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

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Fetal Echocardiography II: Congenital Heart Defects and Management

By Monesha Gupta-Malhotra, MBBS

This is the second in a series of two articles. The first article, "Fetal Echocardiography I," was written by Gurur Biliciler-Denktas, MD, FACC, FAAP of the University of Texas Houston Medical School & Children's Memorial Hermann Hospital, Houston, TX. It was published in the August issue of Neonatology Today, and is available on the website.

Fetal echocardiography has been an evolving field with an increasing number of congenital heart defects being detected and reported in-utero. The implications for prenatal detection and management of these defects are enormous with two main outcomes: firstly, improvement in the outcomes of congenital heart disease and secondly the burden of early termination of pregnancy based on these diagnoses.[1]

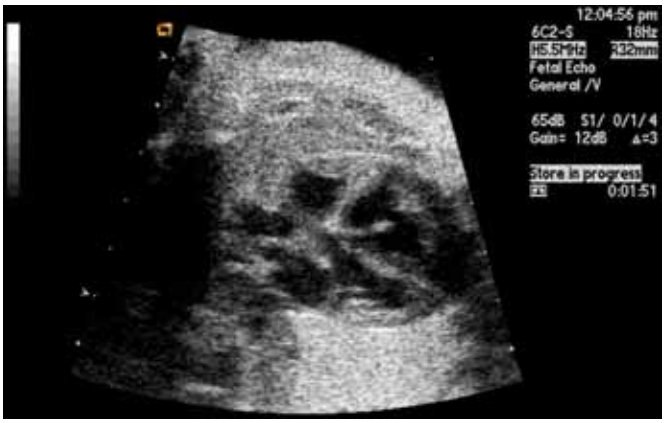

Figure 1. The 4 chambers of the heart with left ventricular outflow tract.

By eight weeks of gestation, the development of the heart is complete, and from then onwards the heart grows in size. The American Institute of Ultrasound in Medicine guidelines for the obstetric ultrasound includes imaging of the 4-chamber view and the left and right outflow tracts of the heart (see Figure 1). The screening obstetric ultrasound at around twenty weeks gestation can detect about 30% of the malformations;[1, 2] this significantly improves in the hands of trained maternal fetal medicine specialists.[3] The fetal echocardiogram, however, can provide detailed diagnosis of 80% of heart defects[4] and can further help in counseling, management and prognostication. The expected survival rate of neonates with prenatal diagnosis is 90%, and that of neonates without prenatal diagnosis is 60% (i.e., 50% improvement in survival with prenatal diagnosis).[5] Fetal echocardiography diagnoses of congenital heart disease guides in-utero and postnatal management[1] including urgent interventions such as balloon atrial septostomy. Furthermore, fetal echocardiography can help in monitoring cardiovascular status during fetal surgery for non-cardiac congenital anomalies.[6]

The prevalence of congenital heart malformations is higher than previously thought and is about 3-4 per 100 live births.[7] However, in-utero the prevalence is much higher with high lethality. The congenital heart lesions detected in-utero are myriad and include simple shunt lesions to complex cyanotic heart disease. On fetal echocardiogram, a de-

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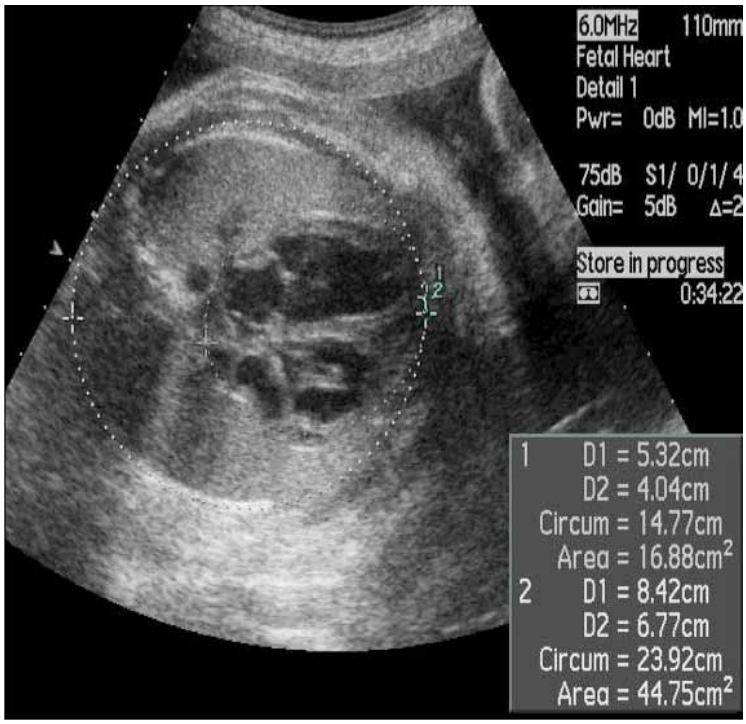

Figure 2. Determining the heart size in the fetus.

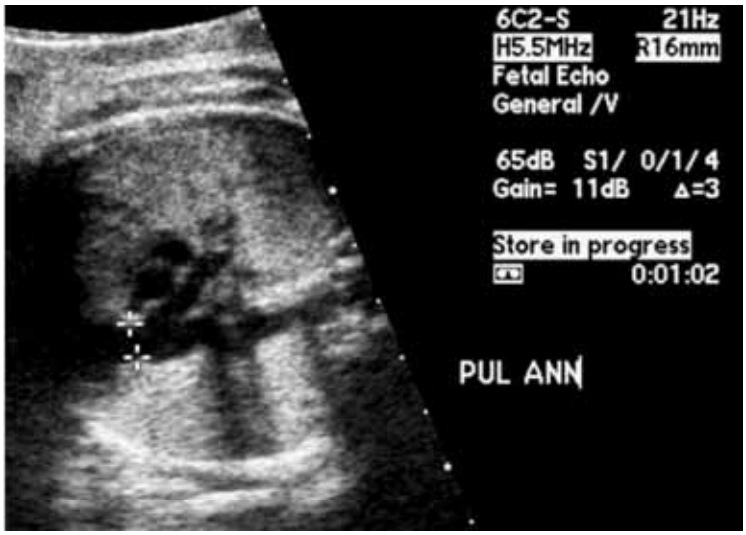

Figure 3. The branch pulmonary arteries and pulmonary valve annulus.

