypotrichosis-lymphedema-telangiectasia Syndrome (HLTS) is an extremely rare diagnosis with a paucity of literature. We describe a case caused by mutation in the SOX18 gene.

Case Presentation

A 41-week-old 3.525 kg boy was born to a 31-year-old Caucasian female who was Gravida 1, Para 0, at the time of delivery. Her prenatal labs were: Blood type A positive, Antibody screen negative, RPR non-reactive, Rubella immune, Hepatitis B sAg negative, HIV negative, GBS negative. The pregnancy was uncomplicated. Delivery was by Normal Spontaneous Vaginal Delivery (NSVD) with epidural anesthesia, with AROM 8 hours prior to delivery productive of meconium stained amniotic fluid. APGARs were 6 at 1 minute, and 8 at 5 minutes. Resuscitation in the delivery room consisted of drying and stimulation, blow-by-oxygen and brief mask CPAP.

The baby continued on blow-by oxygen in the delivery room and could not be weaned, so he was brought to the NICU.

Birth weight 3525 g, Length 49.5 cm, Head Circumference 34.5 cm.

Admission Vital Signs: BP 86/44, Pulse 120, Temp 98.2, Resp 77, SpO_2 94% on blow-by-oxygen.

Exam: Active baby with strong cry, no significant distress. HEENT: Anterior Fontanelle Open and Flat (AFOF), red reflex present, noted absence of eye brow and eyelashes, sparse hair on scalp. CV: RRR without murmur, normal pulses. Lungs: Tachypnea with mild coarse breath sounds, equal bilaterally. **Abdomen:** soft, nontender, not distended, active bowel sounds. GU: patent anus, normal penis and descended testes with b/l hydroceles. Legs: dramatic cutis marmorata with areas of atrophy of subcutaneous tissue over the extensor surface of the knee. The lower extremities thighs feel woody from significant edema. **Neurological:** normal reflexes, slightly increased tone, normal strength, symmetric morrow. Skin: scattered petechiae and several areas of telangiectasia.

CXR (Figure 1)**:** bilateral hazy lung fields with pleural effusion on the left. Mild cardiomegaly.

Initial CBC showed WBC 14 with 59 segs, 26 lymphs, 6 monos, 4 eos, 6 bands. ABG on 100% oxygen blow by was 7.27/47/359/-5.

He was placed on a nasal cannula, IV fluids and ampicillin and cefotaxime. Nasal cannula was weaned off on Day of Life (DOL) #3 and initial left-sided pleural effusion resolved. Cardiac ultrasound on DOL #3 showed mild-to-moderate pulmonary hypertension, small pericardial effusion, PFO (Patent Foramen Ovale) vs. ASD (Atrial Septal Defect) and a moderate to large bidirectional Patent Ductus Arteriosus (PDA). A Genetic consultation obtained on DOL #3 due to skin, hair and dermatologic findings; a diagnosis of probable Hypotrichosis-Lymphedema-Telangiectasia Syndrome was made.

On DOL #4-#6 the patient's respiratory status improved, and he was feeding well.

On DOL #7 his respiratory status worsened, he was placed back on NC oxygen 1L 35%, CxR showed recurrence of bilateral pleural effusions. At this time, he was transferred fromthe Level 2 NICU at the birth hospital to our regional tertiary NICU.

He remained on NC for several days, the effusions increased as did his oxygen requirement. He was started on furosemide. Serial cardiac ultrasounds showed worsening pulmonary hypertension. He was placed on inhaled nitric oxide at 20ppm and 100% oxygen via 2L NC without improvement in his pulmonary hypertension. iNO was increased to 40ppm without any improvement.

PLEASE READ THIS LETTER ON AN IMPORTANT BILL (*ADVANCING HOPE ACT 2015*) THAT IS NOW BEFORE CONGRESS

Extending this act, is a win-win for pediatric patients, physicians and the companies that provide the products and services. After reading this letter, if you agree, download the form letter and send to your Senator.

For additional information, please contact:

Saira Sultan, JD, President of Connect 4 Strategies, LLC at: saira.sultan@connect4strategies.com

SUGGESTED LETTER (See Links Below to Find your Senator and Download this letter)

On your institutional letterhead, if available

[Date]

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RE: The Advancing Hope Act of 2015

Dear [Your Senator],

As a physician who treats and serves hundreds of premature babies suffering from respiratory distress syndrome, I write to you today with great interest and concern regarding proposed legislation which will affect about 65,000 premature infants each year in the U.S. The Advancing Hope Act is a bill intended to reauthorize and make permanent a priority review program at the Food and Drug Administration (FDA), which will encourage development of new treatments for rare pediatric diseases such as RSD.

As a neonatologist at [insert name of your institution] treating these infants, I wanted to write to let you know how much institutions like ours in [insert your state] stand to benefit from additional research in rare pediatric diseases. Historically, our youngest and most vulnerable patients have been underserved and ignored in the drug development arena due to the high risk nature and small size of pediatric patient populations. This is why many drugs used in infants and children have never been tested in these age groups and, therefore, must be used off-label.

