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Upcoming Medical Meetings

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Editorial and Subscription Offices:

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Pericardial Effusion with a Properly-Placed Umbilical Venous Catheter

By Ahmad A. Aboaziza, MD; Darshan Shah, MD; Jennifer Gibson, MD; Otto H. Teixeira, MD

Introduction

Pericardial effusion caused by Umbilical Venous Catheter (UVC) is described with intracardiac location of the tip of the UVC. Mechanisms of injury range from direct myocardial perforation to thrombus formation and myocardial necrosis.

Case Presentation

A preterm, 27-week, appropriate-for-gestational-age female was immediately transferred to the NICU after delivery due to prematurity and Respiratory Distress Syndrome. Her Apgar scores were 6 and 8 at 1 and 5 minutes, respectively.

A physical exam revealed an active preterm female in moderate respiratory distress with subcostal retractions. Vital signs included: a temp of 100.9° F, a pulse of 189bpm, a respiratory rate 61bpm, blood pressure 57/27mmhg, and weight 1335g. On lung auscultation there were diffuse rhonchi over both lung fields. Mild hypotonia was present. The remainder of the exam was unremarkable.

Umbilical artery and venous lines were placed upon the patient's arrival to the NICU. As demonstrated in Figure 1, the umbilical arterial catheter tip was located at the level of the T6, and the umbilical venous

catheter tip projected at the cavoatrial junction.

On Day of Life (DOL) 1, an echocardiogram did not show any pericardial effusion.

Repeat imaging showed the arterial line with its tip at the T7 level and the venous line with its tip at the T6 level.

On DOL 3, an echo showed a small circumferential pericardial effusion. The X-ray showed 'optimal position' of the UVC. Echocardiograms failed to show the catheter tip in the heart on Day 1 or on Day 3. Ejection fraction was 91.7%. Clinically, the infant deteriorated and required intubation for worsening blood gas.

On DOL 4, a repeat echo showed a moderate circumferential pericardial effusion with no evidence of cardiac tamponade. The effusion was mainly located posteriorly and was slightly larger compared to the previous day. The ejection fraction remained unchanged. In view of these findings, the umbilical lines were then removed, and a PICC line was placed.

On DOL 5, the pericardial effusion had decreased as the infant remained stable on vent support.

By DOL 7, there was no pericardial effusion seen on echocardiogram.

“Pericardial effusion caused by Umbilical Venous Catheter (UVC) is described with intracardiac location of the tip of the UVC. Mechanisms of injury range from direct myocardial perforation to thrombus formation and myocardial necrosis.”

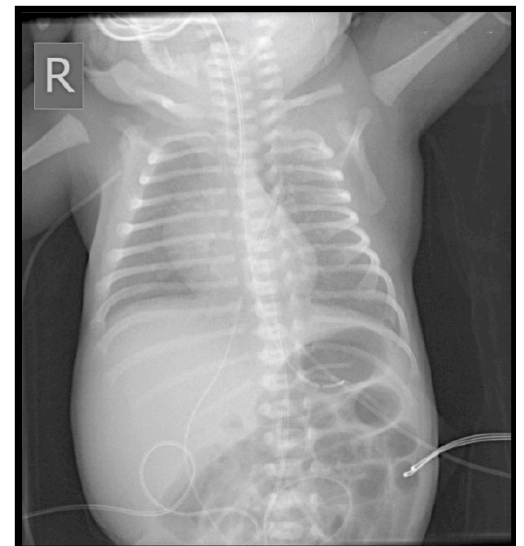


Figure 1. Chest- X-ray (PA view) showing UVC and UAC line placements.

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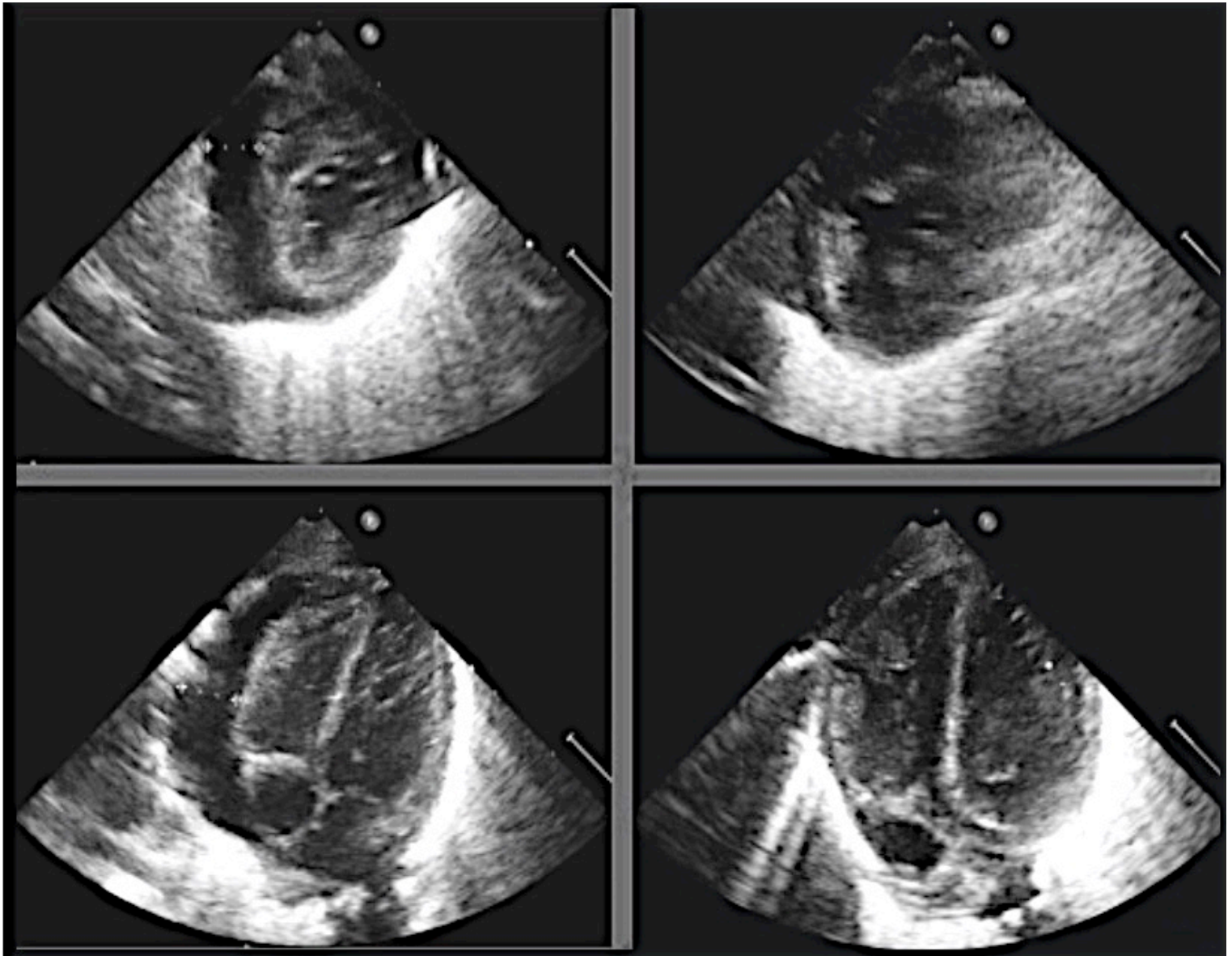