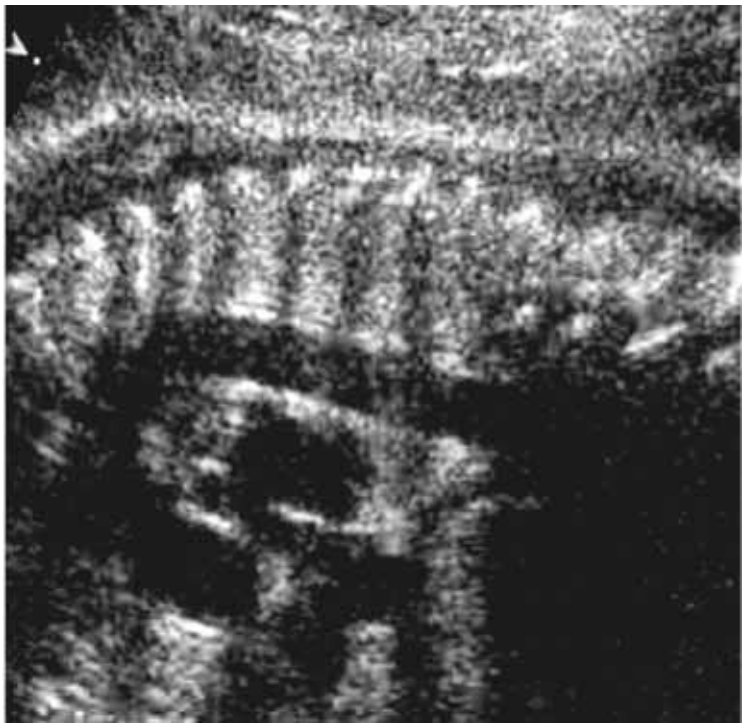

Figure 4. The aortic arch.

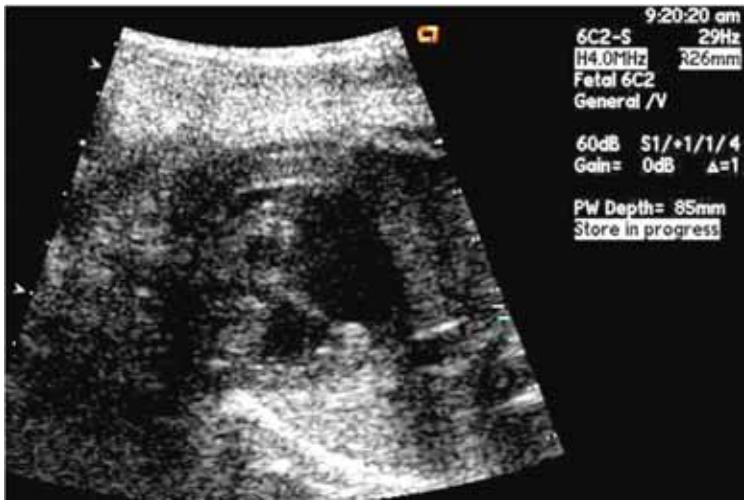

Figure 5. Complete atrioventricular canal defect with mild-left ventricular hypoplasia.

tailed imaging is performed using 2-dimensional (2-D), M-mode and Doppler ultrasound and recently using 3-D[8] and 4-D.[9] Several measurements are made to evaluate the heart size (Figure 2) and function[10]. Standard views are obtained to identify anatomy of the chambers (Figure 1), valves, walls, and vessels of the heart (Figures 3-4).[11] Serial studies throughout pregnancy are important to detect development and progression of valve obstruction, hypoplasia or cardiomegaly, rhythm disturbances and heart failure in some of the heart defects. Determining the z-scores of the chambers and vessels is beneficial in determining the degree of hypoplasia or enlargement. The flow across the patent foramen ovale, ductus venosus and ductus arteriosus requires special attention in the presence of congenital heart malformations. Besides congenital cardiac malformations, one can determine other cardiovascular disease, such as rhythm disturbances, heart failure, hypertrophy of the myocardium, premature ductal constriction, twin-to-twin transfusions, pericardial effusions, and cardiac tumors. The congenital cardiac malformations are several different types and can be divided into following categories for ease in diagnosis: shunt lesions (atrioventricular canal defect), valve lesions (tetralogy of Fallot, Ebsteins anomaly), malpositioning of great arteries (d-transposition of great arteries, double outlet right ventricle), univentricular hearts (hypoplastic left heart syndrome, tricuspid atresia), arch anomalies (interrupted aortic arch), venous anomalies (total anomalous pulmonary venous return), and cardiosplenic syndromes. The following are a few examples of heart defects routinely detected in-utero by fetal echocardiography.

Atrioventricular Canal Defects (AVC)

AVC defects can be diagnosed easily by a 4-chamber view (Figure 5) and have high risk of in-utero demise.[12] It is important to determine whether it is a balanced AVC or unbalanced AVC with hypoplasia of one of the ventricles. Color flow mapping can determine the degree of atrioventricular valve regurgitation, which is crucial as significant valve regurgitation can lead to non-immune hydrops fetalis. Heart blocks and fetal arrhythmias are associated with this lesion. In addition, these defects are associated with abnormal karyotype, in particular, Trisomy. [21]

