

# NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

Volume 6 / Issue 11

November 2011

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## NEONATOLOGY TODAY

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16 Cove Rd, Ste. 200

Westerly, RI 02891 USA

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Neonatology Today (NT) is a monthly newsletter for 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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## Short-term Outcomes of Different Treatment Modalities of Patent Ductus Arteriosus in Preterm Infants - Five Year Qatar Experiences

By Nuha Nimeri, MD; Husam Salama, MRCP  
Pediatrics "UK" - DCH, DCCH

### Abbreviations

- BPD = Bronchopulmonary Dysplasia
- CHD = Congenital Heart Disease
- CPAP = Continuous Positive Air-way Pressure
- IVH = Interventricular Hemorrhage
- NEC = Necrotizing Enterocolitis
- NICU = Neonatal Intensive Ccare Unit
- PDA = Patent Ductus Aarteriosus
- PEEP = Positive End Expiratory Pressure
- ROP = Retinopathy of Prematurity

### Abstract

**Background:** The incidence of PDA ranges from 40 to 60% in infants born before 28 weeks' gestation. In recent years, there has been growing debate regarding the need to treat PDA during the neonatal period.

**Objective:** To study the short-term outcome of PDA treated with different treatment modalities in preterm infant's  $\leq 32$  weeks gestational age.

**Methods:** This study is based on a descriptive retrospective chart review conducted in NICU Women's Hospital, Hamad Medical Corporation, Doha, Qatar. The files of all infants born in Woman's Hospital with a gestational age  $\leq 32$  weeks with a diagnosis of PDA over a five-year period, January 2003 to December 2007 were reviewed.

**Results:** For the five-year period, 82 cases of PDA were diagnosed in infants  $\leq 32$  week's gestational age. Pharmaceutical intervention was used in 63/82 infants (76%), 20/82 infants (24%) required surgical ligation after failed medication, while 32 infants (39%) had their PDA closed spontaneously. Medication was successful in only 30/63 (47%). Large PDA significantly increased the mortality, IVH, and ROP (P value 0.002-0.003). PDA size has no protective effect on BPD or NEC (P value 0.54, 0.06 respectively). Infants who received medication or surgery experienced no significant difference in all adverse outcomes, except for ROP which has P value of 0.003. Preterm infants  $\leq 32$  weeks, who had spontaneous closure of their PDA, experienced lower rates of CLD, ROP, NEC and IVH (P<0.001-0.045).

**"The results suggest that conservative treatment of PDA is the first choice approach before resorting to medical and surgical treatment."**

**Conclusion:** The results suggest that conservative treatment of PDA is the first choice approach before resorting to medical and surgical treatment.

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## Introduction

Ductus arteriosus is a vascular connection between the main pulmonary artery and aorta. The Ductus arteriosus closes spontaneously in most near-term and full-term infants during the first three days of life, but in preterm infants it remains patent during the first week of life.<sup>1</sup> Patent Ductus Arteriosus (PDA) is a common congenital heart defect in preterm infants. The incidence of PDA in preterm infants is increasing due to the improved survival rate of infants born with extremely low birth weight. Similarly, incidence is inversely proportionate to gestational age; in preterm infant's  $\leq 28$  weeks, the incidence is as high as 60%.<sup>2</sup>

The available clinical trials were unable to establish an obvious relationship between different neonatal morbidities, whether secondary to the hemodynamic changes that occur with left-to-right shunt through the PDA or due to therapies used to close PDA.<sup>3</sup> In a small randomized controlled trial conducted 25 years ago, the investigators suggested that persistent PDA is associated with increased pulmonary morbidity.<sup>4</sup>

The debate regarding optimum management of Patent Ductus Arteriosus in preterm infants has heated up in recent years. The majority of clinicians attempt to close clinically significant PDAs using either Indomethacin or ibuprofen. If the PDA does not close or reopens after pharmaceutical therapy, then surgical closure is considered by some clinicians.<sup>5</sup> The decision to surgically close a "significant" PDA is complicated by recent experiences, indicating that surgery of any kind in newborns is associated with poor neurodevelopmental outcomes. Some preterm infants seem to be unable to tolerate a PDA ligation, perhaps because of acute physiological changes that are imposed on the cardiovascular system that has adapted to the PDA.<sup>6,7</sup>

Current conservative measures that have been adopted by some clinicians include: adjustment of ventilation by reducing inspiratory time, increasing positive end expiratory pressure (PEEP), and fluid restriction.<sup>8</sup>

The objective of this study is to assess the short-term outcome of different PDA treatment modalities in premature infants  $\leq 32$  weeks gestation.

## Methods

This study is a descriptive retrospective chart review. All records of preterm infants of  $< 37$  weeks gestation admitted to NICU at Hamad Medical Corporation, Qatar, within a five-year time period, January 2003 to December 2007, were reviewed and assessed. The NICU had 8,604 admissions within this time period. From those admissions, a total of 495 cases had congenital heart disease. PDA was diagnosed in 82 cases born before 32 weeks.

The initial diagnosis of PDA was based on clinical criteria, which are hemodynamic instability, respiratory instability or a combination of both. The hemodynamic criteria included blood pressure instability, bounding peripheral pulses, poor tissue perfusion, and metabolic acidosis. The respiratory criteria included difficulty in weaning from the ventilator, increased ventilatory support, frequent episodes of apnea, carbon dioxide retention and occurrence of pulmonary hemorrhage. All these cases underwent a routine confirmation by echocardiography. The size of PDA was classified into 3 categories: insignificant or small, if diameter was  $\leq 1-1.5$ mm; moderate, if diameter was  $\geq 1.5-3$ mm, and large, if diameter was  $\geq 3$ mm.<sup>9</sup> Management modalities were divided into conservative, medical or surgical. The conservative approach included optimizing ventilation and restricting the total fluid intake to 130 ml/kg/day and augmenting positive pressure ventilation. The pharmaceutical intervention included using either intra-

venous Indomethacin or oral ibuprofen. Patients who failed conservative and pharmaceutical treatment while still clinically compromised were candidates for surgical ligation.