Figure 2. Echocardiograms (apical 4-chamber and short axis view) before and after UVC removal.

Discussion

It is possible for a properly-placed UVC to cause pericardial effusion, as happened with our patient. Even if the UVC is not in the heart, it is always important to take it out ASAP in the event of pericardial effusion. Pericardial effusion associated with UVC may be treated conservatively if signs of cardiac tamponade are absent.

Possible causes of pericardial effusion in this setting include direct trauma to the endothelial wall during UVC placement or

irritation to the endothelial lining caused by hyperosmolar infusates.

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“It is possible for a properly-placed UVC to cause pericardial effusion, as happened with our patient. Even if the UVC is not in the heart, it is always important to take it out ASAP in the event of pericardial effusion. Pericardial effusion associated with UVC may be treated conservatively if signs of cardiac tamponade are absent.”

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Corresponding Author



Ahmad A. Aboaziza, MD
 PGY2
 Pediatric Resident
 East Tennessee State University
 Department of Pediatrics
 Ground Floor, 325 North State of Franklin
 Johnson City, TN, 37604 USA
 Phone: 571.277.2091
 Aboaziza@mail.etsu.edu



Jennifer Gibson, MD
 Assistant Professor
 East Tennessee State University
 Department of Pediatrics
 Ground Floor, 325 North State of Franklin
 Johnson City, TN, 37604 USA



Darshan S. Shah, MD
 Associate Professor
 East Tennessee State University
 Department of Pediatrics
 Ground Floor
 325 North State of Franklin
 Johnson City, TN, 37604 USA



Otto H. P. Teixeira, MD
 Associate Professor
 East Tennessee State University
 Department of Pediatrics
 Carl A Jones Hall (VA Bldg 1)
 Room 2-06
 PO Box: 70578
 Johnson City, TN, 37604 USA

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Expanding the Circle of Influence With Neonatal Telehealth

By Michael Narvey, MD

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All Things Neonatal

<https://winnipegneonatal.wordpress.com>

March 2015; Republished here with permission.



Typical setup in a remote site for Telemedicine

If there is one area of Neonatology that is experiencing rapid growth it would be in telemedicine. Each month I come across new reports of centers utilizing this strategy whether to connect families and their infants (televisitation) when they cannot be present or to connect medical teams with other centres lacking the local expertise to care for newborns with certain conditions.

I am fortunate to work in a centre that has an established telehealth program. The city of Winnipeg in Manitoba, Canada, covers an exceptionally large geographic area. On average we transport between 280 – 300 patients per year from as far as the Arctic Circle to North Western Ontario. To put this in perspective, I had the pleasure of presenting our work at a conference in Ireland in 2013.

Superimposing the country of Ireland over a map of our catchment area provides some perspective of distances I am talking about.

The topic in this case was the impact of using Telehealth to reduce neonatal transports, by supporting care providers in families in their

“If there is one area of Neonatology that is experiencing rapid growth it would be in telemedicine.”

home cities and towns. As care providers, if we have a strategy that can, in some cases, keep babies together with their families and support networks in their own communities, how can we not explore that possibility? We commonly talk about the importance of family-centred care and if you ask me it should begin with doing what is best for the family unit which is minimize the trauma to the family unit after delivery. I thought it was worth sharing as it gives the people of Manitoba and beyond an idea of how dramatic an impact Telehealth can have when used in a clinical manner. Telehealth, of course, is valuable for televisitation and allowing remote meetings, but there is so much more. To our knowledge this is the first such use of Telehealth in Canada and was awarded a leading practice designation by Accreditation Canada in 2013. The effectiveness of this strategy has paid for the cost of implementation many times over and I would strongly urge other centres to explore with their Telehealth services whether it would be right for their centre.

How effective was the strategy? In the year following May 2012 implementation an estimated 4 air and 12 ground transports were averted. Using an average cost of \$10,000 per air and \$5,000 per ground transport it is estimated that the total health care savings is \$100,000.

