



Volume 12 / Issue 4  
April 2017

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### NEONATOLOGY TODAY

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ISSN: 1932-7137 (online)  
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Editorial and Subscription Offices  
16 Cove Rd., Ste. 200  
Westerly, RI 02891 USA

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## A Newborn with Amniotic Band Syndrome

By Kelechi Ikeri, MD; Surendra Gupta, MD; Alexander Rodriguez, MD

### Case Report

A large-for-gestational-age full-term baby was delivered vaginally to a thirty-six-year-old Gravida 4 female with one previous molar pregnancy. She was an early registrant at the prenatal clinic, was fully immunized and took only prenatal vitamins and iron in pregnancy. She had no illnesses in pregnancy and denied alcohol or illicit drug use. There was no history of maternal trauma.

Quad screening done showed an increased risk of having a baby with Trisomy 18 (>1:10), but was negative for Down Syndrome and open neural tube defects. Subsequent amniocentesis results were unremarkable. Serial Ultrasounds, however, revealed a fetus with clubbing of the foot, and possible abnormal bone deformity. Extra soft tissue

### Introduction

Amniotic Band Syndrome (ABS) has been described clinically as rupture of amnion, followed by encircling of developing structures by strands of amnion. These may vary from constricting bands to limb reduction defects. Multiple etiologies may cause this single defect that produces a pattern of congenital abnormalities.

The estimated incidence of ABS ranges from 1:1200 to 1:15,000 live births<sup>1</sup> and 1:70 stillbirths.<sup>2</sup>

We report a case of a newborn with manifestations of ABS.

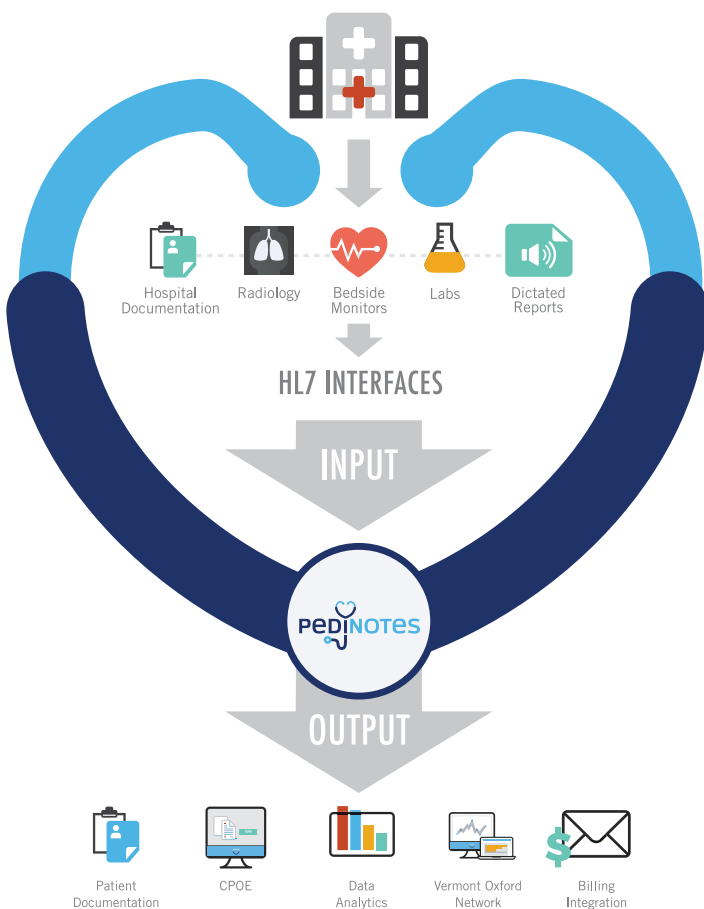


Figure 1. Constrictive band over the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> digit with a spherical mass over the 3<sup>rd</sup> digit.



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was also seen on the arch of the foot and ankle. A round, hyper-echogenic structure on the right hand at the level between the index and middle finger measuring 20mm by 18mm, with no significant flow within the structure on color Doppler, was visualized.

The baby was born through meconium-stained fluid, and with a nuchal cord. APGARS were 9 in 1 and 5 minutes; weight at birth was 4015g.

Physical Examination revealed constriction bands on all extremities. Details include:

- Right hand: constrictive band over the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> digits, and a spherical mass over the 3<sup>rd</sup> digit. Normal thumb and fifth digit (See Figure 1).
- Left hand: constriction band over the 2<sup>nd</sup> and 3<sup>rd</sup> digits with partial amputation of the 4<sup>th</sup> digit. Normal thumb and 5<sup>th</sup> digit.
- Right foot: partial amputation of the 3<sup>rd</sup> digit with constriction bands on all toes (See Figures 2, 3).
- Left foot: constriction band on the lower leg, above the ankle, around the mid-foot. Swelling of the foot and ankle noted with normal appearing big toes (See Figure 2, 4).
- No dysmorphic features were noted and other systemic examination showed no abnormalities.
- Plain radiographs showed no bony involvement of the lower limbs.
- Examinations of other systems were within normal limits.



Figure 2. Constrictive bands over the lower limbs and digits.

In view of the presence of the constriction bands on the limbs, a diagnosis of Amniotic Band Syndrome was made. The mother received extensive counseling on the diagnosis and the baby was referred for elective surgery.

The baby subsequently underwent Z-plasty with release of constriction bands at 1 and 4 months of age with no complications and is currently doing well postoperatively (See Figures 5, 6).

## Discussion

Amniotic Band Syndrome comprises a broad clinical spectrum of defects that include disruptions, deformations and malformations. Disruptions may be caused by adhesions or constrictions causing cleavage of the structures that have already developed normally. Deformation arise due to fetal compression secondary to oligohydramnios and fetal entanglement by amniotic bands. Malformations may result from the presence of amniotic bands in the early embryonic period that interfere with normal embryogenesis.