Outcomes were assessed by analyzing the percentage of infants with PDA, modalities of treatment and major adverse outcome of these modalities. The rate of occurrence of NEC (modified Bell staging 1-3),<sup>10</sup> IVH, BPD, ROP and mortality rate were also documented. Data obtained from patient files were entered into a computerized statistical program (SPSS12®)

This study was approved by the Institutional Review Board. A waiver of informed consent for participation was obtained from the Ethical Committee since it is a chart review study.

## Results

**Study demographic:** A total of 82 infants  $\leq 32$  weeks gestation of equal gender distribution were identified out of 147 infants with isolated PDA. Mean gestational age was 26.9 ( $\pm 2.41$ ) and the mean birth weight 1020  $\pm$  353 grams (Table 1).

**Treatment modalities in preterm infants:** A total of 63 infants received medical treatment with a closure rate of 47%; 20 infants required surgical ligation for their PDA after it failed to close by medication (31%). A total of 13 PDA cases failed to close in response to

Table 1. Demographic Features of the Study Population  $\leq 32$  Weeks

Variables	Total Number = 82
Female	41 (50%)
Mean Gestational Age	26.9 $\pm$ 2.41weeks
Mean Birth Weight	1020 $\pm$ 353 grams
Mechanical Ventilation*	64 (79%)
CLD	30 (36%)
IVH	25 (69.5%)
NEC	16 (19.5%)
ROP **	46 (56.1%)**
Thrombocytopenia	18 (22%)
Mortality	18 (21%)

\* Including CPAP. \*\*ROP of all grades.



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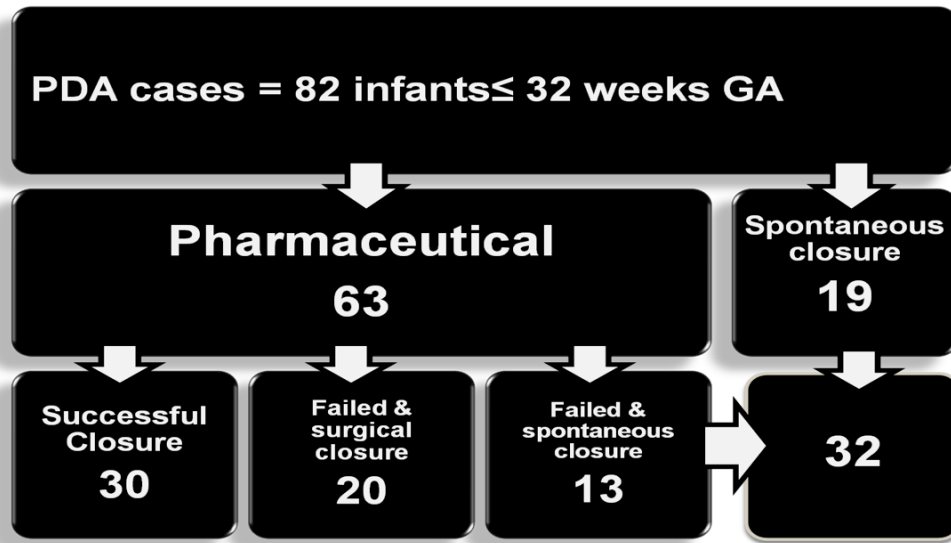


Figure 1. Response of PDA cases according to different treatment modalities.

	Medication + Surgery (50)	Spontaneous (32)	*P Value
Mortality	15	3	0.05
**CLD	27	3	0.001
**IVH	25	6	0.009
**NEC	15	1	0.007
**ROP	41	5	0.001

\*P value in favor of spontaneous. \*\*All grades

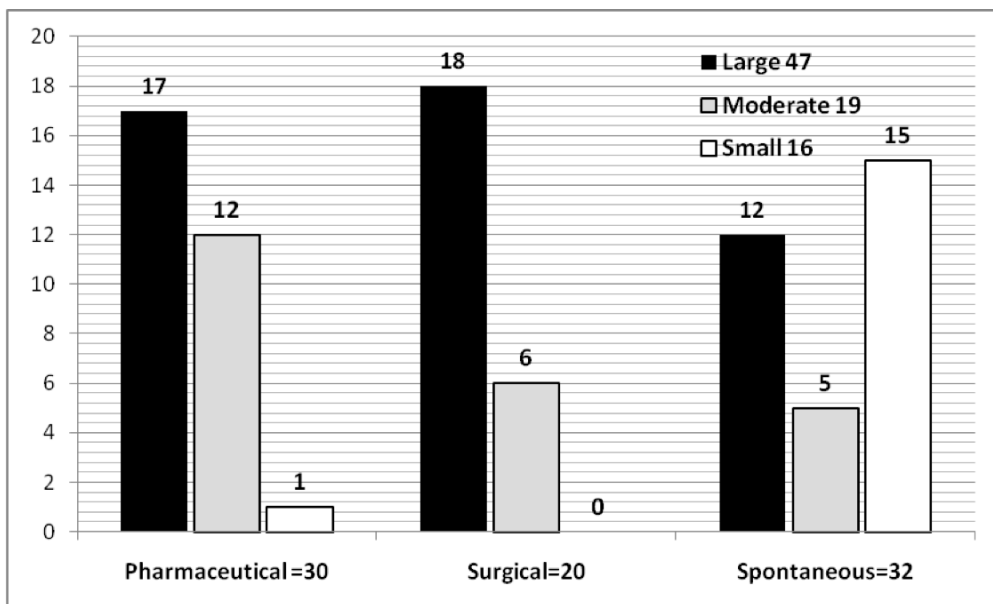


Figure 2. Number of PDA successfully closed according to size and treatment modality.

