NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

Volume 5 / Issue 9
September 2010

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NEONATOLOGY TODAY

Editorial and Subscription Offices
16 Cove Rd, Ste. 200
Westerly, RI 02891 USA
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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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Care of the Preterm Neonate with a Congenital Cardiovascular Malformation

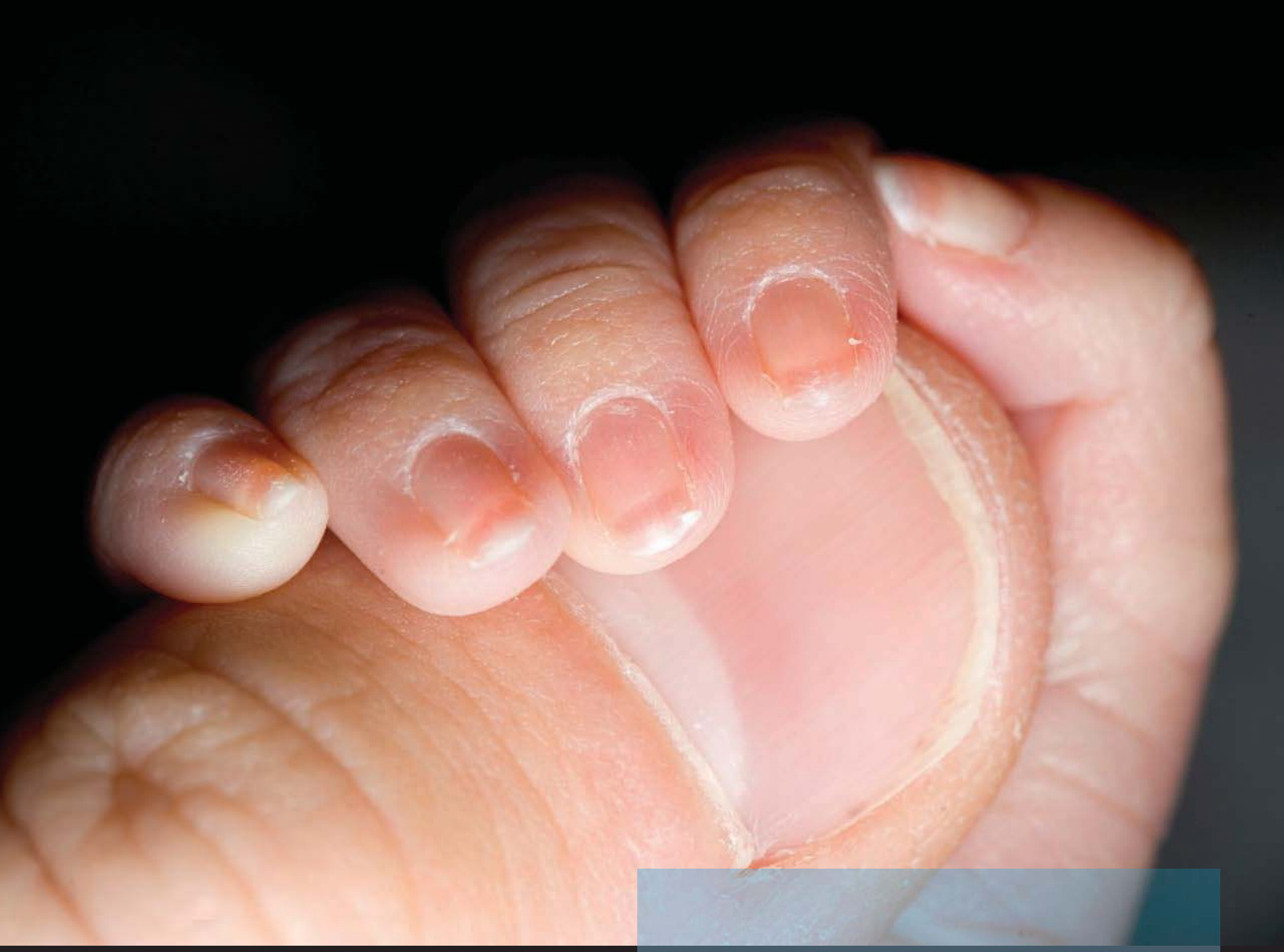
By Jillian Lewis, MBBS, DM Paediatrics and Patrick J. McNamara, MD, MSc, MRCPCH

Congenital heart defects (CHD) represent an important cause of morbidity/mortality in the neonatal population. The incidence has been quoted as up to 8 per 1000 live births in some accounts[1-4]. In one review, as many as 35% of infants with CHD were reported to have low birth weight defined as less than 2500 grams[5]. The Baltimore-Washington Infant Study revealed an incidence of low birth weight in infants with CHD of 6 – 23%[3]. Low birth weight may be a consequence of either prematurity, intrauterine growth restriction or secondary to a genetic malformation or syndromic complex. The preterm population with CHD presents a unique challenge in terms of diagnosis and pre, peri and post-operative care. These infants tend to be at higher risk of morbidity/mortality and this consideration must therefore inform the medical and surgical approach. The purpose of this review is to provide an overview for physicians caring for this high-risk and vulnerable population rather than to detail specifics of all congenital cardiovascular malformations.