ABS is thought to occur sporadically or in association with trauma to the abdomen. It can be a complication after amniocentesis and/or it can indicate early rupture of the amniotic sac.<sup>3</sup>

Pathogenesis of ABS has been explained by multiple theories. The intrinsic theory suggested by Streeter in 1930, also named "Streeter Dysplasia," suggests that the anomalies and the fibrous bands have a common origin caused by the disturbance of the developing germinal disc of the early embryo.<sup>4,5</sup>

Moerman and associates proposed vascular compromise as the primary pathogenic mechanism. They described three types of lesions: constrictive tissue bands, amniotic adhesions and limb body

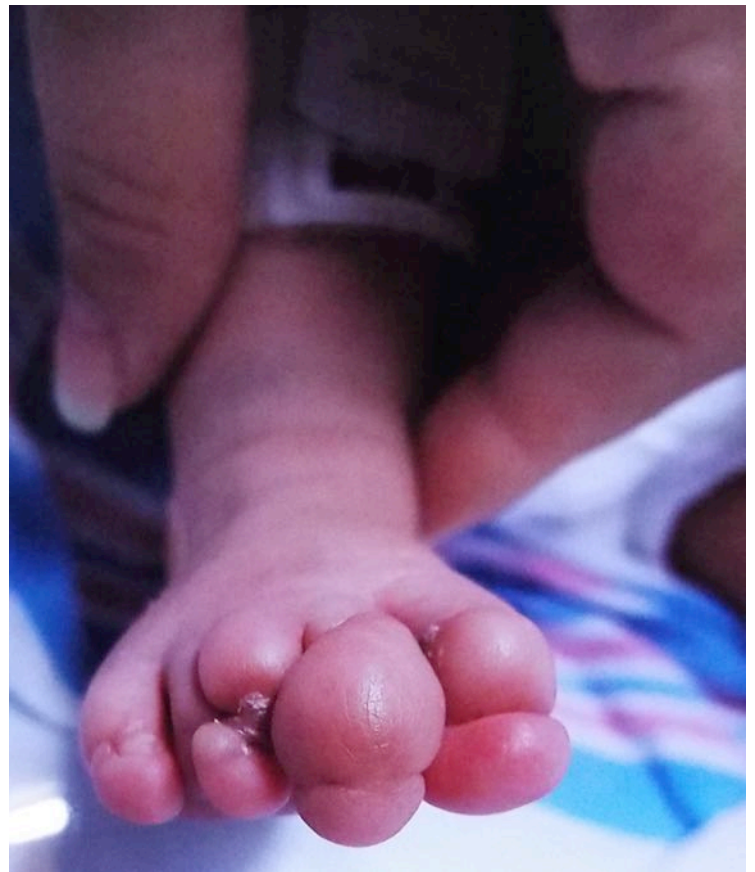


Figure 3. Constrictive bands over the right foot.





Figure 4. Constrictive bands over the left lower limb.



Figure 5. Left hand after z-plasty completed.

wall complex (thoracoabdominoschisis, facial cleft and encephalocele).<sup>6</sup>

The more widely accepted theory is the extrinsic model proposed by Torpin and Faulkner in 1966. This theory suggests that early amniotic rupture occurs leading to formation of mesodermal fibrous strands that entangle limbs and appendages. It was

also postulated that amniotic bands result from amnion rupture without injury to the chorion and encircle the affected parts resulting in constriction rings. He also theorized that oligohydramnios plays a major role in the development of constricting bands and club foot could result secondary to continuous pressure on the feet from the undersized uterus.<sup>7</sup>

Clinical spectrum may vary from single mild defect to severe deformation with multiple anomalies affecting cranium, spine, limb and trunk. Multiple constriction rings may involve multiple digits and limbs and may contribute to the compromise of the vascular supply, as well as bones and nerves.<sup>8</sup>

Anomalies in ABS include, but are not limited to:

- Craniofacial abnormalities - encephalocele, exencephaly, unusual location clefts, anencephaly.
- Body wall defects: especially not in the midline.
- Limb defects: constriction rings, amputation, syndactyly, club foot /hand deformities, lymphedema.
- Visceral Defects: lung hypoplasia, cardiac defects.
- Others: spinal defects, scoliosis, ambiguous genitalia and short umbilical cord, hemangioma, aplasia cutis.<sup>9</sup>

Extremity deformities were classified by Patterson into 4 types:

- I. Simple ring constriction.
- II. Ring constriction accompanied by fusion of distal bony parts with or without lymphedema.
- III. Ring constriction accompanied by fusion of soft tissue parts.
- IV. Intrauterine amputations.<sup>10</sup>

Diagnosis is suggested by the presence of characteristic structural finding on prenatal ultrasound or postnatal physical examination. Approximately 60% of mothers delivering ABS babies report a history of abnormal pregnancies. Prenatal risk factors include: trauma to uterus, low birth weight <2.5kg, maternal illness during pregnancy, maternal drug exposure to cocaine or mifepristone, maternal hemorrhage and attempted abortion in first trimester.<sup>11</sup> ABS has been showed to be associated with elevated maternal alpha-feto-protein, but the association is not diagnostic.

Bands may be difficult to detect on ultrasound and are most times diagnosed by the effect they have on the fetal anatomy. Antenatal Magnetic Resonance Imaging may be helpful in confirming the diagnosis.<sup>12</sup> If ABS is suspected postnatally, immediate investigation of fresh fetal membranes and placenta is important. Amniotic strands can be visualized by immersion of fresh membrane and placenta into a tub of water. Postnatal ultrasound of the brain and abdomen are important to detect structural defects due to vascular disruption.<sup>13</sup>

No known medical treatment is available for ABS. In-utero treatment, which is of unproven efficacy, consists of surgical lysis of the constriction ring to improve blood flow and prevent amputation.<sup>14</sup> Postnatally, surgical release of constriction ring in babies with



Figure 6. Left lower limb after z-plasty completed.

progressive edema distal to the ring is done to enhance function or cosmetic purpose.<sup>15</sup> Other options are prosthesis and physiotherapy of individuals with limb defects.

Recurrent risk is very low and most cases are sporadic, but familial cases have been reported.

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Emory University School of Nursing

### Indication

INOMAX is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

### Important Safety Information

- INOMAX is contraindicated in the treatment of neonates dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOMAX may lead to increasing pulmonary artery pressure and worsening oxygenation.
- Methemoglobinemia and NO<sub>2</sub> levels are dose dependent. Nitric oxide donor compounds may have an additive effect with INOMAX on the risk of developing methemoglobinemia. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.
- In patients with pre-existing left ventricular dysfunction, INOMAX may increase pulmonary capillary wedge pressure leading to pulmonary edema.
- Monitor for PaO<sub>2</sub>, inspired NO<sub>2</sub>, and methemoglobin during INOMAX administration.
- INOMAX must be administered using a calibrated INOmax DS<sub>IR</sub><sup>®</sup> Nitric Oxide Delivery System operated by trained personnel. Only validated ventilator systems should be used in conjunction with INOMAX.

**Please see Brief Summary of Prescribing Information on adjacent page.**



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# INOmax<sup>®</sup> (nitric oxide gas)

## Brief Summary of Prescribing Information

### INDICATIONS AND USAGE

#### Treatment of Hypoxic Respiratory Failure

INOmax<sup>®</sup> is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilator support and other appropriate agents.

### CONTRAINDICATIONS

INOmax is contraindicated in neonates dependent on right-to-left shunting of blood.

### WARNINGS AND PRECAUTIONS

#### Rebound Pulmonary Hypertension Syndrome following Abrupt Discontinuation

Wean from INOmax. Abrupt discontinuation of INOmax may lead to worsening oxygenation and increasing pulmonary artery pressure, i.e., Rebound Pulmonary Hypertension Syndrome. Signs and symptoms of Rebound Pulmonary Hypertension Syndrome include hypoxemia, systemic hypotension, bradycardia, and decreased cardiac output. If Rebound Pulmonary Hypertension occurs, reinstate INOmax therapy immediately.