\*13/63 cases failed to close completely by medication; when followed up before discharge, they were completely closed.

medication, but closed later spontaneously (late spontaneous closure). Conservative treatment was successful in only 19/82 infants (23%) of those who received no treatment. However, the overall spontaneous closure including late spontaneous closure was 32/82 (39%) - Figure 1.

**Response of different PDA size to different treatment modality:** Figure 2 shows the number of PDA successfully closed according to different size and treatment modality. Twelve out of those with large PDA closed spontaneously (26%); moderate PDA has the same percentage of spontaneous closure (26%).

**Complications related to treatment modalities:** When comparing combined surgical and medical treatment to conservative treatment (Table 2), the rate of adverse outcome is significantly less in the latter group with P value of 0.001 to 0.05. Neither the medication approach, nor the surgical approach, showed any significant protection against adverse outcomes when compared, except in ROP where P value is 0.003 (Table 3).

**Effect of PDA size on neonatal outcome:** Adverse outcomes have been significantly influenced by the size of PDA; where the larger the size, the higher the chance to develop adverse outcome (Table 4).

## Discussion

In preterm infants, patency of the Ductus Arteriosus may represent a normal physiologic adjustment to allow shunting from either systemic-to-pulmonary circulation (e.g., in the first day of life) or from pulmonary-to-systemic circulation (e.g., in the presence of severe lung disease).<sup>11</sup>

Several studies have been discussing medical and surgical treatment; few studies have evaluated the outcome of currently popular conservative treatment that includes adjusting ventilation and fluid restriction.<sup>8</sup> The spontaneous closure reported in the current study was 23% of affected preterm infant's ≤ 32 weeks. This rate is not comparable with the rate reported in the literature by Sophie et al, who reported a spontaneous closure rate of the Ductus Arteriosus in moderately premature infants of 67%.<sup>8</sup> However, these figure gaps could be narrowed if the author factored in the 13/63 infants (20%) in whom the PDA was not completely closed after medication and closed later spontaneously without need for further courses of medications (late spontaneous closure) to bring the overall rate of spontaneous closure to 39%. Our rate of spontaneous closure is comparable to the rate reported by Josh and his colleagues. They reported a rate of spontaneous permanent DA closure of > 34% in extremely low birth weight neonates.<sup>12</sup>

	<b>Medication (30)</b>	<b>Surgery (20)</b>	<b>*P Value</b>
<b>Mortality</b>	9	6	0.75
<b>**CLD</b>	16	11	0.86
<b>**IVH</b>	19	6	0.04
<b>**NEC</b>	10	5	0.75
<b>**ROP</b>	29	12	0.003
<i>**All grades</i>			

	<b>Small + Moderate (35)</b>	<b>Large (47)</b>	<b>P Value</b>
<b>Mortality</b>	3	15	0.02
<b>CLD</b>	11	19	0.54
<b>IVH</b>	4	21	0.003
<b>NEC</b>	3	13	0.06
<b>ROP</b>	13	29	0.006

Ronald and his colleagues recommended that therapies designed to close the Ductus Arteriosus are contraindicated in some settings and should not be considered a standard of care at any time until these therapies are proven to decrease long-term clinical morbidities in randomized, placebo-controlled trials.<sup>11</sup> This is reflected in our result that showed no significant difference when medication and surgical approaches were used in terms of decreasing all morbidities. On the other hand, when comparing medication and surgical approach in one arm with the conservative management in the other arm, there was statistically significant reduction in all forms of morbidities. This result is supported by the lack of evidence that treatment of patent Ductus Arteriosus results in long-term benefit.<sup>13</sup>

Interestingly, the ROP was significantly increased in patients who received medication P value 0.003. This can be explained by the need for prolonged respiratory support while receiving medication. Large PDA has no protective role, in comparison to other PDA size in decreasing morbidities. This can be explained by the fact: these infants were subjected to long-standing medical treatment with possible long-standing pathology and hazardous surgical intervention.

Both pharmacologic and surgical treatment options exist for closing a PDA, both of which have their own morbidities. Treatment of a PDA is not gentle and has not been shown to prevent any morbidity associated with prematurity.<sup>14</sup>

In conclusion, acknowledging the limitations of this retrospective analysis, the rate of PDA closure achieved with conservative treatment

at our center was comparable to the rates previously reported with drug management. Our conservative approach resulted in ensuring PDA closure; it did so without exposing the neonates to potential side effects of drug treatment. Although our result is a retrospective chart review analysis, we changed our approach toward treatment of small and moderate PDA by placing more emphasis on a conservative approach before exposing the infants to other active interventions. Further confirmation by way of a properly randomized controlled trial is warranted.

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# Medical News, Products and Information

## Enriched Formula Benefits Developing Brain and Heart

University of Kansas scientists have found new evidence that infant formulas fortified with long chain polyunsaturated fatty acids (LCPUFA) are good for developing brains and hearts.

In the randomized, double-blind study, 122 term infants were fed one of four formulas from birth to 12 months; three with varying levels of two LCPUFAs (DHA and ARA) and one formula with no LCPUFA, and tested at four, six and nine months of age.

By simultaneously measuring the heart rate and visual attentiveness of infants while they looked at images of adult human faces, John Colombo and Susan Carlson found that infants who were fed fortified formula were more cognitively advanced and their heart rates were lower than infants who were fed formula without LCPUFA.

The formula with the lowest level of LCPUFA — 0.3% level — was found to be sufficient to produce these benefits.

The study is the first randomized clinical trial of postnatal DHA supplementation to measure attention.

Colombo, a neuroscientist who specializes in the measurement of early neurocognitive development, said that the findings add to the mounting evidence that these nutritional compounds positively affect brain and behavioral development.

DHA or docosahexaenoic acid is an essential long-chain fatty-acid that affects brain and eye development, and babies derive it from their mothers before birth and up to age two. But the American diet is often deficient in DHA sources such as fish.

ARA or arachidonic acid is another LCPUFA that is present in breast milk and commercial formula.