“Use of Telemedicine to Support Care of Newborns in Rural Manitoba” can be found at: <https://accreditation.ca/node/6785>, which describes in detail what we accomplished, and how it benefited the people of Manitoba.

Dare to Dream

The use of Telehealth need not stop at the assistance of other care providers in caring for sick neonates. As the field is developing, I see

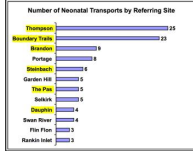


Background

Manitoba, Canada covers a very large geographic area with rural communities having practitioners of varying skill. The two tertiary care NICUs are located in Winnipeg; to improve ready access to specialised neonatal care, the Manitoba Neonatal Transport Team was established in 1981 for ground and in 1986 for air transports. Annual transports were approximately 280 patients with most having respiratory distress. Average transport time is 4 hours. In 2002 the MB Telehealth network was established; a direct link via telehealth was established with the Nursery in a rural community situated 525 miles north of Winnipeg (Thompson) and the NICU at Health Sciences Centre. Two rural sites were linked to the NICU (2010). Despite simplicity of use and full interoperability of the systems, utilisation was sporadic. Increased use of telehealth to improve ready access to specialised care for sick newborns, support to rural health care providers and reduction in the number of newborn transports were the goals of the government funded Manitoba Health Maternal and Child Health Task Force (2011).

Methods

Employing a collaborative model, the project team consisted of members from MB Telehealth, a Clinical Nurse Specialist and two MD co-chairs. The first step was to determine the areas of greatest need in the Province based on past history of Neonatal Transports (highlighted sites).



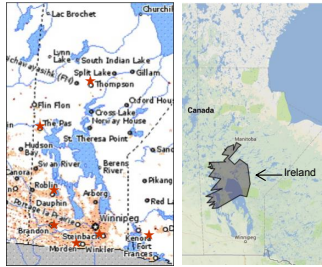
Data from July 2010 - June 2011

Site visits were then carried out to present the project, and to obtain consent to receive equipment and determine timing of training. Surveys were completed by each site to determine levels of experience and needs. Site visits allowed the best determination of type and location of equipment to be installed. Essential to the success of the project was inclusion of high definition video to allow viewing of the small



"Virtual NICU" viewing of "remote" baby

Geographic Perspectives



Sample Distances

Thompson General Hospital	Distance 525 miles
Dauphin Regional Health Centre	Distance 128 miles
Boundary Trails Health Centre (Morden/Winkler)	Distance 63 miles

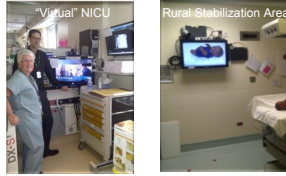
ACoRN Course

Outreach education was delivered at each site as an ACoRN course. The goal of this offering was to both enhance the understanding of common approaches to Neonatal problems and develop relationships with the rural sites to improve familiarity with our team.

- NICU physicians, nurses and respiratory technologists travelled to participating sites to instruct the full day course
- 75 participants have received an ACoRN certificate



Equipment Installed Spring of 2012

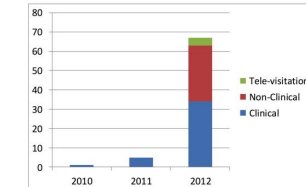


- Integration with work flow patterns
- Fixed videoconferencing equipment
- Headphones for private communication with privacy screens
- Establishment of a digital address book at all sites
- Tertiary care centre capability of establishing remote camera control to view details of interest independently

Results

Deliverable	Description	Outcome
Telehealth Equipment	10 pieces of new equipment in 8 facilities	Completed March 2013
ACoRN Course	Course offered at each rural site	5 of 6 completed by March 2013
Radiographic view station (PACS) for NICU	1 new PACS view station able to display radiographic images immediately from rural sites	Completed March 2013

When comparing the use of telemedicine prior to this initiative we saw a 12 fold increase in usage from 2011 to 2012.



Economic Impact

In the year following May 2012 implementation an estimated 4 air and 12 ground transports have been averted. Using an average cost of \$10000 per air and \$5000 per ground transport it is estimated that the total health care savings is \$100000

Post implementation Evaluation

- After sufficient time for each centre to become accustomed to the equipment a follow-up survey was distributed to each centre.
- 100% felt the tele-neonatology service was very important to the care of sick newborns at the rural facility
 - 100% felt that the videoconferencing equipment was easy to use
 - 75% felt tele-neonatology had improved the relationship between their staff and the NICU

Conclusions

- A solid business case with clear goals and timelines was instrumental to success of the project. Coordination between stakeholders from MB Telehealth, Medicine, our nurse telemedicine coordinator and transport nurses enabled smooth collaboration.
- A reduction in Neonatal transports has occurred since the introduction of telehealth services in our targeted sites. This reduction translates into a significant cost savings from averted air and ground transports.
- Each averted transport has the additional benefit of keeping infants with their families and support networks, thereby reducing stress on the family unit.
- Site surveys suggest enhancement of support and improved communication between tertiary and rural sites.
- By bundling educational outreach with equipment implementation and training we believe an increase in care provider confidence may have contributed to a reduction in Neonatal transports.
- A change in society's acceptance of video enhanced communication since 2002 may have contributed to the acceptance of telehealth with this project.

The Future

- We anticipate expansion of this service to other centres based on the demonstrated cost savings to the health care system. Nearly half of the total cost of the program has been recouped from cost savings in the first year of use.
- A permanent Telehealth coordinator is being hired to maintain the quality of the service and ensure that outreach education is both relevant and provided on a frequent basis to our rural sites.