#### Hypoxemia from Methemoglobinemia

Nitric oxide combines with hemoglobin to form methemoglobin, which does not transport oxygen. Methemoglobin levels increase with the dose of INOmax; it can take 8 hours or more before steady-state methemoglobin levels are attained. Monitor methemoglobin and adjust the dose of INOmax to optimize oxygenation.

If methemoglobin levels do not resolve with decrease in dose or discontinuation of INOmax, additional therapy may be warranted to treat methemoglobinemia.

#### Airway Injury from Nitrogen Dioxide

Nitrogen dioxide (NO<sub>2</sub>) forms in gas mixtures containing NO and O<sub>2</sub>. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.

If there is an unexpected change in NO<sub>2</sub> concentration, or if the NO<sub>2</sub> concentration reaches 3 ppm when measured in the breathing circuit, then the delivery system should be assessed in accordance with the Nitric Oxide Delivery System O&M Manual troubleshooting section, and the NO<sub>2</sub> analyzer should be recalibrated. The dose of INOmax and/or FiO<sub>2</sub> should be adjusted as appropriate.

#### Worsening Heart Failure

Patients with left ventricular dysfunction treated with INOmax may experience pulmonary edema, increased pulmonary capillary wedge pressure, worsening of left ventricular dysfunction, systemic hypotension, bradycardia and cardiac arrest. Discontinue INOmax while providing symptomatic care.

### ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Controlled studies have included 325 patients on INOmax doses of 5 to 80 ppm and 251 patients on placebo. Total mortality in the pooled trials was 11% on placebo and 9% on INOmax, a result adequate to exclude INOmax mortality being more than 40% worse than placebo.

In both the NINOS and CINRGI studies, the duration of hospitalization was similar in INOmax and placebo-treated groups.

From all controlled studies, at least 6 months of follow-up is available for 278 patients who received INOmax and 212 patients who received placebo. Among these patients, there was no evidence of an adverse effect of treatment on the need for rehospitalization, special medical services, pulmonary disease, or neurological sequelae.

In the NINOS study, treatment groups were similar with respect to the incidence and severity of intracranial hemorrhage, Grade IV hemorrhage, periventricular leukomalacia, cerebral infarction, seizures requiring anticonvulsant therapy, pulmonary hemorrhage, or gastrointestinal hemorrhage.

In CINRGI, the only adverse reaction (>2% higher incidence on INOmax than on placebo) was hypotension (14% vs. 11%).

Based upon post-marketing experience, accidental exposure to nitric oxide for inhalation in hospital staff has been associated with chest discomfort, dizziness, dry throat, dyspnea, and headache.

### DRUG INTERACTIONS

#### Nitric Oxide Donor Agents

Nitric oxide donor agents such as prilocaine, sodium nitroprusside and nitroglycerine may increase the risk of developing methemoglobinemia.

### OVERDOSAGE

Overdosage with INOmax is manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO<sub>2</sub>. Elevated NO<sub>2</sub> may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO<sub>2</sub> levels >3 ppm or methemoglobin levels >7% were treated by reducing the dose of, or discontinuing, INOmax.

Methemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation.

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# A Comparison Between C-Reactive Protein and Immature-to-Total-Neutrophil Count Ratio in the Early Diagnosis of Neonatal Sepsis

By Mary Grace S. Tan, MD; Hao Ying, PhD; Woei Bing Poon, MRCPCH, FAMS; Selina Ho, MRCPCH, FAMS

## Definition of Terms

**Confirmed sepsis** - bacteria isolated from blood, cerebrospinal fluid, ETT, surface swabs, wound swab, umbilical catheter tips or urine and started antibiotics or on antibiotics.

**Probable sepsis** - clinical and/or with antenatal risk factors and/or laboratory findings consistent with bacterial infection without a positive culture and started on antibiotics or on antibiotics.

**No sepsis** - may have antenatal risk factors or symptomatic but not started on antibiotics.

## Introduction

To diagnose neonatal sepsis is one of the challenges among medical practitioners. Culture result will take 2 to 3 days, and rapid deterioration of patient's condition may happen if medical treatment is not instituted early.

C-Reactive Protein (CRP) has been used to diagnose and follow the course of infection in neonates. Still, it has some limitations and false positive results. Various haematological results are also being used to diagnose neonatal sepsis like immature-to-total-neutrophil ratios (ITR). With the combination of these diagnostic tests available, delay in treatment of sepsis can be avoided.

## Aims and Objectives

To evaluate the diagnostic efficacy of CRP, or IT Ratio alone, or in combination with the early diagnosis of neonatal septicaemia, so that immediate treatment can be started before a blood culture result is available.

This study was done to look for blood parameters for early diagnosis of neonatal sepsis for better management of neonates.

## Materials and Methods

We performed a prospective study of preterm infants born from March 2013 to March 2014 admitted to the SGH Neonatal Intensive Care Unit (NICU). Infants included were: premature delivery (GA <34weeks), symptomatic neonates who are suspected to be having sepsis and high-risk infants with antenatal-perinatal risk factors like Maternal

	CONFIRMED	PROBABLE	NO SEPSIS
<b>TOTAL EPISODES</b>	<b>17</b>	<b>232</b>	<b>174</b>
<b>BIRTHWEIGHT (median)</b>	1030	2055	2280
<b>MALE</b>	17 (100%)	153 (65.9%)	94 (54%)
<b>FEMALE</b>	0	79 (34.1%)	80 (46%)
<b>emLSCS</b>	15 (88%)	115 (49.6%)	83 (47.7%)
<b>eLSCS</b>	1 (5.9%)	31 (13.4%)	23 (13.2%)
<b>Crash CS</b>	0	9 (3.9%)	6 (3.4%)
<b>NVD</b>	1 (5.9%)	69 (29.7%)	59 (33.9%)
<b>VACUUM</b>	0	6 (2.6%)	2 (1.1%)
<b>FORCEPS</b>	0	2 (0.9%)	1 (0.5%)

	SENSITIVITY for CRP	95% CI
<b>CONFIRMED SEPSIS</b>	0.29	(0.10, 0.56)
<b>PROBABLE SEPSIS</b>	0.34	(0.27, 0.40)
<b>COMBINED (CONFIRMED+PROBABLE)</b>	0.33	(0.27, 0.40)
	SENSITIVITY for ITR	95% CI
<b>CONFIRMED SEPSIS</b>	0.35	(0.14, 0.62)
<b>PROBABLE SEPSIS</b>	0.25	(0.20, 0.31)
<b>COMBINED (CONFIRMED+PROBABLE)</b>	0.26	(0.20, 0.32)
	SENSITIVITY for CRP	95% CI
<b>CONFIRMED SEPSIS</b>	0.77	(0.72, 0.82)
<b>PROBABLE SEPSIS</b>	0.94	(0.88, 0.97)
<b>COMBINED (CONFIRMED+PROBABLE)</b>	0.97	(0.92, 0.99)
	SENSITIVITY for ITR	95% CI
<b>CONFIRMED SEPSIS</b>	0.79	(0.75, 0.83)
<b>PROBABLE SEPSIS</b>	0.83	(0.76, 0.88)
<b>COMBINED (CONFIRMED+PROBABLE)</b>	0.84	(0.78, 0.89)