"Congenital heart defects (CHD) represent an important cause of morbidity/mortality in the neonatal population. The incidence has been quoted as up to 8 per 1000 live births in some accounts[1-4]. In one review, as many as 35% of infants with CHD were reported to have low birth weight (birth weight as less than 2500g)[5]."

1.0 Clinical Presentation

Early identification of a congenital cardiovascular malformation (CCVM), and in particular a duct-dependent lesion, affords the opportunity for focused cardiac interventions which may ultimately improve patient outcomes. The yield from clinical assessment in preterm infants is low, but the possibility of a CCVM should be entertained in all neonates who present with cyanosis, systemic hypoperfusion, pulmonary congestion or heart failure. Occasionally a CCVM is suspected after abnormal findings on a chest x-ray (CXR) or electrocardiogram (ECG). The clinical course is often altered by co-morbid pathophysiologic processes normally associated with prematurity, e.g. Respiratory Distress Syndrome. The gold standard for diagnosis is two-dimensional echocardiography. The approach to management of a preterm infant with a CCVM is dependent on two important physiological considerations: first, whether the lesion is duct dependent, and second, whether there is single-ventricle type physiology. In the latter situation the ductus arteriosus (DA) controls blood supply to both the pulmonary and systemic



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circulations. Hypoplastic Left Heart Syndrome (HLHS) and pulmonary atresia with a hypoplastic right ventricle are two examples of duct-dependent lesions with single ventricle physiology (SVP). The term single ventricle type physiology refers to the anatomic anomalies that result in a single ventricle supporting both pulmonary and systemic circulations. In these lesions, there is complete mixing of both systemic and pulmonary venous return; and as a result, the pulmonary arterial saturation equals systemic arterial saturation.

1.1 Echocardiography and Preterm CCVM

The role of 2D echocardiography in the care of preterm neonates is two-fold: first, to establish the anatomical diagnosis and second to monitor patency of the DA, myocardial performance and pulmonary arterial pressures. Serial echocardiography is often necessary prior to surgical intervention to monitor cardiovascular health and the effects of the CCVM on pulmonary arterial pressures.

2.0 Management of the Preterm Neonate with a CCVM

The care of the preterm neonate with a CCVM should take into account the morbidities peculiar to this population, as well as those related to the particular CCVM. The approach in the initial postnatal period is often predominantly medical. Surgical interventions or other invasive procedures are usually delayed until the neonate reaches a maturity and weight at which the risks of an expectant approach outweigh the risks of the specific intervention. Management of the premature infant with a CCVM requires expertise to ensure both focused cardiovascular and neonatal care, neither of which is mutually exclusive. It is only by ensuring excellence in each, that outcomes will be improved.

2.1 Focused Cardiovascular Care

Medical Management

2.1.1 Prostaglandin Treatment

Neonates with a duct-dependent CCVM require continuous intravenous prostaglandin E1 therapy to sustain patency of the DA. In the early stabilization phase the dose required may range from 0.01 to 0.2µg/kg/min. For neonates with an antenatal diagnosis, the lowest dose should be prescribed immediately after birth since this is usually sufficient to maintain ductal patency; however, in those presenting with acute hypoxaemia or circulatory collapse, high doses are often required. Once clinical and haemodynamic stability has been achieved, the intravenous PGE_1 dose is usually weaned to the lowest effective dose in order to avoid excessive pulmonary vasodilation. This is particularly relevant for neonates with SVP where a profound or sustained fall in pulmonary vascular resistance (PVR) leads to excessive pulmonary blood flow (PBF) at the expense of systemic perfusion. In many cases prostaglandin therapy is required for several weeks or months whilst awaiting surgical intervention. This increases the likelihood of complications related to prostaglandin administration including: apnea, hyperthermia, hypotension, gastric outlet obstruction secondary to gastric foveolar hyperplasia and cortical hyperostosis[6].

2.1.2 Cardiovascular Monitoring

This is particularly relevant in premature infants with single ventricle type physiology because acute physiologic changes in arterial oxygen or carbon dioxide content or common neonatal treatments, e.g. increased ambient oxygen, surfactant replacement therapy or inhaled nitric oxide may affect pulmonary and/or systemic vascular resistance (Table 1). The consequences may include altered ventricular afterload, transductal, pulmonary or systemic blood flow. As pulmonary vascular resistance falls in the immediate postnatal period, increased pulmonary blood flow may occur at the expense of systemic perfusion thereby leading to end-organ compromise and suboptimal tissue oxygenation. Arterial $PaCO_2$, pH, and FiO_2, should be carefully monitored and controlled, therefore, to prevent excessive pulmonary vasodilatation and consequential over circulation.