View a large version of the poster at: <https://winnipegneonatal.files.wordpress.com/2015/03/ireland221.pdf>

a larger benefit to long distance education. How many non-tertiary care centres would benefit from linking to centres with more expertise in the neonatal field and being walked through procedures or equipment that they are unfamiliar with?

The time and cost to travel to these remote locations can be avoided by the use of a high definition camera and regular scheduling of sessions. If we want the best for the babies in our catchment areas, education cannot be limited to the walls of the hospital we work in. Prevention of adverse outcomes must start with providing proper care to the newborns in the place of birth rather than having the transport team address the issues that have already arisen.

As the technology becomes more available and at a lower cost, I have no doubt we will see expansion of services. Retcams exist already which are capable of avoiding transfer of discharged infants back for ROP screening.

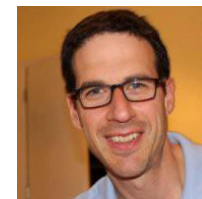
This, in fact, has been recently reviewed by Fierson et al in January of this past year. Alternatively, breastfeeding support is possible by connecting those with expertise

in lactation support to rural centres without such training. Why should breastfeeding success rates in rural communities be any different than in urban centres when the education can be brought to them? Such an opportunity was highlighted recently by Friesen et al in 2015.

Are there other Telehealth modalities that you know of out there that could help

improve the care we provide to these vulnerable infants? The field of Telehealth is exploding and with it opportunities to improve our care, and ideally, outcomes. I encourage everyone whenever possible to ask the question "Can we link up so we can see a patient?" All too often what has been described, and what is actually present in terms of signs and symptoms, may be quite different.

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Michael Narvey, MD
 Children's Hospital Research Institute of Manitoba
 513 - 715 McDermot Ave.
 Winnipeg MB R3E 3P4
 Phone: 204.787.2720
 mnarvey@exchange.hsc.mb.ca

Medical News, Products & Information

Compiled and Reviewed by Tony Carlson, Senior Editor

Therabron Therapeutics Receives FDA Fast Track Designation for rhCC10 for the Prevention of Chronic Lung Disease Related to Premature Birth

Therabron Therapeutics, Inc., a clinical-stage biotechnology company dedicated to advancing a new standard in respiratory care, announced in April that it has received Fast Track Designation from the U.S. Food and Drug Administration (FDA) for rhCC10 (recombinant human Club Cell 10 kDa Protein), specifically for the prevention of chronic lung disease related to premature birth.

Therabron Therapeutics, lead biopharmaceutical product candidate, is a proprietary preparation of recombinant human CC10 protein which has potential clinical applications, based on its potent anti-inflammatory properties, in a variety of respiratory diseases. CG100, the company's lead compound, based on rhCC10 and intended to prevent chronic lung disease in neonates, is currently in a Phase 2 clinical trial enrolling 88 preterm infants. This ongoing Phase 2 study is supported, in part, by a grant from the U.S. FDA Office of Orphan Product Development.

"The receipt of Fast Track Designation signifies further recognition by the FDA of the merits of this program, and allows the company to submit completed portions of the Biologics License Application (BLA) on a rolling basis, thereby expediting the FDA review process," stated Dr. Thomas F. Miller, President & CEO of Therabron Therapeutics. "As such, we look forward to working closely with the FDA and other Global Health Authorities to advance this program and eventually bring CG100 to market." rhCC10 was previously granted Orphan Drug Designation by the FDA.

The Fast Track program was created by FDA to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Drugs that receive this designation benefit from more frequent communications and meetings with FDA to review the drug's development plan, including the design of the proposed clinical trials, use of biomarkers and the extent of data needed for approval. Drugs with Fast Track Designation may qualify for priority review to expedite the FDA review process, if relevant criteria are met.

Therabron Therapeutics, a privately held, clinical-stage biopharmaceutical company, is advancing a platform of novel therapeutic proteins in an effort to change how a variety of neglected and under-treated respiratory and fibrotic conditions are managed. They are developing a new class of drugs based on the naturally occurring secretoglobin family of proteins, which includes the CC10 protein — a molecule with both anti-inflammatory and immunomodulatory mechanisms. For information, visit www.therabron.com.

Subset of E. Coli Bacteria Linked to Deadly Disease in Preterm Infants

Newswise — Necrotizing enterocolitis is an intestinal disease that afflicts about one in 10 extremely premature infants and is fatal in nearly one-third of cases. The premature infant gut is believed to react to colonizing bacteria, causing damage to the intestinal walls and severe infection. In a study that was published in the March 17th *Cell Reports*, researchers at UMass Medical School, University of Trento and Cincinnati Children's Hospital describe an association between necrotizing enterocolitis and a subset of E. coli bacteria, called uropathogenic E. coli, that colonize the infant gut.

"Bacteria start to colonize infants as soon as they are born, but preterm infants colonize and react to colonization differently than term infants.

What we found is that when preterm infants are colonized by uropathogenic subtypes of E. coli, they are much more likely to develop necrotizing enterocolitis," said co-first author Doyle Ward, PhD, Associate Professor of Microbiology & Physiological Systems at UMass Medical School and Director of Operations for the UMass Medical School Center for Microbiome Research.

Uropathogenic E. coli, or UPEC—typically the cause of urinary tract infections—is frequently found in the gut of infants and adults. But according to the new study, when UPEC colonize the gut of extremely premature infants, those infants have a higher risk of developing necrotizing enterocolitis (NEC).

"This is a challenging and complicated disease, and I think that any new information that offers an opportunity to save an infant's life is an important advance," Dr. Ward said. "We have identified a type of pathogen that preterm infants may be uniquely vulnerable to."