	PPV	95% CI
<b>CRP</b>	0.96	(0.89, 0.99)
<b>iTr</b>	0.70	(0.61, 0.78)
	NPV	95% CI
<b>CRP</b>	0.42	(0.39, 0.44)
<b>iTr</b>	0.44	(0.42, 0.47)

PROM, Pyrexia, Chorioamnionitis, leucocytosis and with high CRP. Infants with probable sepsis are those who have increased CRP or IT Ratio, or both infection markers, but

cultures are negative. Confirmed sepsis are those infants with positive cultures and elevated CRP or IT Ratio or both CRP and IT Ratio.



## Results

During the study period, there were a total of 201 infants with a median birth weight of 1320g and a median gestational age of 31 weeks were evaluated. There were 79 infants who had more than one episode of suspected sepsis, thus requiring multiple episodes of CRP and IT Ratio determination. Thus, the 201 infants had a total of 423 episodes of bloods taken for CRP and IT Ratio.

Out of the 423 episodes who were included in the study, there were 90 episodes (21.3%) who have elevated IT Ratio and 79 episodes (18.7%) with elevated CRP. Out of the 91 episodes with elevated IT Ratio, there were 23 episodes who have elevated CRP at the same time. On the other hand, there were 26 episodes where patients had a high CRP level, as well as a high IT Ratio.

There were 6 episodes and 5 episodes with positive cultures from either blood, ETT, surface swabs and wound swab with high IT Ratio and high CRP level respectively. In general, the two most common presenting symptoms in this study were respiratory distress and feeding intolerance.

## Conclusion

This prospective study showed that IT Ratio is a more sensitive tool to detect early and late neonatal sepsis. A combination of elevated CRP and IT Ratio determination will confirm the suspicion of neonatal sepsis and the understanding early intervention is warranted.

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Dear Colleagues,

The Organizing Committee is pleased to announce the **7<sup>th</sup> World Congress of Pediatric Cardiology and Cardiac Surgery (WCPCCS)**, which will take place on July 16 - 21, 2017, in the Centre Convencions Internacional de Barcelona (CCIB), Barcelona, Spain. The aim of WCPCCS is to bring together all professionals involved in the care of children's heart disease and congenital heart disease of all ages, from the fetus to the aged. The Congress will provide a unique opportunity to meet the leaders of specialties worldwide; to learn about the latest innovations and the results of procedures; and to contribute to the discussions, debates and plenary sessions with renowned speakers.

The central philosophy of the Congress is "bridging together" all major specialties in the field. Accordingly, the scientific program is carefully planned to address all interests and expertise with concentration streams on pediatric cardiology, pediatric cardiac surgery, adult congenital heart diseases, anesthesia, intensive care and nursing.

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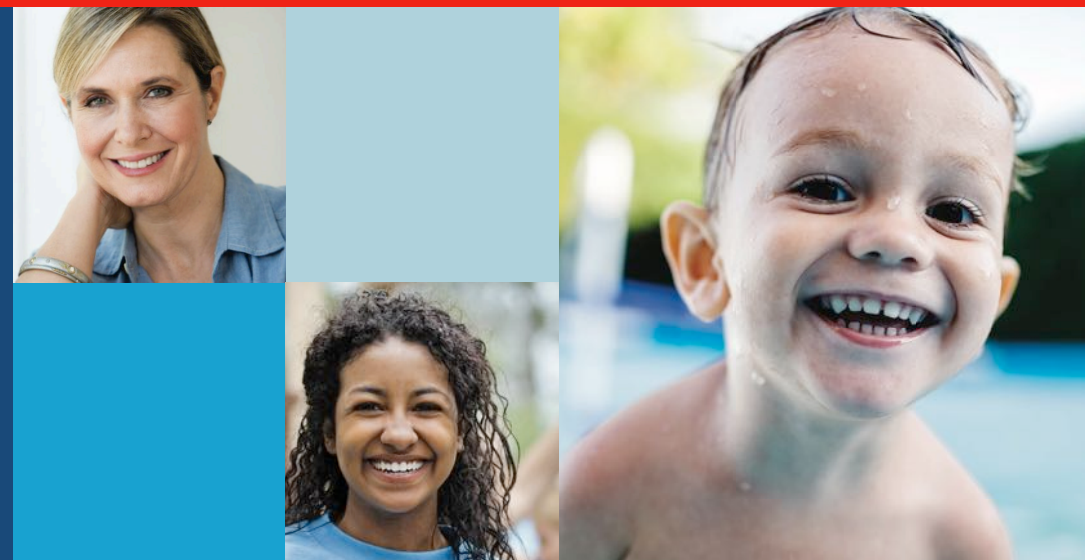
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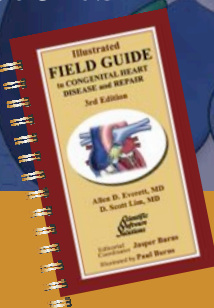


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## Medical News, Products & Information

Compiled and Reviewed by Tony Carlson, Senior Editor

### EchoPixel Announces Progress in the Clinical Adoption of Interactive Virtual Reality for Pediatric Surgery

*World-class sites including Lucile Packard Children's Hospital, Cook Children's Healthcare System, and others are pioneering the use of 3D imaging tools in Pediatric Surgery*

EchoPixel today announced progress in the clinical adoption of its True 3D virtual reality software in pediatric surgical procedures. At several leading clinical sites, surgeons and radiologists are adopting True 3D powered by HP to develop surgical plans, effectively communicate in a common 3D language, and assist in challenging procedures - including a groundbreaking seventeen-hour operation to separate conjoined twins. The progress in clinical applications marks an exciting milestone in the adoption of EchoPixel's breakthrough interactive virtual reality solution in the healthcare system.

In addition to Packard Children's and Cook Children's, pediatric sites including Nicklaus Children's Hospital in Miami and Sick Kids Hospital in Toronto are using EchoPixel's technology. Building on success in clinical uses, the company is looking to expand the role of interactive virtual reality in Pediatrics. EchoPixel's True 3D Viewer powered by HP displays existing DICOM datasets into life-size virtual reality objects, allowing physicians to move, turn, dissect, and closely examine patient-specific anatomy.

"Our True 3D Viewer has demonstrated significant results in a range of applications, from device sizing to virtual colonoscopy, but we're particularly excited about our progress in Pediatric Cardiology," said Ron Schilling, CEO of EchoPixel. "We're honored to play a role in the success of these difficult operations, and to assist physicians in understanding and working with patient anatomy."