As you are surely aware, drug development is expensive and requires many years of effort. The positive impact of an incentive program such as the Pediatric Review Voucher Program is significantly diminished if it is too short-lived or requires frequent reauthorizations. This is because the value of the incentive is not actually realized until many years after the development process has begun. Small companies like mine, our clinical researcher partners, and our investors, need confidence that approval-related incentives like the voucher will still exist when the early-stage discoveries we are developing in the clinic finally make it through the approval process and to the patients' bedsides.

I hope you will consider supporting efforts to make permanent this voucher program described in the Advancing Hope Act of 2015. This bill will significantly benefit the large, under-served population of infants and children who need new innovative therapies to ensure their best healthcare outcomes. There is a tremendous need for new therapies for these patients, many of which bear a terrible lifelong burden not only for these young patients and their families, but also costs the US healthcare system billions per year to support the infants and children who may continue to require medical support throughout their lives. It is incumbent upon us to work together on behalf of those suffering these enormous challenges to create and promote programs that can benefit their health and potentially reduce overall healthcare costs.

Thank you your sincere consideration. Please contact me at [Your phone number or email] if I can be of any assistance on this important issue of making the rare pediatric priority review voucher program permanent.

Sincere regards,

[Your Name]
[Your Title]

Find your US Senator: www.senate.gov/senators/contact/

Download this letter, fill in the appropriate information in the [brackets] and mail - www.neonatologytoday.net/newsletters/ltr.doc

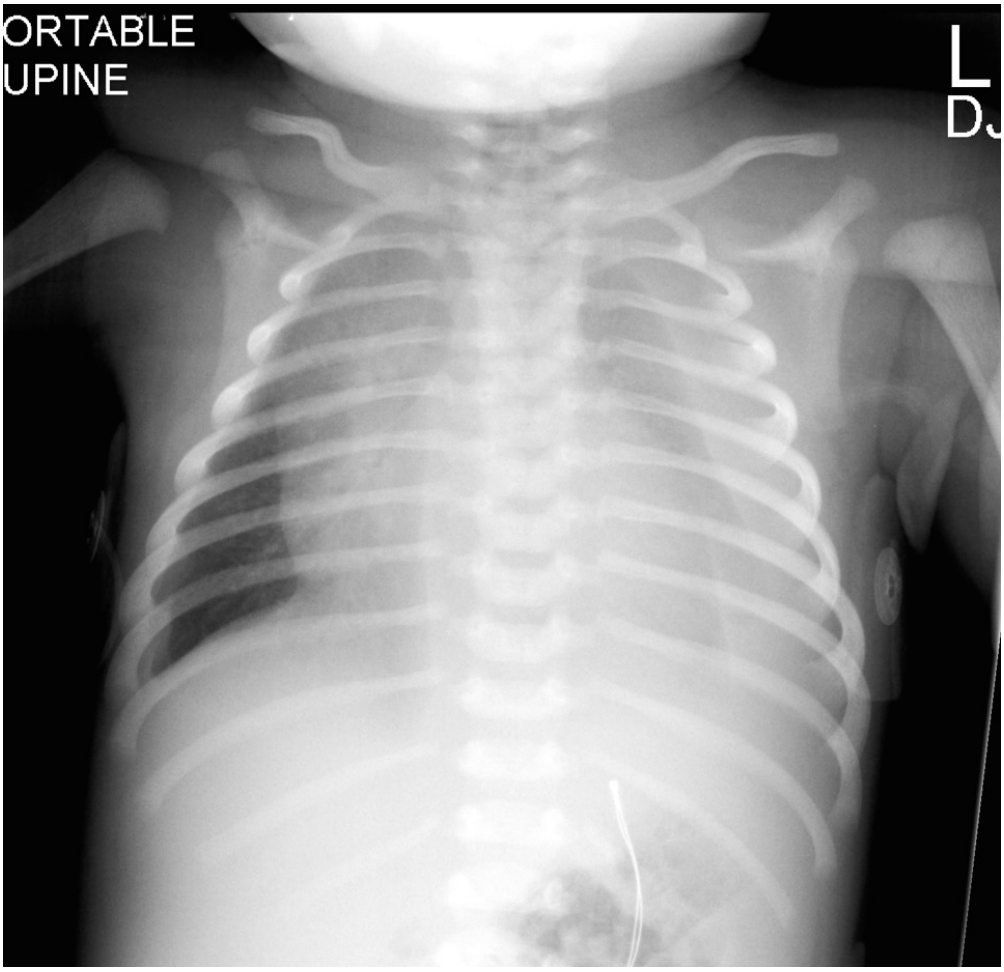

Figure 1.