Table 1. Impact of Common Neonatal Treatments on Pulmonary (PVR) and Systemic (SVR) Vascular Resistance

Intervention	Effect on PVR	Effect on SVR
Increased FiO_2	Reduced	Increased
Reduced CO_2	Reduced	Increased
Surfactant Therapy	Reduced	Limited
Inhaled Nitric Oxhide	Reduced	Limited

Haemodynamic stability and the adequacy of either pulmonary or systemic blood flow may be evaluated both clinically and biochemically. Signs of circulatory compromise include tachycardia, hypotension and decreased urinary output. Biochemical markers of the efficacy of oxygen delivery include: plasma lactate, arterial pH, base deficit and mixed venous oxygen saturation. Lactic acidosis, metabolic acidosis or falling mixed venous oxygen saturation are suggestive of suboptimal systemic perfusion and tissue oxygenation. Arterial access is an essential prerequisite in the care of these patients, particularly in the first 1-2 weeks of life, when major changes in transductal vascular resistance are most likely. The ratio of pulmonary to systemic blood flow (Qp:Qs) is another useful tool to evaluate the adequacy of systemic oxygen delivery. The Qp:Qs ratio is calculated as follows: SaO_2-$SmVO_2$/$SpVO_2$-$SpAO_2$ (where SaO_2 = aortic oxygen saturation, $SmVO_2$ = mixed venous oxygen saturation, $SpVO_2$ = pulmonary venous oxygen saturation and $SpAO_2$ = pulmonary arterial oxygen saturation). In patients with single ventricle physiology, $SpAO_2$ can be assumed to be equal to SaO_2 since blood supply to both great vessels is from the same ventricle. $SpVO_2$ can be assumed to be 100% in the absence of lung parenchymal disease. $SmVO_2$ is obtained from a central venous catheter placed in the SVC. A normal SaO_2/$SmVO_2$ difference is 25 to 30%. Using these assumptions, the optimal Qp:Qs ratio is thought to be 0.5 – 1. In this scenario, both circulations are balanced and the aortic arterial saturation tends to range from 75 to 85%. An aortic arterial saturation of 95% is therefore indicative of pulmonary blood flow 5 times that of systemic.

2.1.3 Cardiotropic Support

There is a paucity of data describing physiologic norms for blood pressure and indices of systemic perfusion in the premature population. The goal of treatment is to ensure that blood pressure is maintained within a range that sustains adequate systemic perfusion. As indicated earlier, monitoring heart rate, urinary output, arterial pH and

lactate are essential components of the stabilization and ongoing care of neonates with a CCVM. Treatment options should be selected based on the underlying pathophysiology and the likelihood of the intervention to correct the abnormal physiologic state. Therapeutic options include volume expansion with crystalloids, the use of inodilators like dobutamine and milrinone, and in special circumstances, pressor agents e.g. dopamine, epinephrine and vasopressin. Volume expansion is useful in neonates with abnormal right ventricular performance to support pulmonary blood flow. Milrinone has been shown to reduce both mortality and Low Cardiac Output Syndrome in post-operative cardiac patients[7]. In many centers milrinone is the first line cardiotropic agent[8]. High-dose dopamine and epinephrine are rarely recommended because of their adverse effects on both myocardial performance and vascular resistance.

Surgical Management

2.1.4 Catheterization Procedures

Cardiac catheterization is occasionally performed in VLBW infants. There are some reports in the literature of successful balloon dilation of the pulmonary valve in neonates at a weight of less than 750 grams[9]. Balloon atrial septostomy can be performed in neonates with Transposition of the Great Arteries (TGA) or other conditions dependent on a transatrial shunt, e.g. HLHS. Surgical intervention in premature neonates with single ventricle physiology is challenging. To avoid the risks of cardiopulmonary bypass and the need for chronic prostaglandin administration in this highly vulnerable population a new technique called the "Hybrid procedure" has been developed to replace the first stage of the Norwood procedure[10]. The procedure is performed in the cardiac catheterization laboratory and involves the placement of a stent in the DA to ensure both pulmonary and systemic blood flow. Pulmonary arterial bands are placed to reduce excessive PBF. This procedure has been performed on a number of premature neonates, and early results are encouraging; however, long-term data are not yet available. The age and weight thresholds for performing these procedures are likely to vary significantly between neonatal cardiac centers.

2.1.5 Surgical Procedures

Determining the optimal time for surgical intervention in the preterm population has proven to be a challenge because of technical issues related to both low birth weight and the co-morbidities inherent within this population. Typically an expectant approach has been employed with a view to intervention at a higher weight, although this is oftentimes a moving target with little consistency between centers and cardiovascular surgeons. Delaying surgery until a predetermined weight is achieved is not without risks which include:

i. prolonged exposure to abnormal physiology and hypoxia,
ii. failure to thrive,
iii. prolonged need for central venous access and total parenteral nutrition administration and the attendant risks of infection, thrombosis and cholestasis,
iv. prolonged volume overload and its possible contribution to the development of pulmonary hypertension and the progression of chronic lung disease.