At Lucile Packard Children's Hospital Stanford, doctors have used EchoPixel's True 3D software - in conjunction with the HP Zvr Virtual

Reality Display and HP Z440 Workstation - to assist in a number of surgical procedures. The system may be particularly effective in understanding challenging or complex cases, such as congenital heart defects in newborn patients. In December, doctors used the joint EchoPixel, HP system to assist with a groundbreaking seventeen-hour surgery that successfully separated twin girls who were conjoined from the sternum down. The system's unique 3D view helped doctors gain a more complete understanding of the unique anatomy prior to, and during, the operation.

At Cook Children's Medical Center in Fort Worth, Texas, physicians have incorporated EchoPixel's True 3D powered HP system into an integrated 3D lab, with the goal of establishing 3D planning as a diagnostic modality. The center has focused on using interactive virtual reality to better understand certain vascular anomalies in congenital heart disease.

"We're excited to establish 3D virtual viewing as part of our 3D program," said Steve Muyskens, MD, cardiologist at Cook Children's Medical Center in Fort Worth, Texas. "Having this technology, in addition to 3D printing capabilities, allows Cook Children's cardiologists and cardiothoracic surgeons to improve the planning of complex procedures and surgeries. We believe this approach will eventually lead to less time in the operating room and fewer complications."

"Our customers rely on HP to help transform lives through innovative solutions," said Reid Oakes, Senior Director, Worldwide Healthcare, HP Inc. "We've seen the value in EchoPixel's technology and our collaborative approach, and we're excited about virtual reality's ability to change the face of healthcare. The success of the EchoPixel True 3D powered by the HP system in Pediatrics really validates this as a game-changing tool for doctors."

EchoPixel is building a new world of patient care with its groundbreaking medical visualization software. The company's FDA-cleared True 3D system uses existing medical image datasets to create virtual reality environments of patient-specific anatomy,

allowing physicians to view and dissect images just as they would real, physical objects. The technology aims to make reading medical images more intuitive, help physicians reach diagnosis, and assist in surgical planning. Leading institutions, including the University of California, San Francisco, the Cleveland Clinic, the Lahey Clinic, and more are using True 3D in clinical and research applications. EchoPixel is a privately held, venture backed company located in Mountain View, CA. For more information, [www.echopixeltech.com](http://www.echopixeltech.com).

### Mapping Brain in Premies May Predict Later Disability

Newswise — MINNEAPOLIS – Scanning a premature infant's brain shortly after birth to map the location and volume of lesions, small areas of injury in the brain's white matter, may help doctors better predict whether the baby will have disabilities later, according to a new study published in the January 18, 2017, online issue of *Neurology*<sup>®</sup>, the medical journal of the American Academy of Neurology.

According to the Centers for Disease Control and Prevention, one in 10 babies is born prematurely in the United States.

Lack of oxygen to the brain is the most common form of brain injury in premature infants, resulting in damage to the white matter. White matter contains nerve fibers that maintain contact between various parts of the brain. Damage to white matter can interfere with communication in the brain and the signals it sends to other parts of the body.

"In general, babies who are born before 31 weeks gestation have a higher risk of thinking, language and movement problems throughout their lives, so being able to better predict which infants will face certain developmental problems is important so they get the best early interventions possible. Just as important is to be able to reassure parents of infants who may not be at risk," said study author Steven P. Miller, MDCM, of The Hospital for Sick Children (SickKids) in Toronto, Canada.

For the study, researchers looked at a group of premature infants who were admitted to the Neonatal ICU at British Columbia's Women's Hospital over seven years. They found 58 babies with white matter injury who had an MRI brain scan at an average of 32 weeks after gestation. These babies were then evaluated for motor, thinking and language skills when they were 18 months old.

Researchers found that a greater volume of small areas of injury, no matter where they were located in the brain, could predict movement problems at 18 months. They also found that a greater volume of these small areas of injury in the frontal lobe could predict thinking problems. The frontal lobe is the area of the brain that regulates problem solving, memory, language skills and voluntary movement skills.

The findings from this study highlight the importance of injury location when considering developmental outcomes. For example, premature infants with larger frontal lobe injuries had a 79 fold greater odds of developing thinking problems than infants without



## DIRECTOR OF CLINICAL RESEARCH NEONATAL INTENSIVE CARE UNIT YALE UNIVERSITY SCHOOL OF MEDICINE

The Department of Pediatrics at Yale School of Medicine is seeking a neonatologist to serve as Director of Clinical Research for a large academic level 4 NICU. This position will include oversight of all research protocols in the NICU, including supervision of research nurses, and mentoring of neonatology fellows and junior faculty. Experience in the NICHD neonatal research network is particularly desirable. This is an outstanding opportunity to join the leadership team of a major academic neonatology division.

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Please address inquiries, along with curriculum vitae and a list of 3 references, to:

Mark Mercurio, M.D., Chief,  
Neonatal-Perinatal Medicine  
Department of Pediatrics  
PO Box 208064  
New Haven, CT 06520  
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such injuries, as well as a 64 fold greater odds of problems with movement development.

Miller said that future studies should evaluate premature infants not just at 18 months, but at various points throughout childhood to determine the long-term consequences of early injuries in the brain.

The study was supported by the Canadian Institutes of Health Research, The Research Training Centre at The Hospital for Sick Children and SickKids Foundation, the Ontario Brain Institute and the NeuroDevNet National Centres of Excellence.

To learn more about the brain, visit [www.aan.com/patients](http://www.aan.com/patients).

The American Academy of Neurology is the world's largest association of neurologists and neuroscience professionals, with 30,000 members. The AAN is dedicated to promoting the highest quality patient-centered neurologic care. A neurologist is a doctor with specialized training in diagnosing, treating and managing disorders of the brain and nervous system such as Alzheimer's disease, stroke, migraine, multiple sclerosis, concussion, Parkinson's disease and epilepsy.

For more information about the American Academy of Neurology, visit [www.aan.com](http://www.aan.com).

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### **Prenatal Infection May Alter Brain Development Via Epigenetic Changes**

Philadelphia, PA, Jan. 24, 2017 - Maternal infection during pregnancy increases the risk for psychiatric disorders in the child, but the path between the two is something of a mystery. In a study published in January *Biological Psychiatry*, Senior Author Professor Urs Meyer of the University of Zurich-Vetsuisse in Zurich, Switzerland and colleagues use a mouse model to show that activation of the mother's immune system may cause long-term alterations in the programming of the offspring's genome, known as epigenetic modifications, which lead to behavioral abnormalities in adulthood.

"This study suggests that immunologic activation may be the connection between maternal infection to epigenetic changes that produce lasting changes in brain development," said Dr. John Krystal, Editor of *Biological Psychiatry*.