Sildenafil was started on DOL #10, PGE on DOL #11 to maintain ductal potency in the face of severe pulmonary hypertension, bosentan started on DOL #13, epoprostenil on DOL #13. Despite these measures he continued with persistent severe pulmonary hypertension with continued desaturation episodes down to the 70s. A chest CT was obtained and showed very mild interstitial lung disease with mild thickened interlobular septa. These findings are nonspecific.

On DOL #20 his effusions worsened, he was intubated, a chest tube was placed and a large chylothorax drained. He was extubated back to NC on DOL #22 with the chest tube left to drain. The patient was gradually weaned off iNO, but he continued to require all other medical therapy for his pulmonary hypertension. Diagnosis of HLTS was confirmed by genetic testing. The patient was heterozygous, with a mutation in the SOX18 gene, specifically c.541 C>T (p.Gln181Stop).

Parents elected to have him transferred to hospice care. He was discharged from the NICU to hospice at 30 days of age. He subsequently passed away from pulmonary hypertension weeks later under hospice care.

Discussion

HLTS has been reported to be caused by autosomal recessive and autosomal dominant mutations in the SOX18 gene. This has been described in the literature by Irrthum et al (2003) in a series of three

families. In animal models, Downes et al (2009) hypothesize that alterations in the SOX18 gene may lead to abnormalities in structural integrity of the microvasculature and lymphatic system. We hypothesize that this abnormal development of the pulmonary microvasculature and lymphatic system led to this patient's ultimately fatal case of persistent pulmonary hypertension of the newborn.

"HLTS has been reported to be caused by autosomal recessive and autosomal dominant mutations in the SOX18 gene.... We hypothesize that this abnormal development of the pulmonary microvasculature and lymphatic system led to this patient's ultimately fatal case of persistent pulmonary hypertension of the newborn."

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The NPA Advocates for Breastfeeding Support in the Workplace

By Raylene Phillips, MD

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

National Perinatal Association

Convene. Educate. Advocate. Integrate.

The National Perinatal Association's (NPA) mission is to provide a forum for all healthcare providers and those involved in the care of babies, mothers and families in order to communicate and work together to provide more effective support during the perinatal period. In order to do this we: "Convene, Educate, Advocate, and Integrate." In previous columns, I have shared opportunities NPA has provided to Convene and Educate. This month I will discuss ways in which NPA participates in Advocacy.

The National Perinatal Association has a long history of advocating for improved perinatal care by taking the lead on issues or by partnering with other organizations to raise awareness and promote support. Advocacy issues NPA has addressed include family support, bereavement, palliative care, quality improvement, promotion of physiologic birth, preconception health, artificial reproductive technology, access to care, medical liability reform, care of late preterm infant, and breastfeeding as the norm for infant feeding.

This month the NPA joins the WHO and UNICEF in supporting World Breastfeeding Week and the United States Breastfeeding Committee in celebrating National Breastfeeding Month. The 2015 theme is "Breastfeeding at Work: Let's Make It Work." While the Gold Standard for infant feeding is six months of exclusive breastfeeding with continued breastfeeding for one or more years after introducing complimentary foods, only 38% of infants are exclusively breastfed for six months globally and less than 25% are doing so nationally. Suboptimal breastfeeding contributes to 800,000 infants deaths a year worldwide.

Over 75% of mothers want to breastfeed their babies in the US. One third of mothers return to work by 3 months after the birth of their babies and two thirds are back to work by 6 months. The Surgeon General has called on all sectors of the community, including employers, to protect, promote and support breastfeeding; yet, only half of mothers have workplace support and the lower a mother's income, the less likely she is to have breastfeeding support at work. Mothers with breastfeeding support are twice as likely to exclusively breastfeed at 3 months. To support breastfeeding, employers should develop a workplace breastfeeding support policy that includes time and a private space for breastfeeding mothers to pump their milk. Several state and federal laws mandate "Break Time for Nursing Mothers." Mothers should know their rights and talk to their employer about maternity leave and breastfeeding support including lactation consults, getting a breast pump, and having a time and place to pump at work.

There are other ways to support breastfeeding for working mothers. Paid parental leave is a hot topic these days. The U.S. is the only developed country in the world that doesn't guarantee paid maternity leave. There are some notable exceptions in our country. Netfix recently announced provision of unlimited paid parental leave for their employees during the first year after the birth or adoption of a child, joining other tech companies who provide 18-22 weeks of paid parental leave including: Google, Apple, and Twitter. Bringing baby to work is an option being trialed by several companies including the Washington Health Department where mothers can bring their infants to work for up to 6 months after birth.

There may be no population needing breastfeeding support more than mothers of babies admitted to the NICU, who often express their milk for weeks or months before being able to actually breastfeed. Many mothers must return to work before their babies are discharged and many have

"When physicians and other healthcare providers have a successful breastfeeding experience, supported by their workplace environment, they are much better equipped to provide positive breastfeeding support for mothers in their healthcare practice. By supporting breastfeeding in our own workplace, we are also supporting breastfeeding nationally and globally and helping to fulfill our mission as healthcare providers to heal and serve."

little or no support at work to provide the milk their babies need for optimal healing, growth, and development.