2.1.5.1 Corrective Surgery

Total anatomic correction is possible in neonates with TGA and anomalous pulmonary venous drainage or coarctation of the aorta. Several studies have demonstrated a more favourable outcome in patients greater than 1500 grams at the time of surgical intervention[11, 12]. For this reason a weight ≥ 1800 grams has been widely accepted as the target weight for intervention; particularly in light of the challenges of cardiopulmonary bypass, the potential need for postoperative Extracorporeal Life Support (ECLS) and the risks to the developing organs, especially the brain. In most centers the average weight at surgery is between 2000 and 2500 gram, although with modified techniques of cardiopulmonary bypass surgical intervention is attempted at less than 1800 gram.

2.1.5.2 Palliative Surgery

Palliative surgical interventions refer to procedures where total anatomic correction is not possible and blood flow is controlled by natural or artificial shunts and a single ventricle. Neonates with HLHS, pulmonary atresia or tricuspid atresia undergo a three stage surgical repair called the "Norwood or single ventricle" track. These patients will have lower oxygen saturation than normal, limited exercise capacity and significant periods of hospitalization during this time period. The final step in this staged approach results in the complete separation of pulmonary and systemic circulations by the fashioning of a Fontan circulation whereby inferior and superior venous blood flow is directed to the pulmonary artery while the single ventricle supplies the systemic circulation. Mortality rates associated with these procedures have improved over the past 10 years; however, significant acute and long-term morbidity remains a reality.

2.2 Focused Preterm Care

Preterm neonates with congenital heart disease should ideally be cared for in tertiary neonatal centers with a critical mass of preterm neonates with CCVM and comprehensive cardiology services. There are no published data or guidelines on best practice for the management of preterm neonates with congenital cardiovascular malformations. Most of the current practices extrapolate from evidence for the care of term neonates with CCVMs.

2.2.1 Respiratory Care

2.2.1.1 Assisted Mechanical Ventilation

Routine intubation of all neonates when PGE_1 is administered is not necessary. The decision to intubate should be made based on the usual clinical indicators. Intubation is recommended in the presence of respiratory failure, clinical signs of cardiogenic shock, the need for cardiotropic support, profound metabolic or lactic acidosis, gestational age less than 28 weeks, and an associated airway disorder. In general, patients should be ventilated to maintain a $PaCO_2$ of 40-50 mmHg and an arterial pH of 7.25-7.35 to avoid excessive pulmonary blood flow in those patients with single ventricle type physiology. The provision of optimal positive end-expiratory pressure may have the additional benefit of limiting left to right shunting across a patent ductus arteriosus and may therefore be useful in controlling transductal flow. One of the most challenging aspects of management is supporting those neonates with evolving chronic lung disease and pulmonary hypertension secondary to pulmonary vascular remodeling. Episodic apnea and/or hypoxaemia occur frequently in these patients necessitating therapeutic intervention. Oxygen therapy is normally administered to preterm neonates when the oxygen saturation falls below 88%, although the optimal saturation for preterm neonates remains controversial. An oxygen saturation range of 75-85% is usually targeted in neonates with duct-dependent CCVMs, particularly if single ventricle type physiology exists. This range has been chosen to minimize an excessive decline in pulmonary vascular resistance in an attempt to maintain satisfactory systemic perfusion. However, the risk of tissue hypoxia and adverse neurodevelopmental outcome must be taken into consideration and judicious oxygen administration may be required. There are limited studies addressing the relationship of CCVM or oxygen saturations to abnormal respiratory outcomes in premature infants and the mechanism of lung injury.

2.2.1.2 Other Respiratory Interventions

The administration of prophylactic surfactant to preterm neonates with an antenatal diagnosis of a duct-dependent systemic circulation may result in an excessive fall in PVR leading to excessive PBF at the expense of systemic perfusion. This may be particularly hazardous for

neonates with HLHS in whom the systemic circulation tends to be extremely tenuous. The radiological confirmation of a diagnosis of Respiratory Distress Syndrome is recommended for these neonates before surfactant administration, unless there are signs of significant respiratory distress in keeping with the clinical diagnosis.

2.2.2 Neurological Care

The risk of an adverse neurological event is significantly increased in neonates with a CCVM requiring cardiopulmonary bypass or postoperative ECLS support due to the fragility of the developing brain, particularly in premature infants. Intracranial hemorrhage and non-hemorrhagic infarction are the most common adverse events in the immediate postoperative period. There is, however, increasing evidence that neurological damage may occur preoperatively and perhaps in utero. Neonates with congenital heart disease have an increased incidence of structural central nervous system and neurobehavioral abnormalities. The incidence of microcephaly was 24-36% in one series[14]. Infants with hypoplastic heart disease have also been reported to have an increased incidence of holoprosencephaly, agenesis of the corpus callosum and abnormalities of the operculum in other series[15]. Magnetic resonance image evaluation preoperatively in newborns with congenital heart defects has revealed periventricular leukomalacia in 16% to 28%[13, 16]. It has been reported that more than 50% of infants with congenital heart disease have poor state regulation and abnormalities of tone preoperatively[14]. There is a strong correlation between these findings and preoperative arterial PaO_2 and blood pressure[13]. Preoperative neurological abnormalities portend a poor neurodevelopmental outcome[14]. In addition, the presence of perioperative hyperthermia or seizures, co-existing genetic abnormalities or associated organ defects also increase the risk of neurological morbidity. The preterm neonate is even more vulnerable to the effects of chronic hypoxaemia and intermittent periods of systemic hypoperfusion on the developing brain because of poor cerebral autoregulation. There is limited published data on the neurodevelopmental outcome of premature infants with congenital cardiovascular malformations.