The researchers collaborated with hospitals in Cincinnati, OH, and Birmingham, AL, to obtain stool samples from a cohort of 166 infants: 144 pre-term and 22 that had been carried to term. The team sequenced the infants' stool and developed metagenomic analysis tools to identify the bacteria colonizing each infant. Previous work had already identified Enterobacteriaceae—a family of bacteria that includes E. coli—as potentially associated with NEC, but Ward and his colleagues used new analysis tools to distinguish the different types of E. coli in the infants.

The team singled out UPEC as the E. coli type most strongly linked to infants who developed NEC. In the study cohort, 27 of the infants developed NEC, all pre-term. The disease was fatal in 15 of those cases. UPEC was found in 44% of the infants who developed NEC, compared to only 16% of the 111 infants who survived without developing NEC.

"Our study suggests that if you can quickly identify UPEC in the microbiome of a pre-term infant, you can know that the infant has a greater risk for NEC before there are any symptoms," Ward said.

Although the team didn't address the question of where UPEC in an infant's gut might originate, they did observe an association between vaginal delivery and death from NEC in these extremely pre-term infants.

"Many infants do have UPEC in their gut," Ward said. "It may be that they're colonized when they pass through the birth canal, and this could be a source of risk. We just don't know yet."

But Ward strongly cautioned against making such generalizations from one cohort, adding that more work is needed. "It's important to realize that infants also acquire many beneficial bacteria from their mothers during vaginal birth—and it's likely that the good bacteria have a role in preventing NEC. We're still at a basic research stage."

"The take-home message is that if we can identify these potentially harmful organisms early enough in a preterm infant, and learn about them in advance, we can arm physicians with information that could help them make care decisions for these vulnerable infants," he said.

MRI Helps Predict Preterm Birth

MRI of the cervix is more accurate than ultrasound at predicting if some women will have a preterm birth, according to a new study from Italy appearing in the online edition of *Radiology*.

Early dilation of the cervix, a neck of tissue connecting the uterus with the vagina, during pregnancy can lead to premature delivery. Women in their second trimester of pregnancy with a cervix measuring 15 millimeters or less, as seen on ultrasound, are considered to be at higher risk of preterm birth. However, ultrasound has limitations as a predictor of preterm birth, as it does not provide important information on changes in cervical tissue in the antepartum phase just before childbirth.

"A better understanding of the process of antepartum cervical remodeling, loosely divided in two distinct phases called softening and ripening, is critical to improve the diagnosis of cervical malfunction and anticipate the occurrence of birth," said the study's lead author, Gabriele Masselli, MD, from the Radiology Department at Sapienza University in Rome.

To learn more, Dr. Masselli and colleagues used an MRI technique called diffusion-weighted imaging (DWI) to examine pregnant women who had been referred for suspected fetal or placental abnormality. DWI reveals differences in the mobility of water molecules in tissue and the results can be used to create apparent diffusion coefficient (ADC) maps that provide a measure of local cell density. DWI has been increasingly used for abdominal and pelvic diseases, but has not been tested for the evaluation of the uterine cervix in pregnant patients.

Each of the 30 pregnant women in the study had a sonographically short cervix and a positive fetal fibronectin test between 23 and 28 weeks of gestation. Fetal fibronectin is a glue-like protein that helps hold the fetal sac to the uterine lining, and the presence of it before week 35 of gestation may indicate a higher risk of preterm birth.

Of the 30 women, eight, or 27%, delivered within a week of the MRI examination. The other 22 delivered an average of 55 days later. The researchers compared differences in ADC values at MRI between two areas of the cervix: the inner, subglandular zone and the outer, stromal area. While stromal ADC and sonographic cervical length showed no difference between both groups, the subglandular ADC was higher in patients with impending delivery, suggesting an increased mobility of water molecules in that area consistent with cervical ripening.

"Our results indicate that a high ADC value recorded at the level of the subglandular area of the cervix is associated with the imminent delivery of asymptomatic patients with a short cervix," Dr. Masselli said. "In detail, the subglandular ADC was inversely correlated to the time interval between MRI and delivery, and therefore, emerged as a powerful imaging biomarker in evaluating patients with impending delivery."

The research team is planning larger, multicenter trials to confirm the role of subglandular ADC analysis in predicting preterm birth, Dr. Masselli said.

"Are Second Trimester Apparent Diffusion Coefficient Values of the Short Uterine Cervix Associated with Impending Preterm Delivery?" Collaborating with Dr. Masselli were Giuseppina Perrone, MD, Karen Kinkel, MD, Marco Di Tola, MD, Francesca Laghi, MD, Gianfranco Gualdi, M., and Roberto Brunelli, MD.

RSNA (RSNA.org) is an association of more than 54,000 radiologists, radiation oncologists, medical physicists and related scientists promoting excellence in patient care and health care delivery through education, research and technologic innovation.

For patient-friendly information on MRI during pregnancy, visit RadiologyInfo.org.

Children Born Prematurely are Disadvantaged at School and into Adulthood, But Delaying School Entry May Not Be the Answer

Children born before 34 weeks gestation have poorer reading and math skills than those born at full term, and the difficulties they experience at

school continue to have effects into adulthood: by the age of 42, adults who were born prematurely have lower incomes and are less likely to own their own home than those born at full term.

These findings are from a study led by Professor Dieter Wolke at the University of Warwick and funded by the Nuffield Foundation. The study analysed data from four large-scale longitudinal studies, and found that the poorer reading and math skills of children born prematurely were associated with lower educational qualifications on leaving school and lower income in middle age.

This is a problem faced by a growing number of people: premature births currently represent 11% of all live births worldwide. On average, any primary school classroom will include two children born prematurely.

The study also looked at whether delaying school entry enabled children born prematurely to do better at school but found no evidence to support this. Children who started school a year later did not perform better in teacher ratings of their academic attainment than children who had started at an age appropriate time.