Another group that often receives less than optimal breastfeeding support is hospital employees, including medical students, residents, and fellows who work long hours with little or no protected time and often no dedicated place to express their milk. We, as a medical profession, must "practice what we preach" and support medical professionals in training to do the same.

When physicians and other healthcare providers have a successful breastfeeding experience, supported by their workplace environment, they are much better equipped to provide positive breastfeeding support for mothers in their healthcare practices. By supporting breastfeeding in our own workplace, we are also supporting breastfeeding nationally and globally and helping to fulfill our mission as healthcare providers to heal and serve.

In addition to joining the National Perinatal Association in supporting breastfeeding in the workplace, we invite you to join us in Nashville, TN, this October as we explore the art and science of helping pregnant women and their babies deal with drug dependency before and after birth.

NT

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Medical News, Products & Information

Compiled and Reviewed by Tony Carlson, Senior Editor

Therabron Therapeutics Reaches 50% Enrollment in Phase 2A Clinical Trial for Lead Pediatric Respiratory Critical Care Program - Company on Track to Complete Trial Enrollment by End of 2015

Therabron Therapeutics, Inc., a specialty biotechnology company dedicated to redefining the management of respiratory disease through innovation, today announced that it has achieved over 50% patient enrollment in the second clinical trial evaluating its lead product candidate, CG100, for the prevention of chronic respiratory morbidities, including Bronchopulmonary Dysplasia (BPD), in premature infants. This Phase 2A study is supported in part by a $1.6 million grant from the U.S. FDA Office of Orphan Product Development.

"We are encouraged by the progress we have made with patient enrollment in this trial and the interest expressed by the neonatology community in our potentially transformative technology platform. Importantly, our data and safety monitoring board has not observed any unexpected safety or tolerability concerns in the trial to date, allowing us to now proceed to the highest dosing group in this study" said Dr. Aprile L. Pilon, Founder, Chairman and CEO of Therabron Therapeutics. "CG100 has the potential to provide a significant respiratory health benefit for very premature infants following discharge from the Neonatal Intensive Care Unit."

The CG100 product candidate is a recombinant human CC10 protein, a secretory protein that is believed to play an important protective role in the lung via maintenance of airway epithelia, delivered by intratracheal instillation in intubated neonates. CG100 has the potential to improve long-term clinical outcomes in preterm infants and significantly reduce the economic burden beyond the infant's initial in-patient stay. In a previously completed clinical study (Levine et al., Peds Research, 2005; Therabron data on file), investigators observed suppression of inflammatory mediators in the respiratory tract and evidence of reduced lung injury in CG100-treated infants. Additionally, infant hospitalizations due to respiratory causes, as well as the need for respiratory medications through six months post-discharge, were reduced in CG100-treated infants compared to controls.

Therabron anticipates completion of enrollment for the current trial by the end of 2015, with multiple data releases in expected in 2016.

About Chronic Respiratory Morbidities in Preterm Infants

Over half a million preterm infants are born in the US every year. Of those infants, about 60,000 are Very Low Birth Weight (VLBW) and experience respiratory distress; and up to 15% of this vulnerable patient population dies. Of those who survive, up to 15,000 will develop neonatal BPD, a chronic lung disorder that predisposes the child to potentially life-threatening respiratory infections and asthma. These infants typically experience repeated hospitalizations for respiratory complications, the need for numerous respiratory medications, and frequent doctor visits throughout their infancy and childhood. An estimated $26 billion are spent annually on medical care during the first year of life in these VLBW premature infants and the emotional cost of families impacted by having a child with this condition is substantial.

Therabron Therapeutics, Inc. is a clinical-stage biotechnology company founded in 2007 and located in Rockville, MD. Therabron is focused on the advancement of respiratory therapeutics with disease-modifying potential. The company's product candidates aim to restore the natural immune balance in the lungs of respiratory patients through the administration of recombinant human CC10 proteins. The family of CC10 proteins, also known as secretoglobins, have the potential to change the course of acute and chronic respiratory diseases, representing large markets into which few truly novel drugs have been introduced. Therabron's product candidates have the potential to be first-in-class, disease-modifying, breakthrough biologic therapeutics. For additional information, please visit www.therabron.com.

"Tele-Rounding" Robots in the Neonatal Intensive Care Unit

Many hospitals lack the resources and patient volume to employ a round-the-clock, neonatal intensive care specialist to treat their youngest and sickest patients. Telemedicine—with real-time audio and video communication between a neonatal intensive care specialist and a patient—can provide access to this level of care.

A team of neonatologists at Children's Hospital Los Angeles investigated the use of robot-assisted telemedicine in performing bedside rounds and directing daily

care for infants with mild-to-moderate disease. They found no significant differences in patient outcomes when telemedicine was used and noted a high level of parent satisfaction. This is the first published report of using telemedicine for patient rounds in a Neonatal Intensive Care Unit (NICU). Results was published online first on June 29th in the *Journal of Telemedicine and Telecare*.