2.2.3 Gastrointestinal Care

The risk of necrotizing enterocolitis is significantly increased in neonates with a CCVM[17]. This is most likely to be related to intestinal hypoperfusion and/or chronic hypoxaemia[17, 18]. Extreme immaturity, higher doses of prostaglandin treatment and episodic low cardiac output syndrome are also strong predictive factors. These newborns required a focused approach to nutrition that balances the risks of prematurity within the context of a fragile circulation. Wherever possible, guidelines should be developed that focus on the unique needs of preterm neonates with cardiac disease. Whilst growth is paramount to achieve target surgical weights these newborns should be fed cautiously. Expressed breast milk is recommended and feeds should be increased slower compared to their gestational-age counterparts, although there is little supporting data for the latter approach in currently published literature.

2.2.4 Miscellaneous

The risk of anemia is likely to be increased in this population due to more frequent blood sampling. Although the threshold for transfusion in preterm neonates remains unclear, it is probably advisable to implement a lower than normal threshold for transfusion. This is particularly relevant for neonates with single ventricle type physiology who are at greater risk of tissue hypoxia. Plasma hemoglobin should probably be maintained > 100 g/dl, but during periods of instability the level should be maintained > 120 g/dl.

The risk of infection is higher in preterm neonates with a CCVM; for this reason, vigilance is required, and the possibility of infection should be entertained in the presence of haemodynamic instability.

Due to the challenges of clinical assessment of preterm neonates for dysmorphism or genetic abnormalities, routine karyotype analysis as well as screening for 22q microdeletion is recommended.

3.0 Outcome

Mortality rates for preterm infants with CCVM of 10 - 43% have been reported by various studies[6]. Few of these studies however take into account the heterogeneity of the cardiovascular malformations. With advances in antenatal diagnosis and postnatal management, there has been a trend towards improved survival in patients with CCVM. As a result the focus has shifted towards evaluating the long-term neurodevelopmental outcome of these infants. Annette Majnemer et al examined the neurodevelopmental outcome of 131 term neonates with CHD who had had surgical intervention at Montreal's Children's Hospital between 1994 and 1998. Evaluation of the patients at 12 –18 months revealed: global delays in 25%; delays in speech and hearing in 34%; locomotor skills in 26%, hand-eye coordination 24%, personal/social 17% and an abnormal neurological exam in 41%[19]. Dittrich et al investigated the neurodevelopmental outcome at one year of age of 90 infants who had had surgical repair of various congenital heart defects. Mean developmental quotient (DQ) was statistically significantly lower in test subjects than controls (who were infants with minor or no congenital heart defect). Thirty-two percent of the index patients had neurological abnormalities compared with 5% of the controls. In each of these scenarios, outcome was worse for those patients offered palliative surgery compared with patients who underwent corrective surgery[20]. Hedwig et al conducted a developmental assessment on 77 children, between the ages of 3 and 9, who had undergone the arterial switch procedure as neonates. They reported reduced intelligence scores in 9.1%, fine motor abnormalities in 22.1% and gross motor dysfunction in 23.4% of the study population[21]. Rogers et al, in a small study, evaluated the neurodevelopmental status of children at the mean age of 38 months who had had surgical repair for hypoplastic left heart disease. Eighteen percent of those studied had cognitive abnormalities; 64% with mental retardation. Forty-five percent of subjects had gross motor delays, 18% were noted to have cerebral palsy. Eighty-nine percent of those with mental retardation or cognitive delay had acquired microcephaly[22]. There is a paucity of data on long-term outcome in the premature population, however. Additionally, outcome data for specific lesions is lacking. This makes accurate counseling of the parents of affected newborns a challenge.

4.0 Summary

With an improvement in the survival rates for neonates with CCVM over the past 10-15 years, the high incidence of cognitive and neurodevelopmental impairment has become a cause for concern. The care of the preterm neonate with a CCVM poses a significant challenge for neonatal intensivists attempting to stabilize a vulnerable circulation within the context of organ immaturity. A multidisciplinary approach with collaboration between neonatologists and cardiac intensivists with careful attention to the issues peculiar to this population is of paramount importance. Prospective research evaluating the physiological and haemodynamic impact of acute therapeutic and surgical interventions on morbidity, mortality and neurodevelopmental outcome is urgently required to further guide and shape the optimal approach to management.