The findings provide new insight into the molecular mechanisms behind the risk factor. The alterations were found in a specific type of epigenetic modification called DNA methylation, which has been increasingly implicated in the origin of neurodevelopmental disorders. Altered DNA methylation appeared throughout the offspring's genome, and differed based on the timing of infection.

First author Dr. Juliet Richetto and colleagues induced a viral-like infection in pregnant mouse mothers at two important time points during brain development of the offspring, in early and late gestation. Immune activation at both time points produced alterations in a few common genes associated with neurodevelopment, but most were distinct. For example, late prenatal infection altered methylation of genes related to the development and function of GABA cells, whereas earlier exposure disrupted genes important for Wnt signaling, a pathway fundamental to early developmental events during embryogenesis. The findings indicate the importance of the timing of prenatal immune activation, and suggest that earlier infection may lead to more serious effects on neurodevelopment.

"Another intriguing finding of our study is that the pattern of DNA methylation in prenatally infected offspring changes over time," said

Meyer, noting that alterations that were present when the mice reached adulthood were not observed when the mice were born. According to Meyer, the findings suggest that the modifications are dynamic and are likely influenced by activity-dependent events as the mice age.

"The adult emergence of multiple epigenetic modifications also raises the clinically relevant question as to whether some of these anomalies could be attenuated or even prevented by early interventions targeting the epigenetic machinery," said Meyer.

This would have important implications because the researchers found that the infection-induced modifications had functional consequences. The mRNA levels of genes showing differential methylation were altered in the offspring, indicating the epigenetic changes were modulating gene expression. Further, the offspring exhibited cognitive and behavioral abnormalities present in animal models of neurodevelopmental disorders, such as schizophrenia and autism, suggesting that prenatal infection may cause genome-wide methylation abnormalities in these disorders. Thus, the possibility of targeting these modifications could open a potential avenue for preventative treatments in people exposed to prenatal infection.

The article "Genome-Wide DNA Methylation Changes in a Mouse Model of Infection-Mediated Neurodevelopmental Disorders," by Juliet Richetto, Renaud Massart, Ulrike Weber-Stadlbauer, Moshe Szyf, Marco A. Riva, and Urs Meyer (doi: 10.1016/j.biopsych.2016.08.010) appeared in *Biological Psychiatry*, volume 81, issue 3 (2017), published by Elsevier ([www.elsevier.com](http://www.elsevier.com)).

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

John H. Krystal, MD, is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interest are available here.

*Biological Psychiatry* is the official journal of the Society of Biological Psychiatry, whose purpose is to promote excellence in scientific research and education in fields that investigate the nature, causes, mechanisms and treatments of disorders of thought, emotion, or behavior. In accord with this mission, this peer-reviewed, rapid-publication, international journal publishes both basic and clinical contributions from all disciplines and research areas relevant to the pathophysiology and treatment of major psychiatric disorders.

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### **Monoclonal Antibody Given to Preterm Babies May Reduce Wheeze Later**

Preterm babies given the monoclonal antibody palivizumab to prevent Respiratory Syncytial Virus (RSV) appear less likely to develop recurrent wheeze, at least until the age of six, according to new research published online, ahead of print in the American Thoracic Society's *American Journal of Respiratory and Critical Medicine*.

In "Palivizumab Prophylaxis in Preterm Infants and Subsequent Recurrent Wheezing: 6-Year Follow-up Study," researchers report on a multicenter case-control study of 444 Japanese infants born at 33-35 weeks gestation. The primary goal of the study was to determine if palivizumab prophylaxis would prevent the onset of atopic asthma. The drug did not, but it did significantly reduce physician-diagnosed recurrent wheezing up to six years of age.

# 3 BIG THINGS



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In nearly 20 years of successfully matching great physicians with great opportunities, I've learned that the right physician placement depends on three primary factors – location, work life and money!

**LOCATION:** Believe it or not, location drives most physician job opportunity decisions, but people often end up in the wrong places for the wrong reasons – the placement doesn't last and they must start their search all over again after a year or so. Conversely, often the best locations are places that people rarely think of, but which offer the lifestyle and family considerations that are at the core of what people are truly looking for.

**WORK LIFE:** Work life is arguably the most complex consideration to evaluate. Do you like the people you are (or will be) working with? Do they inspire you to do your best? Does the organization appreciate you and your contribution? Are you happy there? Do you look forward to starting work each day?

**MONEY:** Contrary to popular belief, money should never be the primary consideration. Money is always important and if it isn't sufficient it will kill the deal – but money is too often used by employers to mask weakness in other areas of consideration. That might be alright if it offsets location, for example - but money alone is a poor trade-off for the ongoing misery of a bad work life.

Of course, this is just a summary of these three considerations – there is more to it as you drill down on each of these areas and evaluate opportunities. If you would like some personalized help finding a great physician practice, please contact me at [mike@hathawayhealthcare.com](mailto:mike@hathawayhealthcare.com) or 954-603-1192.

I look forward to helping you!

Sincerely,

Mike Hathaway

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"Our findings suggest two independent phenotypes of recurrent wheezing in young children: one that is dependent and one that is independent of RSV lower respiratory infection," said lead study author Hiroyuki Mochizuki, MD, PhD, Professor and Chairman of Pediatrics at Tokai University in Japan.

The researchers found that infants who received at least three doses of palivizumab according to standard medical practice had about half the incidence of physician-diagnosed wheeze by age 6, compared to those who did not receive the drug (15.3% vs. 31.6%).

A strength of the study was that it was a long-term prospective study in 52 centers with a high follow-up rate. The latter was achieved using an innovative method involving QR codes on mobile phones for photographing physician documentation of wheezing during outpatient and inpatient visits.

Study limitations include potential bias due to nonrandomized design. The authors noted that there were only minimal differences in family history of asthma, birth weight and gestational age among those who were treated and those who were not. Children in the untreated group, however, were more likely to live in a home with a smoker and have a family member with a history of allergy -- factors that would increase wheezing.

"These results suggest that atopic asthma in children up to age six is probably not due to RSV, but a significant proportion of recurrent wheeze is," Dr. Mochizuki said.

"Long-term observation of these subjects is planned to consider the impact of RSV infection on lung function in later life."

The *American Journal of Respiratory and Critical Care Medicine* (AJRCCM) is a peer-reviewed journal published by the American Thoracic Society. The Journal takes pride in publishing the most innovative science and the highest quality reviews, practice guidelines and statements in pulmonary, critical care and sleep medicine.

### One More Reason to Focus on Prenatal Care -- Stronger Muscles for Newborn Babies

Born too soon, she weighed just over 1 pound at birth and spent the first three months of her life in the Neonatal Intensive Care Unit, (NICU) fighting to live. This tiny baby survived under the care of skilled medical professionals and was sent home with her teenage mother. Today, she's a high school student enrolled in a precollege program. But is it possible that she has health risks that relate to her early life experience?