In light of this, the researchers recommend that children born prematurely should enter school at an appropriate age, but receive additional support. However, their research showed that over 80% of teachers and over 50% of educational psychologists had received no formal training about the effect of preterm birth on children's development and learning, something which needs to be addressed if the growing number of preterm children are to be supported.

The report, *The Impact of Premature Birth on Mathematics Achievement and Schooling*, was launched at a seminar at the Nuffield Foundation. The research team also included: Samantha Johnson from the University of Leicester, Julia Jaekel from the University of Tennessee and Camilla Gilmore from Loughborough University.

Dr Johnson said, "Teachers and educational psychologists receive little formal training about the effects of preterm birth on children's long term development and learning and are often not aware of appropriate strategies to support preterm children in the classroom."

The lead researcher Prof Wolke, who is based at the University of Warwick's Department of Psychology and at Warwick Medical School, concludes: "Our findings lead us to recommend that all preterm children born before 34 weeks of gestation may benefit from regular follow-up after discharge from hospital. Interventions are required around the time of school entry to facilitate preterm children having an optimal start to their schooling career. Delayed school entry is not recommended on current evidence, but more research is needed."

The Preterm Birth: Impact on Mathematics and Achievement (PRIME) study is funded by The Nuffield Foundation. More information is available at www.nuffieldfoundation.org.

Gut Microbes Linked to Deadly Intestinal Disease in Premies

An imbalance of certain gut microbes appears to be the underlying cause of a frequently fatal intestinal illness in premature babies, according to new research led by Washington University School of Medicine in St. Louis. The study appeared online March 8th in *The Lancet*.

Analyzing gut bacteria in premature infants, the study shows that babies who developed necrotizing enterocolitis had a different mix of microbes in their intestines than babies who never developed the condition. The diverging microbial communities were observed before any evidence of disease, suggesting it may be possible to prevent the illness by keeping the balance of gut microbes in check.

"Premature infants who survive the first two weeks of life have a much higher risk of dying of necrotizing enterocolitis than of anything else," said corresponding author Phillip I. Tarr, MD, the Melvin E. Carnahan Professor of Pediatrics. "We're pleased that our work now identifies classes of bacteria on which to focus future investigations of treatment and prevention strategies. We would like this study to open discussions about what the next steps should be to protect premature infants from this destructive disease."

The researchers showed, in general, that babies who developed necrotizing enterocolitis had higher proportions of Gram-negative bacteria and lower proportions of strictly anaerobic bacteria -- those that live without oxygen -- in their guts compared with babies who didn't develop the disease.

The Gram-negative bacteria implicated in the study are classified as Gammaproteobacteria and include organisms well-known for causing serious infections and driving inflammation, such as *Escherichia coli* (*E. coli*), *Klebsiella* and *Enterobacter*. The study also suggested that having more anaerobic bacteria in the gut protects against necrotizing enterocolitis. Such organisms included classes of bacteria called Clostridia and Negativicutes, which might possess anti-inflammatory capabilities.

Conflicting data from past studies have made it difficult to pin down factors that might lead to necrotizing enterocolitis, a leading cause of death among premature infants born throughout the world. Because of this lack of clarity, death rates in premature babies that develop the disease remain at about 30%, essentially unchanged over the past 30 years.

The researchers analyzed data from almost 1,000 premature infants cared for in the neonatal intensive care units at St. Louis Children's Hospital, part of Washington University Medical Center; Children's Hospital at Oklahoma University Medical Center; and Kosair Children's Hospital in Louisville, Ky. Washington University collaborators included Elena Deych, Research Statistician, and William D. Shannon, PhD, Professor of Biostatistics in Medicine, and investigators at The McDonnell Genome Institute.

About 6% of the infants in the study developed the disease. Of those with the condition, 36% died. In the 94% who did not get necrotizing enterocolitis and served as the control group, two babies, about 1.7%, died from other causes.

"The holy grail for necrotizing enterocolitis is prevention," said first author Barbara B. Warner, MD, Professor of Pediatrics. "Despite aggressive treatment with antibiotics and surgery, infants who develop the most severe form of necrotizing enterocolitis die within hours."

Warner described the disease progression as an inflammatory process that starts on the inside of the gut and results in tissue death. Some babies respond to antibiotics, but many need surgery to remove dead tissue. When treatment fails, death is caused by septic shock, an overwhelming inflammatory response to infection.

The new study differs from past efforts to investigate necrotizing enterocolitis because of its large sample size and thorough DNA sequencing strategy that involved collecting and analyzing thousands of babies' stools. This allowed the investigators to monitor the fast-changing gut microbial communities typical of babies in the first weeks of life and to gather these data before disease developed.

Importantly, the researchers noted that differences in the microbial content of the gut were most apparent in the most premature babies, those born before 27 weeks' gestation. These very premature babies also are at higher risk of the disease than babies born after 27 weeks. In addition, the makeup of gut microbe communities in babies that

developed the disease did not diverge from the others until at least one month of life. While the condition can develop at any time during the first two months of life, it often doesn't occur until after the first month, especially in the most premature babies.

Such data suggest there is a window for identifying infants at highest risk of developing the disease -- at about one month after birth, when bacterial differences emerge but before symptoms are apparent.

The investigators pointed out that babies receiving their mother's breast milk have a lower risk of developing necrotizing enterocolitis. But even so, concerted efforts to provide breast milk have not driven down rates of the condition.

Now, Warner and Tarr are focusing on possible ways to prevent or reverse the microbial imbalance they identified, so as to avert the development of necrotizing enterocolitis.