The study was designed to examine the effects of postnatal DHA at levels that have been found to vary across the world, said study co-director Carlson, A. J. Rice, Professor of Dietetics and Nutrition at KUMC.

Colombo and Carlson's earlier work and collaborations influenced infant formula manufacturers to begin adding DHA in 2001.

The study was published in the October 2011 issue of *Pediatric Research*.

## At-Risk Newborns Don't Need Blood Tests to Screen for Group B Strep

For newborn infants at risk of infection with group B streptococcal (GBS) bacteria, screening blood tests cause extra pain and anxiety—without increasing detection of early-onset GBS disease, reports a study in the October issue of *The Pediatric Infectious Disease Journal*.

Repeated blood tests to screen at-risk newborns leads to "a negligible clinical yield and a high rate of technical failure," according to the report by Dr Saar Hashavya and colleagues of Hadassah and Hebrew University Medical Center, Jerusalem.

### Results Question Need for Blood Tests and Cultures to Detect GBS after Birth

Group B strep causes potentially life-threatening infections in newborn infants. The infections are often transmitted at birth from mothers who are carriers of the GBS bacteria. (Being a "carrier" means that the bacteria are present, but aren't causing any disease in the mother.) Beginning in the 1990s, hospitals started giving preventive antibiotics during the last weeks of pregnancy to mothers carrying GBS.

However, sometimes there's not enough time to give the recommended course of treatment before the infant is delivered. In this situation, the infant may undergo blood tests (complete blood count) and blood cultures to detect GBS bacteria.

To evaluate this practice, Dr. Hashavya and coauthors reviewed their medical center's experience with 5,845 GBS-carrier mothers treated from 2005 through 2009. Twenty-eight percent of the mothers were "partially treated," receiving only one dose of antibiotics less than four hours before delivery.

After birth, blood tests and blood cultures were performed in 86% of infants born to partially

treated mothers. In 18% of these infants, a second blood sample was needed because of some abnormal result or technical problems with the first sample.

None of the blood cultures performed within six hours after birth showed the presence of GBS. In a small number of cases (less than one percent), the cultures were contaminated with staph bacteria. These infants required intensive clinical observation and repeated blood cultures to confirm that they didn't have GBS infection.

### Nearly All Cases of Early-Onset GBS Would Be Detected Without Screening.

Overall, early-onset GBS infection occurred in 11 out of nearly 54,000 infants. Only two of these infants had mothers who were GBS carriers; neither was identified by blood screening tests. Most of the infants with GBS infection developed symptoms immediately or within the first 12 hours after birth—again, blood tests were not needed to identify the infected patients.

With the introduction of preventive antibiotic treatment, the rate of early-onset GBS infections has greatly decreased. However, there's no clear approach to treatment for infants whose mothers don't receive the full recommended course of treatment before delivery. The new study strongly suggests that blood tests and cultures are not effective or necessary in detecting early-onset GBS in infants born to these partially treated mothers.

Pending further studies, the results support the recently revised recommendation for "expectant management"—observing the infant for any sign of illness for at least 48 hours—instead of blood tests. In infants without symptoms, early blood tests appear to be of little or no value in detecting GBS infection. "More importantly, [the study] shows the drawbacks in terms of unnecessary stress to the newborn and his or her family," Dr. Hashavya and coauthors conclude.

## Study Shows That New DNA Test To Identify Down Syndrome in Pregnancy

A new DNA-based prenatal blood test that can strikingly reduce the number of risky diagnostic



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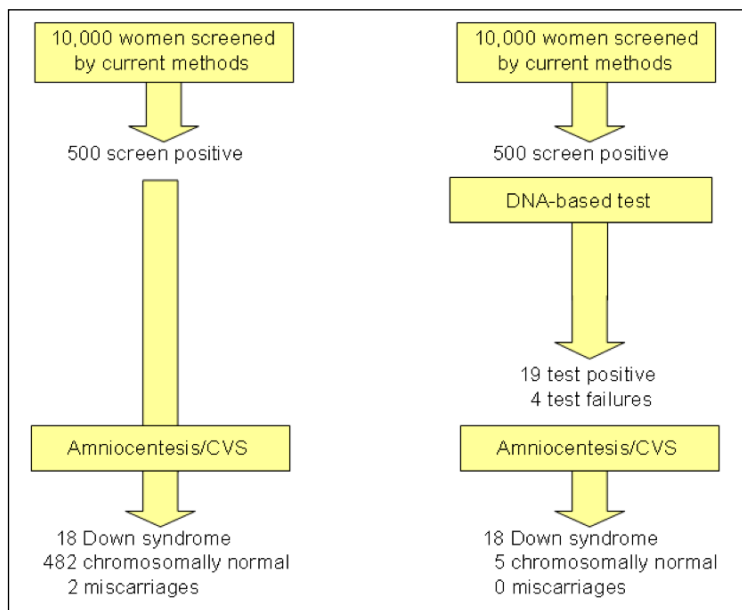
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procedures needed to identify a pregnancy with Down Syndrome is ready to be introduced into clinical practice. The test can be offered as early as 10 weeks of pregnancy to women who have been identified as being at high risk for Down Syndrome. These are the results of an international, multicenter study published online in the *Journal Genetics in Medicine*. The study, the largest and most comprehensive done to date, examined almost 1,700 pregnancies at high risk of chromosomal abnormalities, 212 of which were affected by Down Syndrome.

The research was led by Jacob Canick, PhD, and Glenn Palomaki, PhD, of the Division of Medical Screening and Special Testing in the Department of Pathology and Laboratory Medicine at Women & Infants Hospital and The Warren Alpert Medical School of Brown University, and included scientists at Sequenom, Inc. and The Sequenom Center for Molecular Medicine, San Diego, CA, and an independent academic laboratory at the University of California at Los Angeles.