This baby is one example of a frequent and significant problem in the neonatal population - poor growth following premature birth, "a condition for which causes, optimal management and long-term consequences are still not completely understood," said Dr. Marta Fiorotto, Associate Professor of Pediatrics-Nutrition and of Molecular Physiology and Biophysics at the USDA/Children's Nutrition Research Center at Baylor College of Medicine and Texas Children's Hospital, in whose laboratory the research was performed.



## ACADEMIC NEONATOLOGIST PHYSICIAN-SCIENTIST YALE UNIVERSITY SCHOOL OF MEDICINE

The Department of Pediatrics at Yale School of Medicine is seeking an early career neonatologist, interested in pursuing a career combining laboratory-based research with clinical responsibilities in the Level IV NICU at Yale-New Haven Children's Hospital, in New Haven, CT. The ideal candidate will be on a trajectory toward becoming an independent investigator, or already functioning on that level. Significant protected time and initial research funding are available. Graduating fellows with significant research experience and potential are encouraged to apply.

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Applicants should be Board Certified or Board Eligible in Neonatal-Perinatal Medicine, and qualified for an appointment to the faculty at Yale School of Medicine.

Please address inquiries, along with curriculum vitae and a list of 3 references, to:

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Several studies have found a link between fetal malnutrition, low birth weight and low muscle mass and strength throughout life. "It is important to know how muscles are affected in the fetus because we need muscles to breathe, to eat and swallow and to move," Fiorotto said. "If those muscles are compromised in any way during fetal development, those functions are also likely to be compromised in the newborn baby and affect his or her growth."

#### *Malnutrition and Stress Affect Muscle Development*

Scientists propose that malnutrition and stress are two major environmental factors that affect fetal growth. Interestingly, these two factors expose the fetus to high levels of cortisol, an endogenous glucocorticoid, which is a class of stress steroid hormone.

"Lack of proper nutrition, a form of stress, in an expectant woman raises the levels of cortisol in her blood," said Fiorotto, who also is director of the Mouse Metabolic Research Unit at the USDA/ARS Children's Nutrition Research Center at Baylor and Texas Children's Hospital. "We wanted to know whether it was the lack of proper nutrition during pregnancy itself or the exposure to the associated increases in the levels of glucocorticoids that affected fetal growth. In adults, glucocorticoids have negative effects in the muscles, for instance, they cause atrophy and insulin resistance. Why would the newborn be any different?"

#### *What the Studies in Rats Reveal*

Dr. Ganga Gokulakrishnan, a neonatologist at Texas Children's Hospital and Assistant Professor at Baylor College of Medicine working with Dr. Fiorotto, along with her colleagues investigated how glucocorticoids affect the growth of fetal muscles in the rat.

"You can think of a muscle as a bundle of uncooked spaghetti; each spaghetti is a fiber - a single muscular cell - with many nuclei in a matrix of protein," Gokulakrishnan said. "The number of fibers is already determined by birth and does not increase during postnatal life. So, postnatally, muscles grow by adding both more protein and more nuclei to the fibers. Nuclei are added by muscle stem cells, also called satellite cells, that divide and fuse with the fibers. These muscle stem cells drive muscle growth during fetal development. After puberty, however, the muscles stop accumulating nuclei and grow by adding only protein to the fibers."

Previous studies in rats have shown that exposing fetuses to glucocorticoids impairs muscle growth, and that this is due in part to reduced protein production. In this study, Gokulakrishnan and her colleagues examined the effect of glucocorticoids on the other mechanism of muscle growth, namely the addition of nuclei to the fibers by satellite cells, during early development.

"We were surprised at the magnitude of impairment we observed in the replication of satellite cells in the muscles of fetal rats exposed to glucocorticoids," said Gokulakrishnan. "Taking all the results together, we found that the effect of glucocorticoids on fetal muscle growth is quite complex; it depends on the duration, the level of glucocorticoids and the time during pregnancy when it occurs."

For instance, when the level of stress is mild, such as when the mother's food intake is only approximately 85% of normal, protein deposition in muscles of the fetus is affected quite remarkably. However, this mild restriction in food intake does not affect the accumulation of nuclei.

"However, our results from the current study indicate that treating rats with a dose of glucocorticoids that mimics more severe food restriction affects the reserve of satellite cells, the accumulation of nuclei in the fibers, and therefore, muscle growth," Gokulakrishnan said.

The health of future generations starts with the health of the mother.

"In summary, maternal stress, due to malnutrition or other causes that increase the exposure of her fetus to glucocorticoids, can significantly affect the growth of fetal muscles," Gokulakrishnan said. "Conditions such as stress or malnutrition are factors that could be identified and mitigated by prenatal care, once again emphasizing the importance of a proper diet and antenatal care for all pregnant mothers."

"Maternal stress negatively affects the growth of the fetus at the cellular level. This has been demonstrated for other organs, including the brain," said Fiorotto. "We have now learned that, because this is affecting muscle stem cells, it is possible that these negative effects on the fetus could have life-long consequences. This is another example that illustrates how the health of future generations starts with the health of the mother."

This study also brings the effects of glucocorticoids on the fetus into play when considering treating expecting mothers or newborn babies with steroids for a medical condition. In addition, ongoing research is determining whether the deleterious effects on the fetus can be minimized or eliminated by medical intervention after birth.

The paper was published in the *Journal of Endocrinology*.

Xiaoyan Chang and Ryan Fleischmann at Baylor also contributed to this work.

This work is a publication of the USDA/ARS Children's Nutrition Research Center and the Department of Pediatrics at Baylor College of Medicine.

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#### **Mayo Clinic Enrolls First Patient in Phase 1 Study of Orally Delivered Capsule to Treat Recurrent Clostridium Difficile Infection**

Mayo Clinic announced in January that it has enrolled the first patient in a Phase 1 study of an unfrozen oral capsule formulated to treat Clostridium difficile infection (C-diff).

The capsule is formulated to rehabilitate the human gut microbiome by delivering a broad spectrum of live microbes into the patient's intestinal tract. The gut microbiome hosts trillions of microbes that live in harmony with their human host and perform processes vital for health.

"New therapies are urgently needed to prevent recurrent C-diff, a debilitating, costly and potentially life-threatening infection," says Sahil Khanna, MBBS, a gastroenterologist at Mayo Clinic and Principal Investigator on the study. He says the study will enroll approximately 20 patients in a prospective, two-arm, Phase 1, safety assessment and dosing study at Mayo Clinic's Rochester campus.

"C-diff infections are an increasingly difficult-to-resolve intestinal infection that cause about 29,000 deaths annually in the U.S.," says Dr. Khanna. Dr. Khanna says potential advantages to providing an oral capsule for treatment that is stable at room temperature include flexibility in dosing and at-home treatment. Currently, patients seeking treatment must travel to a medical center for a fecal transplant procedure that involves

the placement of live microbes into the patient's body in a procedure similar to a colonoscopy.