"We wanted to determine if robot-assisted telemedicine could be part of daily clinical practice in order to provide care by a neonatologist where one might otherwise not be present—in remote locations, underserved communities and at times of limited staffing," said Arlene Garingo, MD, neonatologist at CHLA and first author on the study. In an earlier study, the team at CHLA demonstrated the feasibility, safety and accuracy of robot-assisted telemedicine in the NICU.

In this randomized study, infants were treated by either an onsite neonatologist who visited the baby at the bedside during patient rounds, or by an offsite neonatologist who performed daily evaluations of the patient using robot-assisted telemedicine. Twenty pairs of patients were matched by age, weight, diagnosis and disease severity, with one infant from the pair assigned to each treatment group.

There were no differences in average length of stay, age at discharge or hospital charges between the two treatment groups. Nutritional needs, respiratory support, days on antibiotics, phototherapy and number of radiological studies were also the same between the two groups.

"However, there was a significant difference in time spent at the bedside, with the remote neonatologist requiring nearly twice as much time to care for the patient," said Philippe Friedlich, MD, MEpi, MBA, Chief of Neonatology at CHLA and an author on the study. He explained the additional time was largely due to time required to maneuver the robot, as well as issues of internet connectivity.

At the time of discharge, 45% of families completed a survey about their experience. All responded that they were comfortable having their baby treated by an offsite neonatologist via telemedicine and would be comfortable doing it again.

Additional contributors include: Thomas Chavez, Linda Tesoriero, MD, Shilpa Patil, MD, and Paige Jackson, MD, Division of Neonatology and the Center for Fetal and Neonatal Medicine at Children's Hospital Los Angeles; and Istvan Seri, MD, PhD, who was located at CHLA during the study and is now at the Center of Excellence in Neonatology, Saidra Medical and Research Center, Qatar.

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.

Women & Infants Hospital of Rhode Island Receives a $5 Million Grant from National Institutes of Health to Continue Work on Perinatal Biology

Women & Infants Hospital of Rhode Island has recently received a nearly

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$5 million grant from the National Institutes of Health (NIH) to support an Institutional Development Award (IDeA) Center of Biomedical Research Excellence (COBRE) for Perinatal Biology. Of the more than 100 COBREs across the country, Women & Infants is the only one specifically focused on developmental research. The IDeA program builds research capacities in states that historically have had low levels of NIH funding by supporting basic, clinical and translational research; faculty development; and infrastructure improvements.

Under the leadership of James F. Padbury, MD, Pediatrician-in-Chief and Chief of Neonatal/Perinatal Medicine at Women & Infants Hospital and the William and Mary Oh - William and Elsa Zopfi Professor of Pediatrics for Perinatal Research at The Warren Alpert Medical School of Brown University, and Surendra Sharma, MBBS, PhD, research scientist at Women & Infants and Professor of Pediatrics at the Alpert Medical School, the COBRE team will continue its research in perinatal biology, including studies of fetal and newborn development, placental biology, and reproductive diseases including preterm birth and preeclampsia.

"Our projects are focused on critical windows of development and reproductive life. Environmental disturbance or other influences during these critical windows can have lasting effects," said Dr. Padbury. "Our overarching hypothesis is that understanding these effects during critical developmental periods informs the mechanisms of health and disease throughout life."

Work supported by the COBRE in Dr. Sharma's laboratory has identified novel new insights into the pregnancy disorder, preemclampsia, or pregnancy-induced hypertension. "We have recently demonstrated that preeclampsia originates from protein misfolding and aggregation. This leads to disturbances in placental function and many of the mother's symptoms," explained Dr. Sharma. "Remarkably, transthyretin, the protein we have identified that is misfolded in preeclampsia, is also disturbed in some cases of Alzheimers disease. Our current work is focused on the mechanistic similarities between preeclampsia and Alzheimers disease and whether preeclampsia may be a risk factor for later development of Alzheimers."

Dr. Sharma and his colleagues are also working to develop a diagnostic test to confirm that preeclampsia can be identified much earlier in pregnancy. He said, "Identifying preeclampsia earlier will certainly lead to new and better treatments."

This is a Phase III award intended to consolidate the formation of the Center for Perinatal Biology and support the administrative activities of the Center. It will also provide state-of-the-art equipment to support the Center's Molecular Biology and Imaging Core. The Center and the COBRE researchers' laboratories are located in Providence's "Knowledge District" in the Kilguss Research Institute, the Laboratory for Molecular Medicine and the Coro Research building.

Other investigators include: Sunil Shaw, PhD and Shibin Cheng, MD, PhD. Senior investigators also participating in the projects are Ulrike Mende, PhD; Walter Atwood, PhD; Qian Chen, PhD; Pamela Swiatek, PhD; and Karl Kelsey, MD.