The test identified 98.6% of the Down Syndrome pregnancies, while only 0.2% of the normal pregnancies were mistakenly called positive. The test rarely failed to provide a clinical interpretation (0.8%). These findings, along with the detailed information learned from testing such a large number of samples, demonstrate that the new test will be highly effective when offered to women considering invasive testing.

"With current screening methods, about one in every 30 women offered a follow-up invasive diagnostic procedure - amniocentesis or chorionic villus sampling (CVS) - will be found to have a pregnancy with Down Syndrome. We expect the DNA-based test to more accurately determine which women should be offered invasive diagnostic testing. As a result, most of the pregnancies referred for amniocentesis or CVS will be found to have Down Syndrome," said Dr. Canick.



How DNA testing for Down Syndrome works in practice

Dr. Palomaki added, "If this new test is used as we've described, nearly all women with a normal pregnancy could avoid an invasive diagnostic procedure and its associated anxiety, cost, and potential for fetal loss."

Down Syndrome, also called trisomy 21, is a chromosomal disorder that includes mental retardation, characteristic facial features, and, often, heart defects, and affects one in 550 babies born each year in the US. Down Syndrome occurs when each cell in an individual has three rather than the usual two copies of chromosome number 21. Current prenatal screening tests for Down syndrome combine maternal age with information from the measurement of maternal serum markers and ultrasound markers in the first and second trimesters of pregnancy. While these tests can detect up to 90% of Down Syndrome cases, they also incorrectly identify 2% to 5% of normal pregnancies as positive. The new DNA-based test will reduce this "false positive" rate while maintaining the detection rate.

"Prenatal screening and diagnosis of Down Syndrome has been part of routine prenatal care for decades, and it is estimated that nearly two-thirds of all pregnant women in the US are currently screened," said Dr. Canick. "It is possible that with the availability of this new DNA-based test, more women will opt for screening because of the increased safety resulting from far fewer amniocentesis and CVS procedures being performed." The US Centers for Disease Control and Prevention estimated in 1995 that about one in every 200 invasive diagnostic procedures will cause a pregnancy miscarriage.

This industry-sponsored project, awarded to Drs. Canick and Palomaki and Women & Infants Hospital in 2008, enrolled 4,500 women at 27 prenatal diagnostic centers throughout the world. Women & Infants also served as one of the enrollment centers under the direction of maternal-fetal medicine specialist and director of Perinatal Genetics, Barbara O'Brien, MD.

"Screening tests, by their nature, do not diagnose, but rather offer information about the chances that a pregnancy may be affected by a genetic abnormality. For years we have relied on screening tests that have had a fairly significant false positive rate because that was the best screening available," said Dr. O'Brien. "But having access to a DNA-based test that can be done early in pregnancy will give us more information so that we can better guide which patients should consider diagnostic testing."

Women & Infants Hospital has been an international center for prenatal screening research. For more than three decades, Drs. Canick and Palomaki have collaborated with others in developing and improving screening tests for Down Syndrome and other fetal abnormalities. In 1988, Drs. Canick and Palomaki were involved in the development of triple marker screening. The team was able to convert its findings into prenatal screening tests now used throughout the world. Dr. Canick's lab in 1998 was the first in the US to offer quad marker screening and in the past decade was the laboratory center for the National Institute of Health (NIH) funded FASTER Trial which compared first and second trimester screening.

It was announced today that one version of this laboratory-developed test, MaterniT21, has been validated through clinical studies and is now available through The Sequenom Center for Molecular Medicine, a CLIA-certified and CAP-accredited laboratory. Harry F. Hixson Jr., PhD,



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chairman and CEO of Sequenom, Inc., said, "We have been fortunate to partner in the clinical study and are proud to offer the service to assist specialists and high-risk patients in making more informed decisions about their pregnancy."

### Low Birthweight Infants Five Times More Likely to Have Autism

Autism researchers at the University of Pennsylvania School of Nursing have found a link between low birthweight and children diagnosed with autism, reporting premature infants are five times more likely to have autism than children born at normal weight.

The children, some born as small as about a pound, were followed for 21 years making this study, published in the prestigious journal *Pediatrics*, one of the most remarkable of its kind. The infants were born between September 1984 through July 1987 in Middlesex, Monmouth, and Ocean counties in New Jersey at birthweights from 500 to 2000 grams or a maximum of about 4.4 pounds.

"As survival of the smallest and most immature babies improves, impaired survivors represent an increasing public health challenge," wrote lead author Jennifer Pinto-Martin, MPH, PhD, director of the Center for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) at Penn Nursing. "Emerging studies suggest that low birthweight may be a risk factor for autism spectrum disorders."

Links between low birthweight and a range of motor and cognitive problems have been well established for some time, but this is the first study that establishes that these children are also at increased risk for autism spectrum disorders (ASD).

"Cognitive problems in these children may mask underlying autism," said Dr. Pinto-Martin. "If there is suspicion of autism or a positive screening test for ASD, parents should seek an evaluation for an ASD. Early intervention improves long-term outcome and can help these children both at school and at home."

In future studies, Penn researchers will investigate possible links between brain hemorrhage, a complication of premature birth, and autism by examining brain ultrasounds taken of these children as newborns.

The researchers, including a team at The Children's Hospital of Philadelphia, followed 862 children from birth to young adulthood finding that five percent of the children were diagnosed with autism, compared to one percent of the general population in what researchers called "the first study to have esti-

mated the prevalence of ASD . . . using research validated diagnostic instruments."

### Premature Birth May Increase Risk of Epilepsy Later in Life

Being born prematurely may increase your risk of developing epilepsy as an adult, according to a new study published in the October 4, 2011, issue of *Neurology*<sup>®</sup>, the medical journal of the American Academy of Neurology.

"We found a strong connection between preterm birth and risk of epilepsy and the risk appears to increase dramatically the earlier the birth occurs during pregnancy," said study author Casey Crump, MD, PhD, of Stanford University in Stanford, California. "More effective prevention of preterm birth is urgently needed to reduce the burden of epilepsy later in life."