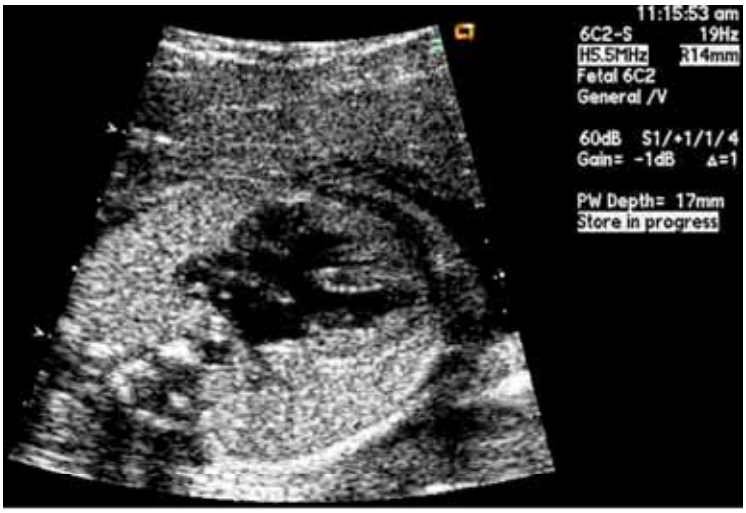

Figure 6. Tetralogy of Fallot with a subaortic ventricular septal defect. Note aorta overriding the interventricular septum.

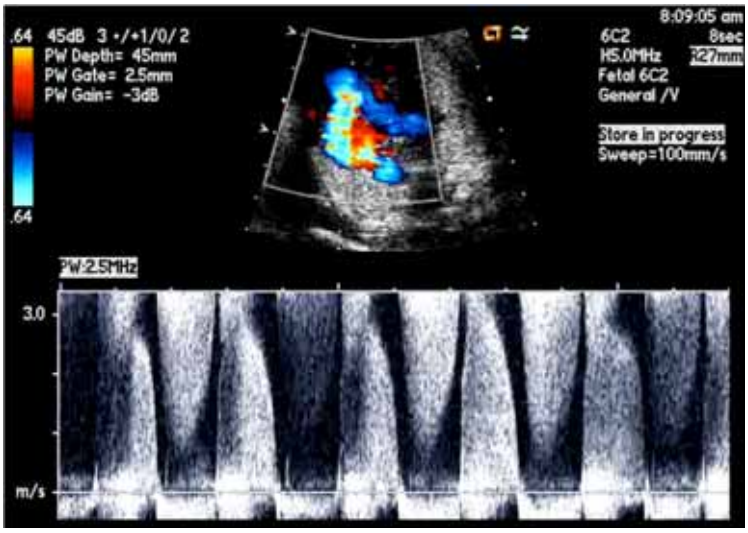

Figure 7. Tetralogy of Fallot with absent pulmonary valve. Note the pulmonary stenosis and pulmonary insufficiency by Doppler interrogation.

Tetralogy of Fallot (TOF)

TOF is the most common cyanotic congenital heart malformation and is associated with an overriding aorta in relation to the ventricular septum (Figure 6) and some degree of right ventricular outflow obstruction and pulmonary valve hypoplasia. An important finding is an abnormal ratio of the diameter of the aortic to the pulmonary valve.[13] In most cases the pulmonary valve velocity is normal or mildly increased and can be determined by spectral Doppler. Severe stenosis and atresia can develop over time.[13] Very rarely, pulmonary valve is rudimentary and hypoplastic resulting in significant pulmonary insufficiency and stenosis or Tetralogy with absent pulmonary valve syndrome (Figure 7). The branch pulmonary arteries can be hypoplastic in varying degrees in TOF to aneurysmal in absent pulmonary valve syndrome. These defects are seen in association with 22q11 deletion and the fetus should be evaluated for other non-cardiac malformations and thymic hypoplasia.[14]

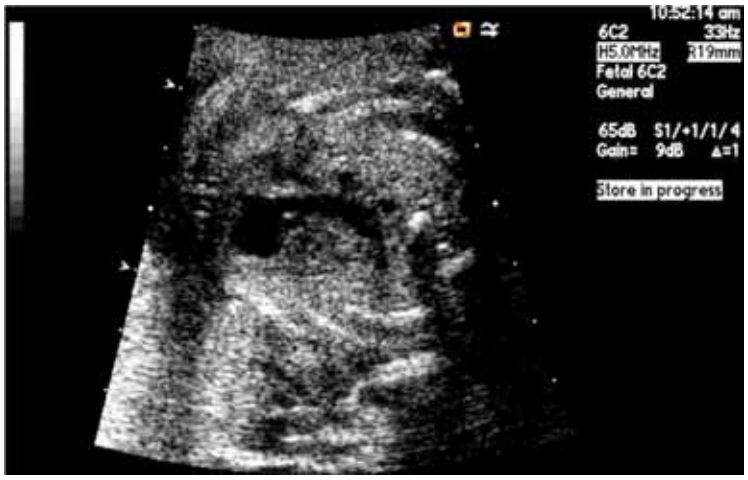

Figure 8. D-transposition of great arteries. Note aorta coming off from the right ventricle.

D-Transposition of Great Arteries

The diagnosis of D-Transposition of the Great Arteries is made by demonstrating ventriculoarterial discordance[15] in the presence of atrioventricular concordance (Figure 8). In the absence of a non-restrictive ventricular septal defect, defining the patency of the foramen ovale is of utmost importance in this lesion, as restriction at atrial level could result in prenatal[16] or postnatal demise. Early identification and emergent balloon atrial septostomy can thus be planned. The fetal diagnosis of d-TGA has improved the clinical status of child before surgery[17] and outcomes post-surgery.[17, 18] Double outlet right ventricle is a type of heart defect with a variety of cardiac configurations and can be associated with malpositioning of great arteries, including d-malpositioning.[19]

Hypoplastic Left Heart Syndrome

The finding of hypoplastic left-sided structures can help in making the diagnosis of this syndrome (Figure 9).[20] The lesions are usually progressive with a range of disease leading to mild hypoplasia and multiple levels of left heart obstructive disease (Shones anomaly) to true Hypoplastic Left Heart Syndrome with ductal dependent circulation. The prenatal prognosis for this lesion is usually poor.[21] Right ventricular function[22] and tricuspid regurgitation should be followed closely. Atrial level flow should be assessed by evaluating the foramen ovale and the pulmonary venous Doppler for restriction.[23, 24]