"Antibiotics delivered to the bloodstream tend not to penetrate into the gut," Warner said. "So the route of administration may make a difference." Past efforts to give antibiotics directly into the gut were stopped because of concerns about bacteria developing resistance, but also because of possible safety and toxicity issues for the baby.

"Since then, we've learned a lot about how a premature baby's body processes these antibiotics, so future studies would be designed with these concerns in mind," she added. "Our first rule is 'Do no harm.' For prevention studies in particular, safety is extremely important because we will be treating premature infants who potentially won't get the disease."

This work was supported by the National Institutes of Health (NIH), grant numbers UH3AI083265, U54HG004968, and P30DK052574; by the National Institute of Allergy and Infectious Diseases; the Eunice Kennedy Shriver National Institute of Child Health and Human Development; the Foundation for the National Institutes of Health, made possible by support from the Gerber Foundation; the Melvin E. Carnahan Professorship; and by the Children's Discovery Institute of Washington University and St. Louis Children's Hospital.

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Profusion of Medical Advances for Premies

Newswise — For World Prematurity Day on November 17th, 2015, CHU Sainte-Justine Children's Hospital, affiliated with the University of Montreal, presented an overview of recent discoveries that are changing the lives of premature babies and their families at three critical periods of their lives: before birth, during their stay in the Neonatal Intensive Care Unit (NICU) and after discharge from the unit. Numerous advances by clinical researchers at the mother and child hospital – Canada's largest – promise to help prevent, treat, and comfort preterm babies and their families. Their work is particularly important given that prematurity is the world's leading cause of death at birth and can cause severe and lasting physical, intellectual, and psychological complications for children born preterm worldwide.

CRITICAL PERIOD 1 – BEFORE BIRTH

[A new molecule is found to prevent preterm birth](#)

Premature births are intimately linked with inflammation of the uterine

tissue, a biological response that induces contractions and preterm labour. In their search for a means to prevent this phenomenon and complications related to preterm deliveries, Mathieu Nadeau-Vallée, a doctoral student in Pharmacy, and Sylvain Chemtob, a neonatologist with multiple drug patents to his credit, discovered an agent that shows efficacy in inhibiting inflammation and preventing or delaying uterine contractions and premature delivery, without adversely affecting the fetus or mother. This discovery is a giant step towards preventing prematurity.

Higher risk of preterm delivery for women born preterm

Women who were born preterm have a higher risk of giving birth to preterm children. “The difference is not alarming considering that the vast majority of women born preterm gave birth at term. But it is significant enough to consider premature birth a risk factor in monitoring pregnancies,” said Dr. Anne Monique Nuyt, who led the study. Dr. Nuyt is also the principal investigator of a major study on the future of premature babies in adulthood.

Parents of preemies: “We are more than just statistics”

Medical association recommend that doctors discuss all potential problems faced by preemies, but parents want more than a list of risks. They want to know what these risks mean for the future of their child and their family, and how preterm birth will affect their quality of life. They want to know how Neonatology works and how to be parents in an intensive care unit. Drs. Antoine Payot and Annie Janvier, both who are both neonatologists and clinical ethicists, study communication between parents and health professionals.

CRITICAL PERIOD 2 – STAY IN THE NICU

Blocking light improves preemies' survival rates

Premature babies need to be fed intravenously due to the immaturity of their digestive system and their high nutritional requirements during their first days of life. The survival rate of preemies is improved by blocking light from reaching the intravenously-fed infused nutritious mixture, thus preventing serious potential complications such as pulmonary and kidney dysfunction or generalized infection.

Probiotics reduce inflammatory bowel disease in preterm infants

The neonatologist and clinical researcher Dr. Keith Barrington has conducted numerous studies to optimize the care of newborns, on subjects from nutrition to cardiovascular and respiratory support. The CHU Sainte Justine is the first Canadian institution to use probiotics to treat neonates to prevent serious bowel inflammation, or Necrotizing Enterocolitis (NEC), which is a major cause of mortality and morbidity in preterm infants. Dr. Barrington and his team demonstrated that it is possible to optimize the nutrition of preterm infants and reduce NEC using probiotics.

Encouraging skin-to-skin contact over incubators using zero-gravity chairs

With many benefits for both premature infants and their parents, the Kangaroo-Mother Care (KMC) method is internationally recognized as the ideal environment for the family in the neonatal unit. In KMC, the infant is placed not in an incubator but in skin-to-skin contact with the

parent. The most recent recommendations encourage the use of KMC as early, often, and long as possible. Isabelle Milette, a nurse practitioner specializing in Neonatology and Developmental Care, evaluated the efficacy of three models of zero-gravity chairs with parents and practitioners to select the ideal model and optimize KMC in the NICU and the parental experience. The use of zero-gravity chairs improved the duration of KMC episodes up to two hours per day on average while increasing their frequency.

Learning to intubate premature babies by viewing their throats on a screen

Each year, thousands of premature babies have difficulty breathing at birth. To help them, a ventilator and tube are inserted in their lungs. This delicate procedure requires expertise that pediatricians learn during their training. The videolaryngoscope is a tool that allows doctors to view an infant's throat structure on a screen during intubation, with better lighting. A clinical study conducted by the neonatologist Dr. Ahmed Moussa demonstrated that use of this tool helped pediatricians in training to learn this procedure more quickly, and will improve the learning of future pediatricians.

In the NICU, parents still want to care for their preemies

A few years ago, visiting hours for parents in NICU were restricted, and physical contact between parents and children was minimal. This approach has been replaced by integrated care, in which families team with practitioners to care for sick newborns. Still, in an intensive care environment, infants require technological assistance, and nurses and doctors assume greater responsibility for care. However, parents generally want to participate in caring for their child. A study conducted by Dr. Annie Janvier, in collaboration with the team Parents en néonatalogie, surveyed the views and experiences of parents and practitioners in neonatology. It was shown that they felt the need to be informed clearly and transparently of their potential role in neonatology, that they should be taught how to participate in care, and that parenting practices deemed “priority” should be supported and encouraged.