For the study, 630,090 adults in Sweden ages 25 to 37 were followed for four years. Participants who developed epilepsy were identified through hospital records as well as monitoring prescriptions for drugs that treat epilepsy. Of the participants, 27,953 had been born prematurely and 922, or 0.15% of the total study participants, had been hospitalized for epilepsy during the study.

The study found adults who were born very preterm (23-31 weeks gestational age) were five times more likely to be hospitalized for epilepsy as an adult compared to those adults who were born full-term (37-42 weeks gestational age). Adults who were born between 32-34 weeks of pregnancy were almost twice as likely to be hospitalized for epilepsy and adults who were born between 35 and 36 weeks were one-and-a-half times as likely to be hospitalized for epilepsy compared to those born full-term. The results remained the same regardless of fetal growth, birth order or related disorders that may be associated with preterm birth.

"Other disorders were also more common in people born preterm, including cerebral palsy and other diseases of the central nervous system," said Crump. "It's possible that the association between preterm birth and epilepsy may be explained by a decreased flow of oxygen to the brain in the uterus during pregnancy that leads to preterm birth or abnormal brain development resulting from preterm birth itself."

This study was conducted at the Center for Primary Health Care Research at Lund University in Sweden and was supported by the National Institute of Child Health and Human Development, the Swedish Research Council, the Swedish Council for Working Life and Social Research, and the ALF project grant.

## FEBRUARY MEDICAL MEETING FOCUS

### Specialty Review in Neonatology/ Perinatology 2.0 (SR 2.0)

Feb. 23-27, 2012; Walt Disney World Dolphin Resort, Orlando, FL USA  
[www.specialtyreview.com](http://www.specialtyreview.com)

SR 2.0 is a comprehensive review of neonatal-perinatal medicine, and offers an updated, intensive and comprehensive review course designed to strengthen knowledge and skills in the field of neonatal-perinatal medicine. The meeting is a collaboration between Dr. Dharmapuri Vidyasagar and The Pediatrix Medical Group's Center for Research, Education and Quality.

#### Topics Include:

- Maternal-Fetal Medicine
- General Care of the Neonate / Fluids & Electrolytes / Growth and Nutrition
- Neonatal Respiratory System
- Neonatal Brain Injury
- Neonatal Cardiovascular System
- Core Scholarly Activities and Biostatistics for the Neonatologist / Neonatal Radiology
- Central Nervous System
- Neonatal Gastroenterology
- Neonatal Infectious Diseases
- Genetics and Inborn Errors of Metabolism
- Neonatal Nephrology
- Neonatal Immunology
- Endocrinology/ Calcium and Phosphorus/ Glucose Metabolism
- Neonatal Hematology / Bilirubin
- Plus, The Legends of Neonatology Gala & Award Ceremony - **Honorees:** William Oh, MD & Abraham Rudolph, MD

**Planning Committee:** Dharmapuri Vidyasagar, MD (Course Co-Director); David L. Weisoly, DO (Course Co-Director); Matthew A. Saxonhouse, MD (Associate Course Director); Lucky Jain, MD, MBA (Senior Consulting Faculty); Arwa Saidi, MB DCH; David Askenazi, MD, MsPH; Tandy Aye, MD; Hilton Bernstein, MD; Sean Blackwell, MD; Dara Brodsky, MD; David Burchfield, MD; Michael Gambello, MD; Martin Keszler, MD; Robert Lawrence, MD; Pedro Mancias, MD; James Moore, MD, PHd; Suma P. Pyatil, MD; J. Deane Waldman, MD, MBA; Michael Weiss MD; Jon L. Williams, MD; James Wynn, MD; John Zupancic, MD

Don't forget to join the CQI Pre-Conference Day - February 22, 2012



# Clinical Trials From ClinicalTrials.gov

## Follow-up of Children With Gastrointestinal Malformations and Postnatal Surgery (FraMal)

*This study is currently recruiting participants.*

### Purpose:

- The aim of this single center study is to measure the impact of standardized neonatal pediatric surgeries due to gastrointestinal malformations on the children's motor and cognitive development and psycho-emotional competence.
- To measure the neurodevelopment, the children will be tested with the Bayley Scales of Infant Development II Assessment.

**Condition:** Digestive System Abnormalities

**Study Type:** Observational

**Observational Model:** Case Control

**Time Perspective:** Cross-Sectional

### Primary Outcome Measures:

Score of Bayley Scales of Infant Development II Assessment [Time Frame: 18 - 36 months ] [Not designated as safety issue] Score consisting of cognitive, verbal, nonverbal and motor development levels

### Secondary Outcome Measures:

Anthropometric and psychological changes [Time Frame: 18 - 36 months] [Not designated as safety issue]:

- Growth of patients compared to a healthy control group
- Post-traumatic stress situations in families
- Psycho-emotional competence of the children

**Estimated Enrollment:** 80

**Study Start Date:** September 2011

**Estimated Study Completion Date:** January 2014

**Estimated Primary Completion Date:** July 2013

### Groups/Cohorts:

- Gastrointestinal malformations - Children who underwent standardized neonatal pediatric surgery due to gastrointestinal malformations
- No gastrointestinal malformations - Control group of healthy children matched concerning gestational age, weight class and gender

### Objectives:

The primary objective of this study is to compare differences in the score of Bayley Scales of Infant Development II Assessment (consisting of cognitive, verbal, nonverbal, motor development levels) between children with gastrointestinal malformations and early postnatal surgery at the age of 2 years and a control group. The secondary objective is to measure the growth of the patients compared to healthy children in the control group, to capture post-traumatic stress situations in families, and to capture the children's psycho-emotional competence.

### Study Design:

The study is designed as a cross-sectional single center study. The study patients are children of 2 years of age who underwent neonatal surgery in our clinic since June 2008 due to a gastrointestinal malformation.