Hypoplastic Right Ventricle

Tricuspid and pulmonary valve obstruction can result in a variety of heart defects including pulmonary atresia with intact ventricular septum

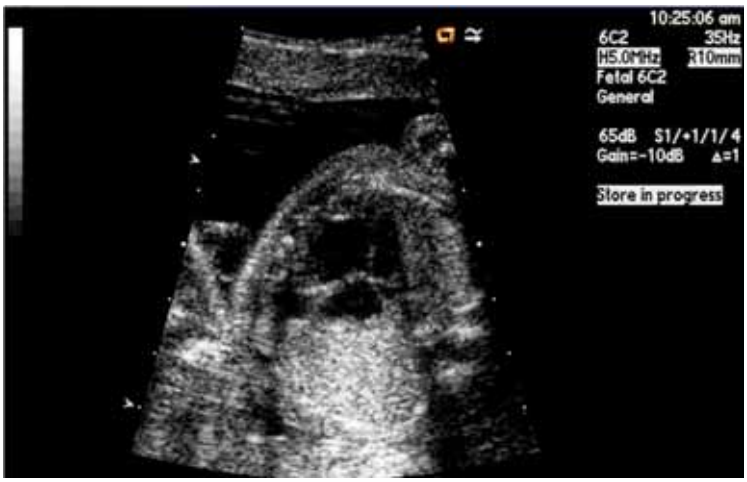

Figure 9. Hypoplastic Left Heart Syndrome. Note hypoplasia of the left atrium as well.

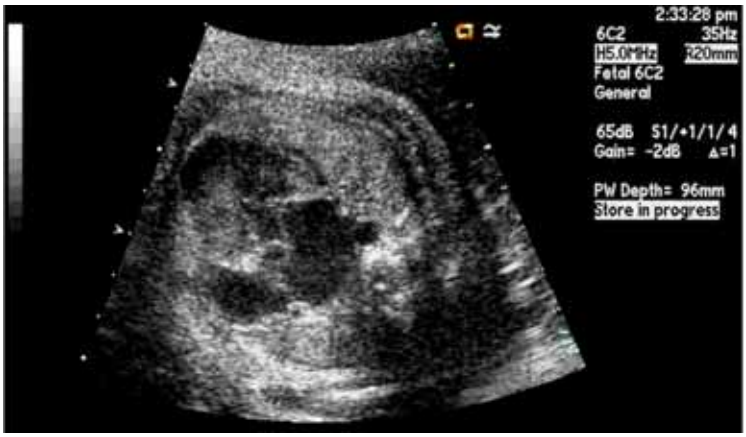

Figure 10. Tricuspid atresia with hypoplastic right ventricle.

and tricuspid atresia. Tricuspid atresia (Figure 10) has several different configurations with malpositioning of the great arteries. Again the atrial and ductal level shunts need to be closely monitored along with the growth of the structures including the branch pulmonary arteries. Ebstein's anomaly can also lead to right ventricular and pulmonary hypoplasia and has a high degree of lethality in-utero.[25]

Total Anomalous Pulmonary Venous Return

If the pulmonary venous return is obstructed, this defect is one of the remaining true pediatric cardiac emergencies if the pulmonary venous return is obstructed. It requires not only urgent diagnosis, but also an emergent surgery in a matter of hours after birth. Hence, in-utero diagnosis would be the key to management of this defect, but the defect is seldom recognized in fetal life by an obstetric ultrasound.[1] and not usually referred for a fetal echocardiogram. Furthermore, it can be a difficult diagnosis by fetal echocardiogram as well.[26] The growth of the left heart structures should be monitored carefully and evaluation for associated lesions such as cardiosplenic syndromes should be made.

Aortic Arch Anomalies

Arch anomalies can be a challenging diagnosis in utero and coarctation of the aorta can develop over days even after birth with closure of the ductus. Hypoplasia of the isthmus and transverse arch are considered the most definitive signs of coarctation of aorta.[27] The fetus should be evaluated for associated lesions such as a bicuspid aortic valve with obstruction. Right aortic arch and double aortic arch can also be determined by a careful scan.[28]

Cardiosplenic Syndromes

The visceroatrial situs is routinely ascertained by fetal echocardiograms and any discrepancy along with congenital heart malformations is suggestive of Heterotaxia.[29] A stomach-distance ratio has been proposed in the diagnosis of right atrial isomerism by one study[29]. There is a high incidence of dextrocardia and venous anomalies; however, some cardiosplenic syndromes can be very subtle and can be missed in-utero.

Management of Fetus with Congenital Heart Defect

A. Multidisciplinary approach: There is a high association rate of extracardiac and chromosomal anomalies with congenital heart malformations which requires a multidisciplinary team effort including consults from neonatologist, geneticist and pediatric surgery.[30] Congenital cardiac malformations are a multifactorial disease, and a detailed maternal history is often necessary to determine the causative factors, although often none are found. Controlling maternal blood glucose levels is very important in prevention of congenital heart malformations. Every effort should be made to avoid preterm delivery as immature lungs often can complicate the prognosis in complex congenital heart defects.

B. Medical Management: Maternal transplacental digitalization can help with fetal cardiac failure and hydrops;[31] however, the risk of intrauterine demise remains high once hydrops fetalis has occurred. Direct fetal therapy with drugs such as furosemide and digoxin has proven to be successful in certain cases.[32] Pharmacological management of rhythm disturbances and early delivery, where hemodynamically significant and persistent rhythm disturbances occur, is also crucial as certain rhythms such as complete heart block in presence of congenital heart disease can be lethal if not treated early.[33]

C. Intrauterine Cardiac Procedures: Fetoscopic surgery and transcatheter management such as in-utero treatment with balloon angioplasty and septostomy are being routinely considered by some centers in concert with maternal fetal medicine and the perinatal cardiologist. Fetal balloon valvuloplasty is being offered for critical aortic stenosis and pulmonary atresia with intact ventricular septum and balloon atrial septostomy for d-transposition of great arteries and Hypoplastic Left Heart Syndrome[34, 35] in order to alter postnatal outcomes. In-utero pericardiocentesis can be helpful in the presence of large effusions.[36, 37]