Women & Infants Hospital of Rhode Island, a Care New England hospital, is one of the nation's leading specialty hospitals for women and newborns. A major teaching affiliate of The Warren Alpert Medical School of Brown University for obstetrics, gynecology and newborn pediatrics, as well as a number of

specialized programs in women's medicine, Women & Infants is the 11th largest stand-alone obstetrical service in the country with approximately 8,400 deliveries per year. A *U.S.News & World Report* 2014-15 Best Children's Hospital in Neonatology and a 2014 Leapfrog Top Hospital, in 2009 Women & Infants opened what was at the time the country's largest, single-family room neonatal intensive care unit.

Women & Infants and Brown offer fellowship programs in gynecologic oncology, maternal-fetal medicine, urogynecology and reconstructive pelvic surgery, neonatal-perinatal medicine, pediatric and perinatal pathology, gynecologic pathology and cytopathology, and reproductive endocrinology and infertility. It is home to the nation's only mother-baby perinatal psychiatric partial-hospital, as well as the nation's only fellowship program in obstetric medicine.

Women & Infants has been designated as a Breast Center of Excellence by the American College of Radiography; a Center of Excellence in Minimally Invasive Gynecology; a Center for In Vitro Maturation Excellence by SAGE In Vitro Fertilization; a Center of Biomedical Research Excellence by the National Institutes of Health (NIH); and a Neonatal Resource Services Center of Excellence. It is one of the largest and most prestigious research facilities in high risk and normal obstetrics, gynecology and newborn pediatrics in the nation, and is a member of the National Cancer Institute's Gynecologic Oncology Group and the Pelvic Floor Disorders Network.

Hospital to Create Emergency Experiences Using Virtual Reality: Walk Around Inside Crisis Situations, Educate Medical Professionals

Next Galaxy Corp. recently announced the signing of an agreement with Miami Children's Hospital. Next Galaxy will develop immersive Virtual Reality medical instructional content for patient and medical professional education using the Company's VR Model. Per the multi-year agreement, Next Galaxy and Miami Children's Hospital are jointly creating VR Instructionals on cardiopulmonary resuscitation (CPR) and other lifesaving procedures, which will be released as an application for smartphones.

Incorporating eye gaze control, gestures, and voice commands while "walking around" inside an emergency medical experience or crisis, Next Galaxy's Virtual Reality Model engages participants far beyond today's methodology of passively watching video and taking written tests.
"Assessments are incorporated directly into the medical VR models. We will design situations where participants are required to make the appropriate decisions about proper techniques. The Virtual CPR instructional will measure metrics and provide real-time feedback ensuring participants accurately perform CPR techniques. Further, the instructional will explain any mistake and prompt users to try again when errors are made. Supportive messages are delivered upon success," states Mary Spio CEO, Next Galaxy Corp.

The medical VR models will be viewable through smartphones and desktops as 3D, and via VR devices such as Google Cardboard, VRONE and Oculus Rift.

Next Galaxy Corporation is a leading developer of innovative content solutions and fully Immersive Consumer Virtual Reality technology. The Company's flagship consumer product in development is CEEK, a next-generation fully immersive entertainment and educational social virtual reality platform featuring a combination of live action and 3D experiences. Next Galaxy's CEEK simulates the communal experience of attending events, such as concerts, sporting events, movies or conferences through Virtual Reality. Next Galaxy is developing entertainment and educational experiences for VR Cinema, VR Concerts, VR Sports, VR Business, VR Tourism and more. In short, Next Galaxy is building the meeting places of the future. For further information, visit www.nextgalaxycorp.com.

Low Birth Weight and Childhood Infections Predict Ankylosing Spondylitis

The results of a study presented June 11th at the European League Against Rheumatism Annual Congress (EULAR 2015) Press Conference showed that a diagnosis of Ankylosing Spondylitis (AS) can be predicted by low birth weight, having older siblings and hospitalisation for infection between the ages of 5-16 years. These data suggest that these factors play an important role in the pathogenesis of the disease.

AS is a painful and progressive form of arthritis caused by chronic inflammation of the joints in the spine. Prevalence of AS varies globally, and is estimated at 23.8 per 10,000 in Europe and 31.9 per 10,000 in North America.

The cause of AS is unknown. Although AS is strongly associated with the genotype HLA-B27, not everyone testing positive for the marker goes on to develop the disease.

"A link between AS and the HLA-B27 genotype was established more than three decades ago, yet studies on the environmental risk factors are few," said study investigator Dr. Ulf Lindström, Institute of Medicine, Rheumatology and Inflammation Research, Sahlgrenska Academy, Sweden. "Our research has identified three factors associated with significantly increased risk of the disease in later life. These data strengthen our understanding of the interplay between genetics and environment in AS, and bring us closer to pinpointing the underlying cause of the disease."