The control group consists of matched pairs concerning gestational age, weight and gender.

The study consists of five parts:

- Introductory interview including the medical history
- Bayley Scales of Infant Development II Assessment
- Pediatric examination with anthropometry
- Questionnaire survey of post-traumatic stress situation
- Final conversation with the parents about the results

The neurodevelopmental testing is performed by the child psychologist and the pediatric examination by the pediatrician.

### Study Population:

The study is purely exploratory and based on the number of patients born in our hospital with the malformations mentioned above (approx. 40). Each patient is compared against a healthy child of the same gestational age, weight class and gender (control group).

**Eligible for Study:** Accepts Healthy Volunteers of both sexes, age 18 -36 months

**Sampling Method:** Non-Probability Sample

### Inclusion Criteria:

Patients:

- At follow-up between 18 and 36 months of age
- At birth a gastrointestinal malformation
- Postnatal surgery
- No other serious malformations
- No serious complications of birth (e.g. asphyxia)
- > = 33 week of gestation at birth
- Follow-up appointment when not acutely ill
- Parental Consent



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## Opportunities available in neonatology

HCA, the largest healthcare company in the US, owns and/or manages over 160 hospitals in 20 states. Listed below are our current opportunities in Neonatology. Whether you are looking for your first position post fellowship or somewhere to complete your career, chances are we have something (or will in the future) that will fit your needs. Call or email today for more information!

### Trident Medical Center, Charleston, South Carolina

We are searching for an additional Neonatologist to join our Level II NICU. The candidate should be proficient in: UAC, UVC, peripheral venous and arterial access (including PCCL placement), ET intubation, chest tubes, lumbar puncture, paracentesis and thoracentesis. The successful candidate will be BE/BC and licensable in the state of South Carolina. Our health system has been serving the beautiful Charleston community for three decades, and between our Trident and Summerville Medical Centers, we deliver more babies than anywhere else in the city! Boasting a comfortable climate, great location, historical charm and a variety of resources, the Charleston area is one of the best places to live in the nation.

### Terre Haute Regional Hospital, Terre Haute, Indiana

Neonatologist Needed To Expand NICU - Medical Directorship Opportunity! Currently we have a 3-bed Level II NICU. We are seeking a Neonatologist to expand our services to a 9-12 bed Level III unit. We are initially seeking one physician with plans to add additional in the future. Pediatricians will provide back up support. We offer a competitive compensation and benefits package including paid malpractice, PTO, CME and more!

### Sunrise Children's Hospital, Las Vegas, Nevada

Largest NICU in the state of Nevada (72 beds) seeks 2 more Neonatologists to join our group of 8. We handle 450 deliveries per month, 200 heart surgeries annually and 10,000 patient days per year. Sunrise also has the state's only high risk OB unit and offers a full complement of Pediatric Specialists, clinical trial research, device development and teaching opportunities. We offer competitive salary, bonus and incentive program in a very busy practice. BC/BE in Neonatology and licensure or the ability to be licensed in Nevada are required.

**Please send a letter and current CV to: Kathy Kyer  
Pediatric Subspecialty Recruitment Manager  
Kathleen.Kyer@HCAHealthcare.com  
937.235.5890**



### Inclusion Criteria (continued):

Healthy individuals:

- At follow-up between 18 and 36 months of age
- Uncomplicated postnatal period
- No malformations
- No surgery until follow-up appointment
- > = 33 weeks of gestation at birth
- Follow-up appointment when not acutely ill
- Parental consent

**Exclusion Criteria:** Absence of parental consent (both groups)

### Contacts (Principal Investigator):

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**Sponsors and Collaborators:** Goethe University

**ClinicalTrials.gov identifier:**  
NCT01451307 (processed on October 30, 2011)

**Other Study ID Numbers:** 01072011FraMal

**Study First Received:** August 4, 2011

**Last Updated:** October 11, 2011

**Health Authority:** Germany: Ethics Commission of the University of Frankfurt

The information on this trial is from  
ClinicalTrials.gov.

For more detail and to find information about other clinical trials in neonatology and perinatology, visit [ClinicalTrials.gov](http://ClinicalTrials.gov).



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# Global Neonatology Today Monthly Column - The Seven Billionth Baby

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

Danica May Camacho, a girl born in a packed government-run hospital in the Philippines capital of Manila, was chosen by the United Nations (UN), along with several other children around the world, to symbolically mark the global population milestone: the world's seven billionth baby. Weighing 2.5 kg (5.5 lbs), Danica was delivered just before midnight on Sunday amid an explosion of press camera flashes at Manila's Jose Fabella Memorial Hospital. But, what are these festivities about?

October 31st 2011, chosen by the UN to celebrate the arrival of the 7 billionth baby, marked a milestone in the history of mankind. However, it is difficult to accurately state which of the millions of babies around the world born on that day is the real 7 billionth baby. Countries around the world announced their own arrival of the 7 billionth baby. While we welcome these babies into the world, we also worry about their future in this overcrowded globe.

Back in 1805, in the face of a growing population, Thomas Malthus, the British contemporary of Darwin, raised concerns about the future of human race in the face of a growing population. When the population was only one billion, Malthus predicted an acute shortage of food leading to human disaster if the world's population continued to rise. The population reached 1.65 billion in 1900 at the dawn of 20th Century. It took more than a century to reach the second billion in 1927, but it took just another 32 years to reach the 3rd billion in 1959. Fifteen years later in 1974, the population count was 4 billion. Because the population grows at a geometric rate, the time between billions started to shorten. The mark of 5th billion baby was reached in 1987, only 13 years later. Nineteen-ninety-nine marked the milestone of the 6th billion baby. Now, in 2011, we have the 7 billionth baby!

Here are some fascinating facts about the 7 billion people of the world. If all 7 billion people formed a human chain, they would be 7 million kilometers which will encircle the earth 175 times, or 9 times the distance between earth and moon! How much does the sea of humanity breath? About 80 trillion litres a day with about 560 billion beats per minute, breathing 56 billion liters of air a minute.