D. Postnatal Management: The delivery can be planned according to the congenital heart malformation, i.e., delivery at a tertiary care center for finding of d-transposition of great arteries. Very rarely is emergent delivery needed for heart defects unless there is evidence of fetal compromise or sustained hemodynamically significant arrhythmia. Neonatology, pediatric cardiology and pediatric cardiac surgery should be involved in postnatal period. Most infants with congenital heart malformations require routine care, however, a small number require emergent intervention after birth which can be predetermined by the perinatal cardiologist.[38]

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New Method for Neonatal ICUs Reduces Infection and Lung Distress in Premature Infants

A new method for improving quality of care can reduce hospital-acquired infections and chronic respiratory distress with oxygen dependency in premature infants in neonatal ICUs, according to a new study in *CMAJ (Canadian Medical Association Journal)* www.cmaj.ca/press/cmaj081727.pdf.

The researchers developed the Evidence-based Practice for Improving Quality Method, and applied it to 12 Canadian Neonatal Network hospitals over a 3-year period. Working in multidisciplinary groups, each hospital developed a list of hospital-specific practice changes and priorities to implement in the neonatal ICU.

The study included 6,519 infants divided into 3 groups: infection, pulmonary and a control group. After adopting practice-change strategies, the incidence of hospital-acquired (nosocomial) infection decreased 32% and 45% in the first two groups. Respiratory distress (bronchopulmonary dysplasia) in the pulmonary group decreased 15%, and there was a 12% decrease in death from this condition.

Based on pooled hospital data, the authors showed previously that 40% of infections in neonatal ICUs were associated with central lines and central catheters inserted into organs. They looked at individual hospital data which revealed different patterns of infection associated with catheter insertions.

"Our method enables hospitals to select practice changes pertinent to them for targeted intervention," writes principal investigator Dr. Shoo Lee of Mount Sinai Hospital and the University of Toronto, and coauthor. "This is potentially more efficient and cost-effective."

The study involved researchers from pediatric departments at University of Toronto (U of T); Memorial University; University of Calgary; University of Manitoba; University of Western Ontario; University of British Columbia (UBC); University of Saskatchewan; University of Ottawa; Dalhousie University; Department of Health Care and Epidemiology and Department of Obstetrics and Gynecology, UBC; the Department of Nursing, U of T.

"We found that interventions aimed at one outcome may affect other outcomes," wrote the authors. "We speculate that the decrease in the incidence of nosocomial infections in the pulmonary group was related to improved lung status and a reduced need for assisted respiration, invasive interventions, improved feeding and growth, and better overall health."

The method used in the study may be applicable in other areas of health care and may increase efficiency and reduce the costs.

In a related commentary www.cmaj.ca/press/cmaj091243.pdf, Dr. William McGuire of the Hull York Medical School in York, UK, and co-author, writes that variations in practice contribute to uneven outcomes for premature infants. "Benchmarking and audit studies in neonatal networks have revealed marked variation in practice even when good evidence exists for specific interventions." They conclude that this study "adds to the accumulating evidence that multifaceted interventions may change practice and outcomes in neonatal intensive care settings," although more analysis is needed to ensure the best use of resources to help infants and their families.

Seizures During Pregnancy Associated with Risk of Pre-Term and Small Babies

Women with epilepsy who have seizures during pregnancy appear more likely to give birth to pre-term, small or low-birth-weight babies than women without epilepsy, according to a report in the August issue of *Archives of Neurology*, one of the JAMA/Archives journals.

An estimated 0.2% to 0.7% of pregnant women have epilepsy, the most common major neurologic complication in pregnancy, according to background information in the article. "While approximately 40% of the 18 million women with epilepsy in the world are of childbearing age, managing maternal epilepsy and monitoring the health of the developing fetus remain some of the most perplexing and engaging issues in the fields of neurology and obstetrics," the authors write.

Yi-Hua Chen, PhD, of Tai Pei Medical University, Taiwan, and colleagues used data from the Taiwan National Health Insurance Research Data set and analyzed records from 1,016 women with epilepsy who gave birth between 2001 and 2003. Of these, 503 had seizures during pregnancy and 513 did not. A control group of 8,128 women, who were the same age and gave birth during the same years, but did not have epilepsy or any other chronic disease, were selected for comparison.

Compared to women without epilepsy, women who had seizures during pregnancy had a 1.36-fold greater risk of having a low-birth-weight baby (weighing less than 2,500 grams), a 1.63-fold increased risk of giving birth pre-term (before 37 weeks) and a 1.37-fold increased risk of having a baby who was small for gestational age (having a birth weight below the 10th percentile for age). In addition, when compared with women who had epilepsy but did not have seizures, the odds of women who had seizures during pregnancy having a baby who was small for gestational age were 1.34 times greater.

Some previous studies had reported a link between adverse pregnancy outcomes and mothers' epilepsy, but others found no association, the authors note. "Our study further illuminates these conflicting data to suggest that it is the seizures themselves that seem to contribute greatly to the increased risk of infants being delivered preterm, of low birth weight and small for gestational age. For women who remained seizure-free throughout pregnancy, null or mild risk was identified compared with unaffected women."

Several mechanisms might explain the association between seizures and adverse pregnancy outcomes. Trauma caused by a woman's seizures could rupture fetal membranes, increasing risk of infection and early delivery. Tension and acute injury may result from contractions in the uterus that occur during seizures. However, additional research is needed to understand how seizures interfere with fetal development.

"Neonates born pre-term, of low birth weight and small for gestational age may be predisposed to diseases during infancy and later life, highlighting the significance of proper intervention strategies for prevention," the authors write. These could include helping women control seizures for a period of time before pregnancy, assisting them in sleeping better, providing education about the risks of seizures while pregnant and teaching improved strategies for coping with stress.

Ask Permission to Use Newborn Data, Parents Say

Newswise — More than three-quarters of parents would be willing to permit the use of their children's newborn screening samples for research purposes if their permission were obtained beforehand, a University of Michigan survey shows.