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From the Desks of the Founder and the Publisher:
Neonatology Today is Going Green

By Anthony Carlson, Founder and
Richard Koulbanis, Publisher & Editor-in-Chief

In May of 2006, we published the first edition of *Neonatology Today*, the sister publication of *Congenital Cardiology Today*. Since then, we have produced:

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Neonatal Diarrhea

Diarrhea represents a major condition responsible for pediatric mortality worldwide. The onset of neonatal diarrhea may rapidly lead to life threatening dehydration and malnutrition. Clinical and epidemiologic studies defining severity and etiology are needed in order to improve diagnostic and therapeutic approaches for the management of neonatal diarrhea.

A research team from Italy did a retrospective, nationwide study involving 5801 subjects observed in neonatal intensive care units during 3 years. The results of the investigation showed that, in particular settings, diarrhea is a relatively uncommon but insidious condition underlying a broad spectrum of illnesses. The list of diseases and mechanisms responsible for diarrhea in neonates is large and the number of possible etiologies is higher compared with older pediatric patients. Thus, early diagnosis and timely treatment are both crucial in the management of diarrhea in neonates. Their study was published on June 7, 2010 in the *World Journal of Gastroenterology.*

This is the first systematic study describing diarrhea in patients hospitalized in the neonatal intensive care unit in an industrialized country and outside outbreak conditions. This study will help neonatologists to become more confident with all the possible etiologies of diarrhea in neonates in order to recognize and correctly manage rare chronic cases who need the assistance of a specialized team dedicated to their long-term treatment. Specific guidelines for the management of diarrheal disorders in neonates are advocated.

This research opens the way to new investigations in the area of diarrheal diseases with neonatal onset. The results could be of importance for other experts in the field of infectious diseases, nutrition, cell biology, histology and genetics.

Reference: Passariello A, Terrin G, Baldassarre ME, De Curtis M, Paludetto R, Berni Canani R. Diarrhea in neonatal intensive care unit. World J Gastroenterol 2010; 16(21): 2664-2668 www.wjgnet.com/1007-9327/full/v16/i21/2664.htm.

The *World Journal of Gastroenterology* (WJG), a leading international journal in gastroenterology and hepatology,

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Annual Federal Statistics Compilation Reports Second Straight Decline In Preterm Births

Eighth graders' Math and Reading Scores Increase, Adolescent Births Decline

Preterm births and adolescent births declined, eighth graders' math and reading scores increased, and more children had health insurance, according to the federal government's annual statistical report on the well-being of the nation's children and youth. The report also showed several economic changes that coincided with the beginning of the economic downturn: increases in child poverty and food insecurity, as well as a decline in secure parental employment.

The report, America's Children In Brief: Key National Indicators of Well-Being, 2010 was compiled by the Federal Interagency Forum on Child and Family Statistics, a working group of 22 federal agencies that collect, analyze, and report data on issues related to children and families. The report groups the most recently available major federal statistics on children and youth under several domains: family and social environment, economic circumstances, health care, physical environment and safety, behavior, education, and health. The purpose of the report is to provide statistical information on children and families in a nontechnical, easy-to-use format in order to stimulate discussion among data providers, policymakers, and members of the public.

"The decline in preterm births is encouraging," said Alan E. Guttmacher, MD, Acting Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. "Preterm infants are at higher risk for death in the first year of life, for serious illness in infancy, and, in later life, for obesity and its associated complications."

"Also of note is the decrease in births to teens," said Edward Sondik, PhD, Director of the Centers for Disease Control and Prevention's National Center for Health Statistics. "This drop occurred after two years of increases, and we will be interested to see if this is the beginning of a new trend."

Dr. Sondik said that the report on the well-being of the nation's children is a significant vehicle in informing the nation about key issues in their lives.

"The impact of the federal agency collaboration cannot be understated — our commitment to the future is evidenced in our measured analysis of the past."

Among the statistically significant changes seen in the period 2007-2008 are:

- A drop in the proportion of infants born before 37 weeks, from 12.7% to 12.3%.
- A drop in births to adolescents, from 22.2 per 1,000 girls ages 15-17 to 21.7 per 1,000.
- A rise in the rate of children from birth to 17 years of age covered by health insurance at some time during the year, from 89% to 90%.
- A rise in the proportion of related children from birth to 17 years of age living in poverty, from 18% to 19%.
- A drop in the percentage of children from birth to 17 years of age living with at least one parent employed year round full time, from 77% to 75%.
- A rise in the percentage of children from birth to 17 years of age living in food insecure. homes, from 17% to 22%, the highest prevalence since monitoring began. The report defines food security as access at all times to enough food for active, healthy lives for all family members.

For the period 2007 to 2009:

- Eighth graders' average mathematics scale score increased, from 281 to 283, while fourth graders' scores were flat after rising for a number of years.
- Eighth graders' average reading scale score increased, from 263 to 264, but fourth graders' scores were unchanged.

From 2008 to 2009:

- The proportion of youth ages 16-19 neither enrolled in school nor working increased from 8% to 9%.

Members of the public may access the report online at http://childstats.gov. Printed copies of the report are also available from the Health Resources and Services Administration Information Center by e-mailing ask@hrsa.gov.