While in the early 20th century the Western world contributed to fast growing global population, in the later part of century, the fast growth has moved to the developing countries of Asia, Africa and Latin America. It raises grave concerns of a population "bomb" and population "explosion" unless the population is curbed.

Great stress has been placed on family planning, and China took drastic steps curbing population by enforcing a "one child" national policy attached with severe penalties. This policy has succeeded in curbing the Chinese population to a great extent. However, democracies, such as India, have taken a less conservative approach, with voluntary family planning, and a relatively limited government population control.

Thankfully, with the Green Revolution, (introducing high-yielding varieties of seeds, improved fertilizers and irrigation methods), the world food supply has started to improve. Although there are two times the number of people living in the world now than 50 years ago, there is more food available now than before (320/kg/per person/yr.). Thus, we are ahead of the population bomb explosion predicted by Ehrlich and Malthus. However, the clock is ticking, and we need to pay attention to controlling population, and meet the UN's MDGs (Millennium Development Goals) by 2015.

With these enormous population numbers, no wonder there is great concern about the world being able to sustain ever-increasing numbers of human beings on Earth. Only time will tell!

Finally, as neonatologists we may wonder how many newborns are born each year? The number is approximately 130 million!

**"The Clock is Ticking!"**

NT

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© 2011 by Neonatology Today  
ISSN: 1932-7129 (print); 1932-7137 (online).  
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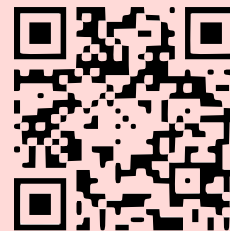
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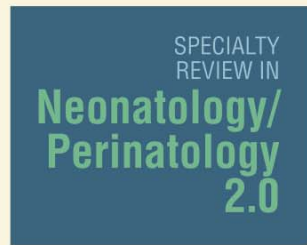
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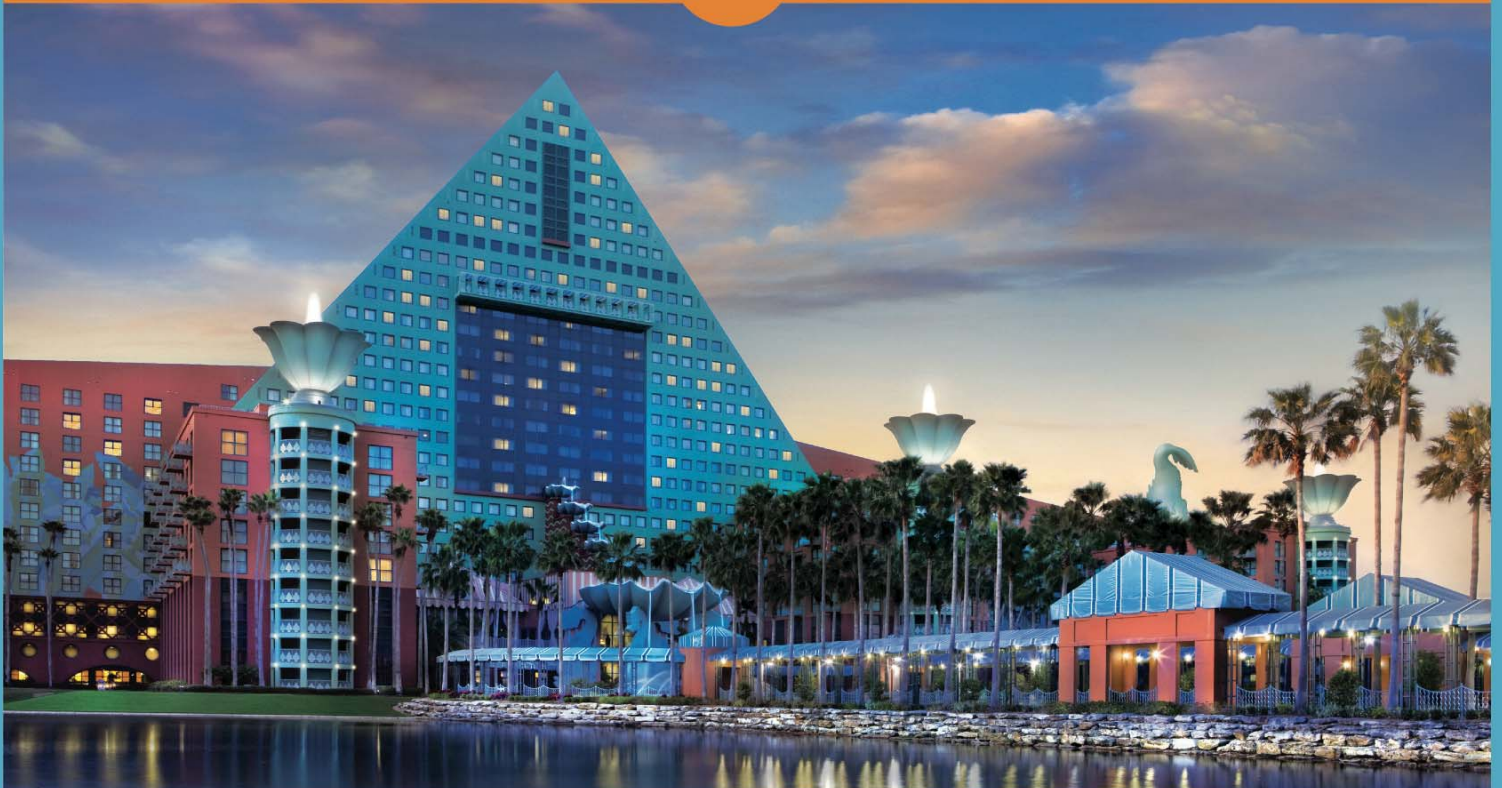
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