Statistically significant increased risks were observed for birth weight under 3,000g (18% vs. 15%), having older siblings (63% vs. 58%) and for hospitalisation due to infections at age 5-12 (5% vs. 3%) and age 13-16 (2% vs. 1%). These factors have been implicated in other, associated disease; the triggering effect of infections in reactive arthritis has been established, birth weight has been shown to predict development of autoimmune disease (diabetes and rheumatoid arthritis), and a link between older siblings and disease risk has been demonstrated in asthma.

Data from several Swedish national registers were used for this study, with five matched controls (sex, age, county) identified for each case of AS. Exposures assessed were birth weight, gestational age, type of birth (single/multiple), number of older siblings and exposure to infections.

How Does Human Behavior Lead to Surgical Errors? Mayo Clinic Researchers Count the Ways - Four to Nine Factors Contributed to Each `Never Event'

Newswise- Why are major surgical errors called "never events?" Because they shouldn't happen — but do. Mayo Clinic researchers identified 69 never events among 1.5 million invasive procedures performed over five years and detailed why each occurred. Using a system created to investigate military plane crashes, they coded the human behaviors involved to identify any environmental, organizational, job and individual characteristics that led to the never events. Their discovery: 628 human factors contributed to the errors overall, roughly four to nine per event. The study results were published in the journal *Surgery*.

The never events included performing the wrong procedure (24), performing surgery on the wrong site or wrong side of the body (22), putting in the wrong implant (5), or leaving an object in the patient (18). All of the errors analyzed occurred at Mayo; none were fatal.

The Mayo Rochester campus rate of never events over the period studied was roughly 1 in every 22,000 procedures. Because of inconsistencies in definitions and reporting requirements, it is hard to find accurate comparison data, but a recent study based upon information in the National Practitioner Data Bank estimated that the rate of such never events in the United States is almost twice that in this report, approximately 1 in 12,000 procedures.

Nearly two-thirds of the Mayo never events occurred during relatively minor procedures such as anesthetic blocks, line placements, interventional radiology procedures, endoscopy and other skin and soft tissue procedures.

Medical teams are highly motivated and skilled, yet preventing never events entirely remains elusive, says senior author Juliane Bingener, MD, a gastroenterologic surgeon at Mayo Clinic. The finding that factors beyond "cowboy-type" behavior were to blame points to the complexity of preventing never events, she says.

"What it tells you is that multiple things have to happen for an error to happen," Dr. Bingener says. "We need to make sure that the team is vigilant and knows that it is not only OK, but is critical that team members alert each other to potential problems. Speaking up and taking advantage of all the team's capacity to prevent errors is very important, and adding systems approaches as well."

For example, to help prevent surgical sponges from being left in patients, Mayo Clinic installed a sponge-counting system and uses that bar code-scanning system and vigilance by the surgical team to track sponges. Other preventive systems include use of The Joint Commission Health Care Quality Organization's Universal Protocol, team briefings and huddles before a surgery starts, a pause before the first incision is made, and debriefings using a World Health Organization-recommended safety checklist.

To investigate the never events, the researchers used human factors analysis, a system first developed to investigate military aviation accidents. They grouped errors into four levels that included dozens of factors:

- "Preconditions for action," such as poor hand-offs, distractions, overconfidence, stress, mental fatigue and inadequate communication. This category also includes channeled attention on a single issue: In layman's terms, focusing so much on a tree that one cannot see the forest.
- Unsafe actions, such as bending or breaking rules or failing to understand. This category includes perceptual errors such as confirmation bias, in which surgeons or others convinced themselves they were seeing what they thought they should be seeing.
- Oversight and supervisory factors: Inadequate supervision, staffing deficiencies and planning problems, for example.
- Organizational influences: Problems with organizational culture or operational processes.

In addition to systems approaches and efforts to improve communication, attention should be paid to cognitive capacity, such as team composition, technology interfaces, time pressures and individual fatigue, the researchers say.

The stakes are high for patients, physicians and hospitals, Dr. Bingener says.

"The most important piece is the patient perspective. You don't want a patient to have to experience a never event. The breach in trust that happens with that is the most important part," she says.

The study was funded in part by National Institute of Diabetes and Digestive and Kidney Diseases grant K23DK93553. The research team included members of the Mayo Clinic Department of Surgery, the Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Quality Management Services and Pulmonary and Critical Care Medicine.

Disclosures: Dr. Bingener is supported through an NIDDK research grant, specified research through Nestle and

Stryker Endoscopy, has received travel support from Intuitive Surgical, and serves on Titan Medical's Surgeon Advisory Board. Co-author Susan Hallbeck, PhD, receives grant funding from Stryker Endoscopy.

Genetic Risk Factor for Premature Birth Found

Newswise — Researchers at the University of California, San Diego School of Medicine have discovered a genetic risk factor for premature birth. The risk factor is related to a gene that codes for a protein that the scientists have found helps the body's immune cells recognize and fight Group B Streptococcus (GBS) bacteria.