The Forum's website contains all data updates and detailed statistical information accompanying this year's America's Children in Brief report. As in previous years, not all statistics are collected on an annual basis and so some data in the Brief may be unchanged from last year's report.

The National Institutes of Health (NIH) — The Nation's Medical Research Agency — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information, visit www.nih.gov.

Teen Moms More Likely to Have Premature Babies

Pregnant women aged 14-17 years are at higher risk of preterm birth and of having a child with low-birth-weight, especially if they are having their second child. Researchers writing in the open access journal *BMC Preg-*

nancy and Childbirth demonstrate this association and call for better health education and the promotion of contraception after a teenager has given birth for the first time.

Ali Khashan, from University College, Cork, Ireland, worked with a team of researchers to study all 14-29 year-old women who had a live baby in the North West of England between January 2004 and December 2006. The researchers identified 3,636 people who were between 14 and 17 at the time of birth, 7,506 who were aged between 18 and 19, and 45,211 who were 20 to 29. The rates of teenage pregnancy increased with increasing social deprivation such that more than one third of the teenage mothers came from the most socially deprived areas. Teenage mothers were more likely to be underweight and of white ethnic background. Women who gave birth during the teenage years were at increased risk of preterm and very preterm delivery. This risk was higher for younger teenager mothers than for older teenagers, and in the 14-17 age group the risk was greater in second pregnancies than in first.

Speaking about the results, Khashan said, "It is possible that the increased risk of poor pregnancy outcome is related to biological immaturity. It is also possible that the increased risk of poor pregnancy outcome in the second teenage pregnancy is related to numerous complicating factors such as greater social deprivation and less prenatal care."

Professor Kenny, a Health Research Board clinician scientist and consultant Obstetrician and Gynaecologist at Cork University Maternity Hospital, who led the study, said, "These results highlight the importance of ensuring pregnant teenagers have appropriate antenatal care. Moreover, a vital component of this care is post-natal contraception to prevent a second teenage pregnancy with potentially higher risks of adverse outcomes. A first pregnancy may be the first and only time a pregnant teenager interacts with health services and this opportunity should not be overlooked".

The article is available: www.biomedcentral.com/bmcpregnancychildbirth/

This study was funded by the Health Research Board (Ireland). The database is housed at the North Western Perinatal Unit which is run by the University of Manchester.

B*MC Pregnancy and Childbirth* is an open access journal publishing original peer-reviewed research articles in all aspects of pregnancy and childbirth. *BMC Pregnancy and Childbirth* (ISSN 1471-2393) is indexed/tracked/covered by PubMed, MEDLINE, CAS, EMBASE, Scopus, Cinahl, CABI and Google Scholar.

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Fetal X-ray Exposure Interferes with Memory in Adulthood

Learning and memory impairments are important contributors to the disability associated with schizophrenia. These functional impairments emerge long before the onset of other symptoms associated with schizophrenia, suggesting that they are a consequence of a disturbance in brain development.

In order to investigate the impact of early life disturbances in brain development upon learning and memory, researchers at the Yale University School of Medicine conducted a study that required a remarkable degree of commitment and planning. They exposed fetal monkeys to x-rays and then examined their behavior when they were adults, approximately 5 years later.

They found that irradiated adult monkeys exhibited a profound deficit in working memory ability compared to adult monkeys that had not been exposed to x-rays. Notably, these same irradiated monkeys had not shown any working memory impairment when tested as juveniles (1 - 2 years old). These findings suggest that this relatively mild insult to the developing brain early in gestation, even before cortical neurons are generated, produced profound cognitive dysfunction that emerged only with maturation to adulthood.

"Our non-human primate study mirrors what has been observed in human populations: that mild prenatal stressors increase the risk for developing neuropsychiatric illness in adulthood," explained Dr. Selemon.

It is important to note that this study evaluated the effects of exposure to x-rays at a much higher level than would be associated with the typical x-ray, so the authors do not suggest that typical clinical x-ray exposures cause schizophrenia in humans.

However, notes Dr. Selemon, "this study reaffirms the importance of the early gestational period as a critical window of vulnerability to environmental factors that may have adverse effects on brain development and insidious consequences for brain function."

The article is "Fetal Irradiation Interferes with Adult Cognition in the Nonhuman Primate" by Harriet R. Friedman and Lynn D. Selemon. The authors are affiliated with the Department of Neurobiology, Yale University School of Medicine, New Haven, Connecticut. The article appears in *Biological Psychiatry*, Vol. 68, Issue 1 (July 1, 2010), published by Elsevier.

The authors' disclosures of financial and conflicts of interests are available in the article.

Biological Psychiatry is the official journal of the Society of Biological Psychiatry. It covers a broad range of topics in psychiatric neuroscience and therapeutics. For more information: www.sobp.org/journal.

Future Continues to Brighten for Children with Velocardiofacial Syndrome

Newswise — Research about quality of life is improving the treatment of children with Velocardiofacial Syndrome, a chronic, genetic condition with a wide range of symptoms, including congenital heart disease, palatal abnormalities (e.g. cleft palate), and learning difficulties.