But permission is crucial; more than half of the parents surveyed said they would be "very unwilling" to permit use of their child's newborn screening sample for future research unless they were allowed a chance to grant or deny permission.

This national survey was conducted as part of the University of Michigan C. S. Mott Children's Hospital National Poll on Children's Health to shed light on the emerging issue of how to square parents' concerns about privacy with medical researchers' desire to use the amazing array of health data available in newborn blood samples. These are routinely collected from infants in all 50 states at birth via a tiny needle-prick in the heel.

These state-required samples, taken to alert doctors to rare, serious inherited diseases that can be corrected if treated early, are stored by health agencies for years. Most parents are unaware the samples still exist, unless a sample proves useful for identification or to shed light on a child's health condition. Realizing the samples' collective value, researchers are beginning to use them to study the origins of childhood leukemia and toxin exposures in utero, and see potential for other beneficial research as well.

"Prior to this study, there was some debate about whether or not parents supported the idea of using the data for research, and whether they wanted their permission to be asked. We did the study to inform policy makers and others involved in the issue," says Beth A. Tarini, MD, MS, Assistant Professor of Pediatrics at the University of Michigan Medical School.

"Clearly, most parents want to be involved in this process," says Tarini, who is a researcher at the Child Health Evaluation and Research (CHEAR) Unit in the U-M Division of General Pediatrics. "Asking parents' permission to use their children's blood samples for future research looks like a critical issue."

The survey results appear online in the *Journal Public Health Genomics*. The survey was conducted using an Internet-based survey of a nationally representative sample of parents.

Researchers see the large existing database of newborn screening records as a rich resource for exploring a variety of diseases, but privacy advocates have raised concerns that have led to a lengthy legislative and court battle in Minnesota over whether the state's newborn screening program violates privacy by storing and making samples available to researchers without formal consent from parents. In Texas, a group sued the state earlier this year, arguing that storage of the samples without obtaining informed consent is unconstitutional.

Parents in most states are not asked to give informed consent for storing or allowing use of the samples for research when private health information has been removed from the samples.

Several states, most notably Michigan, are now evaluating more comprehensive policies for how the data are stored and used. The Michigan BioTrust for Health, established by the Michigan Department of Community Health, is seeking input from state residents on how best to store samples and under what conditions they should be studied.

Public policy that would allow use of newborn screening bloodspots for anonymized or de-identified research purposes without obtaining some form of permission from parents does not appear to be palatable to the public, says Tarini.

"If policy makers fail to engage in a discussion with parents and the public about using the screening results for research, that could create a public backlash and threaten the viability of a potentially valuable public health resource."

Additional U-M authors include: Dianne Singer, MPH, Sarah J. Clark, MPH, Amy Butchart, MPH, and senior author, Matthew M. Davis, M., MAPP. Aaron Goldenberg, PhD, of Case Western Reserve University is also an author.

This study was funded by the Clinical Science Scholars Program at the University of Michigan.

Leading Pathogen in Newborns Can Suppress Immune Cell Function

Group B Streptococcus (GBS), a bacterial pathogen that causes sepsis and meningitis in newborn infants, is able to shut down immune cell function in order to promote its own survival, according to researchers at the University of California, San Diego School of Medicine and the Skaggs School of Pharmacy and Pharmaceutical Sciences. Their study, published online July 13, 2009 in the *Journal of Experimental Medicine*, offers insight into GBS infection – information that may lead to new medical therapies for invasive infectious diseases that affect nearly 3,500 newborns in the United States each year.

The UC San Diego researchers describe how GBS fools the immune system into reducing production of antibiotic molecules. "We have discovered that the bacteria have evolved to use a trick we call 'molecular mimicry,'" said Victor Nizet, MD, UC San Diego Professor of Pediatrics and Pharmacy. "Like a wolf in sheep's clothing, GBS can enter our body without activating the immune cells that are normally programmed to kill foreign invaders."

The findings represent a collaborative effort between the laboratories of senior authors Nizet and Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular medicine. Varki is also co-Director of the UCSD Glycobiology Research and Training Center, where the investigators have been exploring the interaction of bacterial pathogens with the innate immune system. Their most recent focus has been on the special role of Siglecs (short for sialic acid binding Ig-like lectins), members of the immunoglobulin family of antibodies.

Siglecs sense a chemical structure known as sialic acid – a sugar molecule that is abundant on the surface of all human cells –

and send signals that control the gene expression and function of immune cells. Many specialized Siglecs receptors send negative signals, recognizing sialic acids as "self." These signals help keep the immune cells turned off under baseline conditions, avoiding unnecessary inflammation in the absence of infection or injury. Earlier this year, in a manuscript published in the journal *Blood*, the same UC San Diego team demonstrated that GBS decorates its own surface with sialic acid, closely resembling human molecules, and is thus able to bind Siglecs on immune cells, shutting down the cells' normal functions.

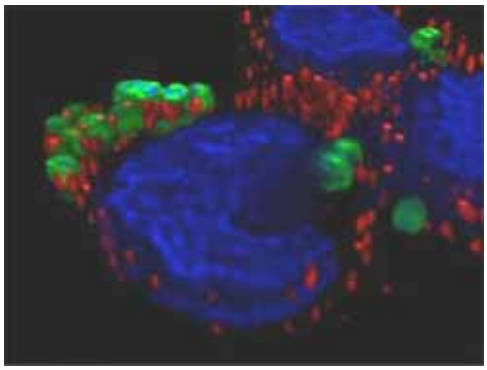
In the new study, the researchers discovered that GBS can also bind a human Siglecs receptor through a particular protein expressed on the bacterial surface. This is the first time a protein has been reported to functionally interact with Siglecs, and presents the possibility that additional pathogenic microbes may have evolved similar ways to manipulate the human immune system.

According to the study's lead author, Aaron Carlin, MD, PhD, when GBS proteins bind to Siglecs, it profoundly affects immune-cell function by decreasing its ability to engulf the bacteria, a process known as phagocytosis.