CRITICAL PERIOD 3 – AFTER DISCHARGE FROM THE UNIT

The Best in Daily Life: (www.developpementenfant.ca/wp/en/) - a new web tool for parents to support the healthy growth of their preterm child

After leaving the hospital, families need to be supported, guided, and reassured in the daily life of their preterm child. Dr. Thuy Mai Luu, a pediatrician in the neonatal follow-up clinic and researcher has developed, with Julie Gosselin, a professor in rehabilitation, workshops and a web platform to help equip parents in caring for and supporting the development of their preterm child from birth to two years. Infant behaviour, the sensory environment, body position, oral nutrition, parent-child interactions, and developmental stages are discussed. The program was validated with 50 families. Overall satisfaction of the parents has been great because the program fulfills a parental need.

It is known that adults who were born preterm are at risk for developing chronic diseases such as hypertension, obstruction of the lungs, sugar intolerance, and osteoporosis. The HAPI project aims to assess the



cardiovascular, respiratory, metabolic, bone, and kidney health of 200 young adults born preterm. Drs. Anne Monique Nuyt and Thuy Mai Luu, who lead the project, seek to better understand this influence of prematurity and the risks and protective factors involved. The results of this study will certainly help provide important guidelines to health professionals with regard to the follow-up and prevention of chronic diseases in this population.

Fall in One-to-One Nursing Care of Very Sick Newborns Linked to Higher Death Rate - Provision Fell by Around a Third in England Between 2008 and 2012

Newswise — University of Warwick research indicates that a fall in one-to-one nursing care of very sick and premature new-borns is linked to a higher death rate in neonatal intensive care.

The findings, which have been published in the *Archives of Disease in Childhood (Fetal & Neonatal Edition)*, showed the proportion of this type of nursing care provided in intensive care units fell by around a third between 2008 and 2012.

The British Association of Perinatal Medicine (BAPM) recommends one-to-one nursing care for newborns in a Neonatal Intensive Care Unit (NICU) in the UK, and a ratio of one nurse for every two infants in high dependency units. For infants in receipt of special care, the recommended ratio is 1:4.

Yet few neonatal units have achieved the required staffing ratios.

Lead author Dr Sam Watson, of the University's Warwick Medical School said: "We believe the results in this study provide some evidence in support of a one-to-one nurse to patient ratio in neonatal intensive care in England, in line with BAPM guidelines, and therefore provide increased nursing labour provision on neonatal units in England."

The academics wanted to assess the impact of one-to-one nursing on the monthly death rate in tertiary level neonatal units - those designated to provide intensive care - in England.

They, therefore, extracted monthly data supplied to the National Neonatal Research Database (NNRD) on infants admitted to 43

tertiary level care units between 2008 and 2012.

Using these figures, they calculated the proportion of neonatal intensive care days or intensive care admissions for which one-to-one nursing care was provided during this timeframe.

Between 2008 and 2012 the proportion of one to one nursing care provided in tertiary level neonatal units fell by a third, from an average of 9% to an average of around 6%.

Similarly, the proportion of infants admitted who received one-to-one nursing care fell from around 39.5% to just under 36%.

During this period, an average of 4.5 infants out of every 100 (4.5%) in receipt of intensive care died every month.

They calculated that a 10 percentage point fall in the proportion of intensive care days on which one to one nursing care was provided was linked to a monthly increase in the inpatient death rate of 6 per 1000 infants (0.6%) in intensive care.

Dr Watson said, "While these findings from an observational study support an increase in one-to-one nursing provision in tertiary level neonatal units, they do not inform us whether a one-to-one nurse-to-patient ratio for all intensive care days would have a beneficial effect."

In a linked editorial in the research, Drs Fenton and Turrill, and the Chief Executive of new-born baby charity, Bliss (www.bliss.org.uk), point out that over 90,000 babies were admitted to neonatal units in England, Scotland, and Wales in 2014: just under 14% of the care days these babies received was in intensive care.

They highlight the health secretary's ambition, announced at the end of last year, to cut the rate of stillbirths, neonatal and maternal deaths in England by 30% by 2030.

Laudable though this might be, "the announcement has so far singularly failed to acknowledge the importance of improving staffing levels in order to reduce neonatal deaths, despite consistent information from neonatal professionals," they write.

And recent government policy may worsen shortages, they suggest.

"In addition, while the Secretary of State has acknowledged the mistake made by the coalition government in 2010 in cutting the number of student nurse places commissioned, it is still far from clear whether the government's plans to replace student nurse bursaries with loans, as outlined in the 2015 Comprehensive Spending Review, will have the desired effect of increasing the number of nurses trained, or will just put a barrier in the way of those who wish to join the profession," they conclude.

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PO Box 444
Manzanita, OR 97130 USA
www.NeonatologyToday.net

Publishing Management:

- Tony Carlson, Founder, President & Senior Editor - TCarlsonmd@gmail.com
- Richard Koulbanis, Group Publisher & Editor-in-Chief - RichardK@Neonate.biz
- John W. Moore, MD, MPH, Group Medical Editor - JMoore@RCHSD.org

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Key Contacts

Tony Carlson - *Founder, President & Senior Editor* - TCarlsonmd@gmail.com or call +1.301.279.2005
Richard Koulbanis - *Group Publisher & Editor-in-Chief* - RichardK@neonate.biz
John W. Moore, MD, MPH, *Group Medical Editor* - JMoore@RCHSD.org

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