These bacteria are found in the vagina or lower gastrointestinal tract of approximately 15 to 20 percent of healthy women, but may cause life-threatening infections, such as sepsis or meningitis in newborns, especially those born prematurely.

The study was published online in the May 5th, 2014 issue of the *Journal of Experimental Medicine*.

"Pregnant women are universally screened for these bacteria during pregnancy and administered antibiotics intravenously during labor if they test positive to protect the infant from infection," said Victor Nizet, MD, Professor of Pediatrics and Pharmacy and co-author. "Our research may explain why some women and their infants are at higher risk of acquiring severe GBS infections than others."

In the study, scientists identified two proteins on fetal membranes of the placenta that are involved in immune function. One of the proteins (known as Siglec-5) binds to the GBS pathogen and suppresses immune response to the microbe, while the other protein (known as Siglec-14) binds to the pathogen, and activates killing of the bacteria. Siglecs are cell surface receptors found typically on immune cells. They recognize (bind) sialic acids - sugar molecules that densely coat our cells.

"We have one protein that tells the body to attack the pathogen and another that tells the body not to attack it," said Raza Ali, PhD, a project scientist in the Nizet laboratory and the study's lead author.

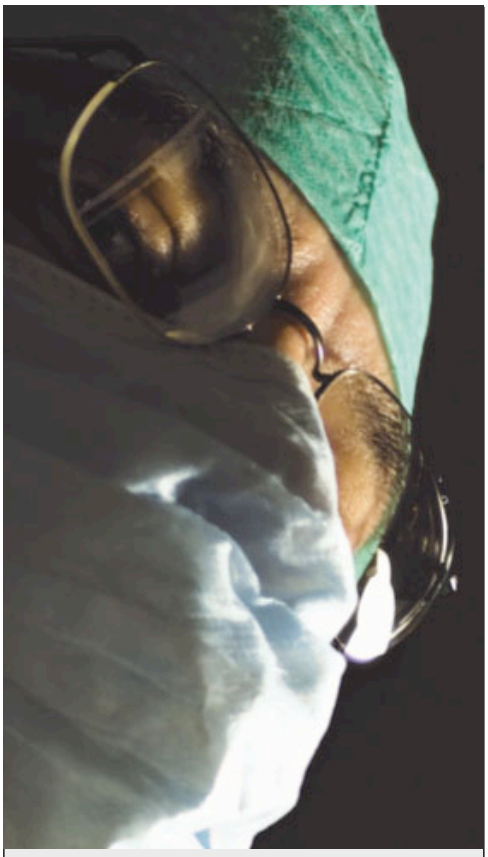
Scientists believe that the pair of proteins together helps balance the body's immune response to pathogens, by directing some antimicrobial response without provoking excessive inflammation.

"Identifying the dual role of these receptors and how they are regulated may provide insight for future treatments against GBS," Ali said.

Interestingly, the gene for Siglec-14 is missing in some individuals, and the researchers have found that fetuses that lack the Siglec-14 protein are at higher risk of premature birth, likely due to an imbalanced immune response to the bacterial infection.

"We found this association in GBS-positive but not GBS-negative pregnancies, highlighting the importance of GBS-siglec crosstalk on placental membranes," said Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular Medicine and study co-author.

For reasons not completely understood, GBS infections are not found in any other animals, including chimpanzees, which share 99% of human protein sequences. "The expression of the two siglec proteins on the fetal membranes is also unique to humans," Varki said. "Our study offers intriguing insights into why certain bacterial pathogens may produce uniquely human diseases."



The scientists believe that identifying the mechanisms of siglec protein action may help in designing therapeutic targets against bacterial infections that are becoming increasingly resistant to antibiotics and could have important implications for other disorders, such as blood clotting, chronic diseases and HIV infections. Co-authors include: Jerry J. Fong, Aaron F. Carlin, Rebecka Linden, Mana Parast, UC San Diego; Tamara Busch and Jeffrey Murray, University of Iowa; Takashi Angata, Academia Sinica, Taiwan and Thomas Areschoug, Lund University, Sweden.

Funding for this research came, in part, from the National Institutes of Health (grants P01HL107150 and AI057153).

Disclosure: Ajit Varki has an equity interest in Sialix, Inc., which is developing products based on new discoveries of non-human sialic acids and their potential impact on cancer, cardiovascular and other inflammatory-mediated disease. He is also a scientific advisor to the company and a member its board of directors.

Upcoming Meetings

9th International Conference on Brain Monitoring and Neuroprotection in the Newborn - 2015 Symposium
Oct. 1 – 3, 2015; Cork, Ireland
http://newbornbrain2015.com

NPA & National Advocates for Pregnant Woman - Pregnant Women, Drug Use, and NAS: Experts Share Science & Strategies That Help Women, Babies, and Families
Oct. 2 – 3, 2015; Nashville, TN USA
www.nationalperinatal.org

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Oct. 8-10, 2015; Miami, FL USA
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