"The immune cells reduce their production of antibiotic molecules, allowing the GBS bacteria to survive the encounter and proliferate," said Carlin, who recently completed his doctoral studies in UC San Diego's Medical Scientist Training Program.

Knowledge of the mechanisms by which crafty pathogens engage Siglec receptors to fool the immune system may reveal new targets for medical therapy. "Blocking engagement of the Siglec could help boost the immune system and aid in clearing GBS infection in the critically ill newborn," said Nizet. "Alternatively, perhaps the bacterial molecule could be exploited as a novel treatment for human diseases involving abnormal inflammation, for example, rheumatoid arthritis."

Siglecs are among the most rapidly evolving parts of the human genome. This suggests that strong natural selection pressures are present to modify their expression, according to Varki, with pathogenic microbes likely playing a critical role.



Group B Streptococcus (green) binds Siglec-5 (red) on the surface of a human macrophages, shutting down their activity. DNA strain (blue) highlights nuclei of the human cells and bacteria.
Credit: Aaron Carlin and the UCSD Light Microscopy Facility.

"There are important variations in Siglec expression and function between humans and other species, among human populations, and across the age spectrum. Evidence is accumulating that Siglecs may profoundly affect susceptibility or resistance to several important infectious diseases," said Varki.

According to the UC San Diego researchers, the new study likely has broad implications for understanding the propensity of certain bacterial pathogens to produce human disease. It also explains why some individuals or groups may be more predisposed to suffer more severe outcomes than others.

Approximately 20 to 25% of women of childbearing age are asymptomatic carriers of GBS on their vaginal mucosal surface. Newborns can become infected with GBS that invade through the placenta to initiate infection in the womb, or during delivery by exposure to contaminated vaginal fluids. Screening of pregnant women for GBS and antibiotic prophylaxis during labor is used to reduce the risk of newborn transmission, yet it estimated that approximately 3,500 newborns still develop invasive GBS infections annually in the United States. In addition to neonatal disease, GBS is increasingly associated with serious infections in adult populations such as pregnant women, diabetics, and the elderly.

This study was financed by grants from the National Institutes of Health. Co-authors contributing to the study were Yung-Chi Chang, PhD and Charles King, PhD, of the UCSD Department of Pediatrics; Nancy Hurtado-Ziola, PhD of the UCSD Department of Cellular and Molecular Medicine, and Thomas Areschoug, PhD, and Gunnar Lindahl, PhD, of Lund University in Sweden.

Newborn ICUs Seeing More Antibiotic-Resistant Staph Infections

Newswise — The rate of methicillin-resistant Staphylococcus aureus (MRSA) infections in U.S. neonatal intensive care units (NICUs) has more than tripled in recent years, reports a study in the July issue of The *Pediatric Infectious Disease Journal*. The journal is published by Lippincott Williams & Wilkins, a part of Wolters Kluwer Health, a leading provider of information and business intelligence for students, professionals, and institutions in medicine, nursing, allied health, pharmacy and the pharmaceutical industry.

The study highlights the need for redoubled efforts to follow routine infection control steps to prevent MRSA transmission to infants in NICUs, according to Dr. Fernanda C. Lessa and colleagues of The Centers for Disease Control and Prevention.

Using a national database on hospital-acquired infections, the researchers analyzed data voluntarily reported by NICUs from 1995 through 2004. The analysis focused on "late-onset" infections, developing more than three days after birth. The study included information on nearly 5.9 million patient-days in 149 NICUs.

Of approximately 4,400 Staph infections tested for antibiotic resistance, 23% were MRSA. From 1995 to 2004, the rate of late-onset MRSA infections increased by 308%: from less than one to about three infections for every 10,000 hospital days. The sharpest increase in MRSA infections occurred after 2002.

The smallest infants—those with very low birth weights of 1,000 grams (about 35 ounces)—had the sharpest increase in

MRSA infections. However, the infection rate rose in all birth weight groups.

The types of MRSA infections did not change during the study period. About 30% were bloodstream infections; other common MRSA infections included pneumonia and eye infections (conjunctivitis).

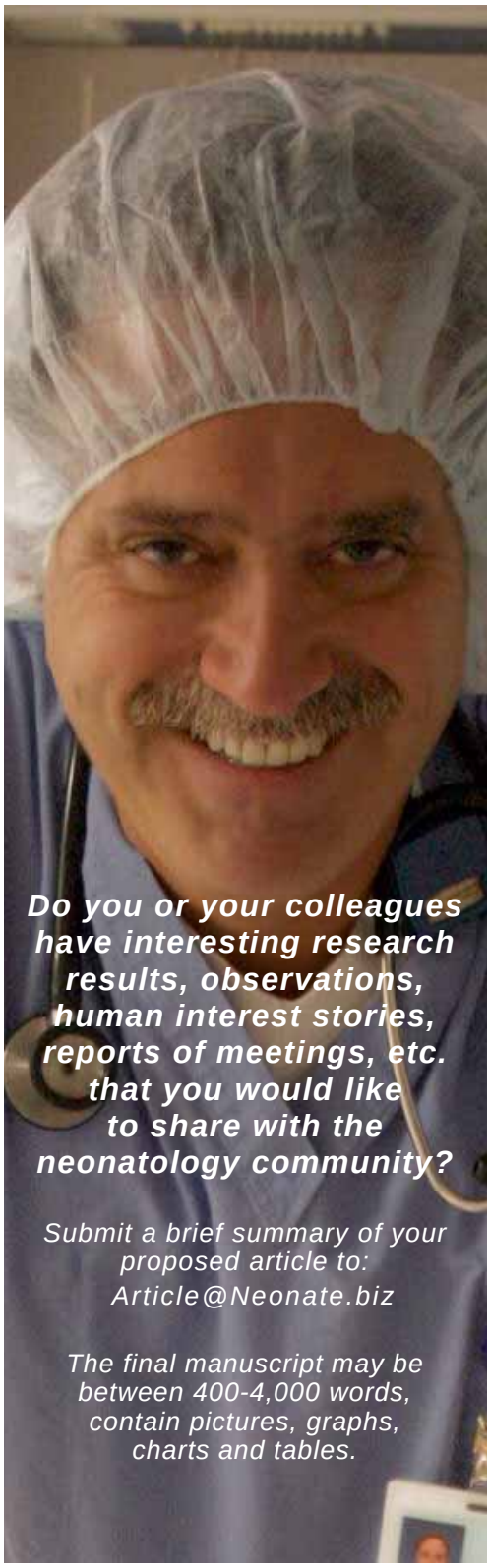
The rising rate of MRSA is a worldwide public health problem, with Staph bacteria developing resistance to commonly used antibiotics. In recent years, MRSA has moved out of hospitals and health care settings to spread in the community. In the new study, however, the MRSA strains found in NICUs were more similar to the strains responsible for hospital-acquired infections, rather than those which spread in the community.