Studies have examined the physical and cognitive aspects of pediatric Velocardiofacial Syndrome, but until now quality of life has not been explored. “Quality of Life Among Children With Velocardiofacial Syndrome” adds to the growing body of knowledge that is aimed at improving the health and wellbeing of children faced with the physical, psychological, social, and spiritual challenges associated with this genetic condition.

Children with Velocardiofacial Syndrome, especially boys, struggle with fatigue and have trouble functioning in school. With the exception of physical health, boys and girls scored lower in emotional, social and school functioning than children with other chronic conditions. However, humor, caring, kindness, persistence and enthusiasm were identified as the top character strengths that help children with Velocardiofacial Syndrome cope with their condition.

The relationship between treatment and quality of life is a feedback loop. Quality of life is a reflection of the effectiveness of treatment. Understanding the various dimensions of quality of life helps researchers and clinicians develop better treatment strategies.

Although Velocardiofacial Syndrome presents formidable challenges to the children with this condition and to family and health care providers, the future is looking brighter as studies continue to provide methods of improving treatment and quality of life.

Full text of the article, "Quality of Life Among Children With Velocardiofacial Syndrome," is available at: www2.allenpress.com/pdf/cpcj47.3FNL.pdf *The Cleft Palate–Craniofacial Journal* is an international, interdisciplinary journal reporting on clinical and research activities in cleft lip/palate and other craniofacial anomalies, together with research in related laboratory sciences. It is the official publication of the American Cleft Palate–Craniofacial Association (ACPA). For more information, visit www.acpa-cpf.org/.

Hospital Formulary Decisions Often Ignore Important Factors

Newswise — Pharmacoeconomic methods rank low as a decision influencer on formulary changes, according to a new survey released today by the Society of Hospital Medicine (SHM) and the American Society of Health-System Pharmacists (ASHP). Respondents reported that only 13% of formulary system decisions made by Pharmacy and Therapeutics (P&T) committees in hospitals is influenced by pharmacoeconomic methods.

The findings in the new report are based on a survey of 319 ASHP members that were either directors of pharmacy or members of ASHP's Pharmacy Practice Managers Section.

Pharmacoeconomic methods evaluate the value of effects compared to the cost of pharmaceutical products when making decisions on changes to the formulary system. Hospital formularies identify medications and medication-use policies used within a particular hospital. Decisions on the management of a formulary system have a significant impact on the quality and safety of patient care.

"Pharmacoeconomics is all about balancing the costs of medications with the outcomes they provide and this survey pointed out that many P&T Committees underutilize this approach," said SHM CEO, Laurence Wellikson. "Just like the collaboration between SHM and ASHP in conducting and analyzing this survey, we expect hospitalists and pharmacists to work together to provide the safest, most effective medications for our hospitalized patients."

In the study, 87% of respondents felt that pharamacoeconomic methods should be used when considering additions or deletions to their hospital formulary. However, when making formulary decisions, respondents reported that clinical and therapeutic factors contribute most to these decisions (54%), followed by drug costs (24%), pharmacoeconomic methods (13%), and patient quality of life (9%).

Although, more than nine out of ten survey respondents (93%) reported having pharmacoeconomic analysis available during their most recent P&T committee discussion, only 26% found it helpful and 71% desired additional pharmacoeconomic information. Barriers to the use of pharmacoeconomic analysis include a lack of understanding of these methods, a lack of pharmacoeconomic information available for use by the committee, and lack of staff resources to compile pharmaeconomic information.

"Pharmacoeconomic analyses are essential to efforts to improve patient outcomes while minimizing costs," said Henri R. Manasse, Jr., PhD, ScD, Executive VP and CEO of ASHP. "The survey demonstrates that clinicians recognize the importance of these tools, but also identifies barriers to their use. For next steps, we plan to assist our respective members with addressing those barriers."

As both hospitalists and pharmacists take on leadership roles in quality of care and patient safety initiatives, many are now serving on important hospital committees, such as P&T committees that serve as the communication link between the pharmacy and medical staff. As part of the SHM- ASHP joint survey, 60% of respondents indicated a hospitalist serves on their P&T committee and 81% of respondents indicated a hospitalist works in their hospital. More information on the role of the P&T committee is available in the ASHP Guidelines on Pharmacy and Therapeutics Committee and the Formulary System.

ASHP and SHM share interest in jointly optimizing the care of patients in hospitals and promoting the use of pharmacoeconomic methods in making decisions on hospitals' formulary systems.

Sanofi Aventis sponsored SHM-ASHP Pharmacoeconomics survey. Additional results from the SHM-ASHP pharmacoeconomics survey can be found at www.hospitalmedicine.org/pharmacoeconomicsurvey.

SHM is the premier medical society representing hospitalists. For more information about SHM, visit www.hospitalmedicine.org.

For more information on ASHP's visit www.ashp.org, or its consumer website, www.SafeMedication.com

NEONATOLOGY TODAY

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ISSN: 1932-7129 (print); 1932-7137 (online).
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