In newborns, infections occurring during the first three days of life are generally transmitted during labor and delivery. In contrast, the late-onset infections like the ones evaluated in the new study are more likely transmitted by parents, health care personnel, and other contacts.

The study—the largest to date of MRSA in NICUs—emphasizes the need to reinforce infection control measures shown to be effective in limiting the spread of MRSA (hand washing, etc.) among infants in the NICU. The researchers also call for further studies to explore potential sources and routes of transmission of MRSA infection to critically ill newborns.

The characteristics of MRSA infections among infants in the NICU "may be more complex than in other types of populations," Dr. Lessa and colleagues write. "Further strategies to prevent MRSA transmission among NICU patients may need to be developed."

The *Pediatric Infectious Disease Journal*® (www.pidj.com) is a peer-reviewed, multidisciplinary journal directed to physicians and other health care professionals who manage infectious diseases of childhood. The journal delivers the latest insights on all aspects of infectious disease in children, from state-of-art diagnostic techniques to the most effective drug therapies and other essential treatment protocols. The *Pediatric Infectious Disease Journal* is the official journal of the Pediatric Infectious Diseases Society (www.pids.org) and the European Society for Paediatric Infectious Diseases (www.espid.org).



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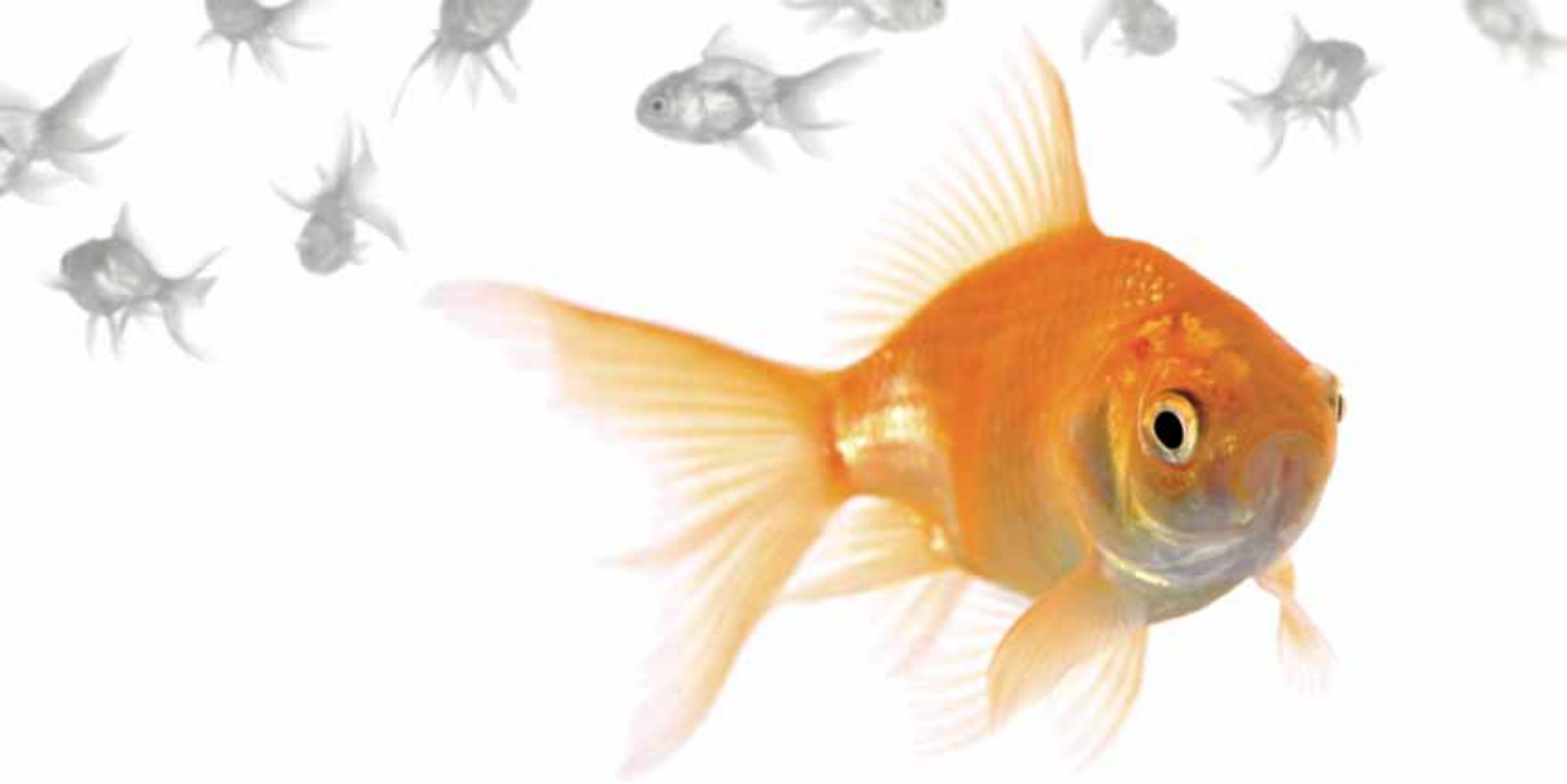

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