Mayo Clinic is a nonprofit organization committed to clinical practice, education and research, providing expert, whole-person care to everyone who needs healing. For more information, visit [www.mayoclinic.org/about-mayo-clinic](http://www.mayoclinic.org/about-mayo-clinic).

### More Extremely Preterm Babies Survive, Live Without Neurological Impairment

Babies born at just 22 to 24 weeks of pregnancy continue to have sobering outlooks -- only about 1 in 3 survive.

But according to a new study led by Duke Health and appearing Feb. 16<sup>th</sup> in the *New England Journal of Medicine*, those rates are showing small but measurable improvement. Compared to extremely preterm babies born a decade earlier, the study found a larger percentage are developing into toddlers without signs of moderate or severe cognitive and motor delay.

Changes to prenatal care, including greater use of steroids in mothers at risk for preterm birth, could have contributed to increased survival and fewer signs of developmental delay in these infants, the authors said.

"The findings are encouraging," said lead author Noelle Younge, MD, a neonatologist and Assistant Professor of Pediatrics at Duke. "We see evidence of improvement over time. But we do need to keep an eye on the overall numbers, as a large percentage of infants born at this stage still do not survive. Those who survive without significant impairment at about age 2 are still at risk for numerous other challenges to their overall health."

The researchers analyzed the records of 4,274 infants born between the 22<sup>nd</sup> and 24<sup>th</sup> week of pregnancy, far earlier than the 37 to 40 weeks of a full-term pregnancy. The babies were hospitalized at 11 academic medical centers in the Neonatal Research Network, part of the Eunice Kennedy Shriver National Institute of Child Health and Human Development at the National Institutes of Health.

About 30% of infants born at the beginning of the study (between 2000 and 2003) survived. That proportion increased to 36% for babies born toward the end of the study (from 2008 to 2011), with the best outcomes for children born at 23 and 24 weeks. Overall survival for babies born at 22 weeks remained the same throughout the study, at just 4%.

Over the 12-year study period, the proportion of infants who survived but were found to have cognitive and motor impairment at 18 to 22 months stayed about the same (about 14% to 16%). But the proportion of babies who survived without evidence of moderate or severe neurological impairment improved from 16% to 20%.

"Researchers in the Neonatal Research Network reported in 2015 that survival was increasing in this vulnerable population," Younge said. "One concern was that the improved survival might have been accompanied by a greater number of infants who went on to have impairments in the long term, such as cerebral palsy, developmental delay, hearing and vision loss. However, we actually are seeing a slight improvement. Because children continue to develop over years, it's important to continue to track this data so families and providers can make the best decisions in caring for these infants."

Improvements in survival and neurodevelopment may be the result of a number of factors, including declining rates of infection in the infants, along with the increased use of steroids in expectant mothers that can help mature and strengthen the fetus's lungs prior to birth. At the beginning of

## Family Centered Care is trendy, but are providers really meeting parents needs in the NICU?

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You may be surprised to see what NICUs are doing right and where their efforts are clearly falling short.

Graham's Foundation empowers parents of premature babies through support, advocacy and research to improve outcomes for their preemies and themselves.



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the study, 58% of the expectant mothers had received steroids to boost fetal development. That figure increased to 64% by the end of the study.

"The culture of Neonatal Intensive Care Units has really changed in the past decade," said senior author C. Michael Cotten, MD, a neonatologist and Professor of Pediatrics at Duke. "We've taken a big focus on preventing infections, and there's a lot more encouragement and support for the use of mother's milk than there was 15 years ago, which has also been linked to better outcomes."

Extremely preterm infants are highly susceptible to infections. Neonatal Intensive Care Units have reported steady decreases in infection rates among extremely preterm infants over the past two decades.

"This is important because infections have been associated with greater risk of neurologic problems," Cotten said.

In addition to their work with the Neonatal Research Network studying strategies to improve outcomes for preterm babies, the Duke researchers continue to study environmental and genetic factors, as well as the babies' gut bacteria and metabolomics.

"We're always looking at how we can make further headway and continue to improve survival and reduce illness in this population," Cotten said. "The results of this study are encouraging, but there's still a long way to go."

In addition to Younge and Cotten, study authors were: Ricki F. Goldstein; Carla M. Bann; Susan R. Hintz; Ravi M. Patel; P. Brian Smith; Edward F. Bell; Matthew A. Rysavy; Andrea F. Duncan; Betty R. Vohr; Abhik Das; Ronald N. Goldberg; and Rosemary D. Higgins.

The research was supported by the National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Center for Research Resources, and the National Center for Advancing Translational Sciences, which provided grant support for the Neonatal Research Network's Generic Database and Follow-up Studies through cooperative agreements (U10 HD27904, U10 HD21364, M01 RR80, U10 HD68284, U10 HD27853, M01 RR8084, U10 HD40492, M01 RR30, U10 HD27851, M01 RR39, U10 HD27856, M01 RR750, U10 HD68278, U10 HD36790, U10 HD27880, M01 RR70, UL1 TR93, U10 HD53119, M01 RR54, U10 HD34216, M01 RR32, U10 HD68270, U10 HD40461, U10 HD53109, M01 RR59, U10 HD21397, M01 RR16587, U10 HD27881, U10 HD53089, M01 RR997, U10 HD68244, U10 HD68263, U10 HD40521, UL1 RR24160, M01 RR44, UL1 TR42, U10 HD21415, U10 HD21373, U10 HD40689, M01 RR633, U10 HD53124, M01 RR64, UL1 TR105, U10 HD40498, M01 RR7122, U10 HD21385, U10 HD27871, UL1

RR24139, M01 RR125, UL1 TR142). Younge received support from National Institutes of Health (5T32HD043728-10, HD060558-05; 4K12HD043494-14).

**E-mail comments to:**  
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## Upcoming Medical Meetings

### 14<sup>th</sup> National Advanced Practice Neonatal Nurses Conference

*Apr. 19-27, 2017; Waikiki Beach, HI USA*  
[www.academyonline.org](http://www.academyonline.org)

### 1<sup>st</sup> World Congress on Maternal Fetal Neonatal Medicine

*Apr. 23 - 26, 2017; London, UK*  
[www.worldmfmf.com](http://www.worldmfmf.com)

### 15<sup>th</sup> Annual AirBorne Neonatal and Pediatric Transport Conference

*May 10-12, 2017; Austin, TX USA*  
<http://int-bio.com/events-news/airborne-conference/>

### The 28<sup>th</sup> Annual Meeting of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC 2017)

*Jun. 6-9, 2017; Lisbon, Portugal*  
<http://espnice2017.kenes.com>

### 3<sup>rd</sup> International Neonatology Association Conference (INAC 2017)

*Jul. 7-9, 2017; Lyon, France*  
<http://2017.worldneonatology.com/>

### 6<sup>th</sup> National Neonatal Simulation Conference

*Sep. 26-27, 2017; Southampton, UK*  
[www.mproveonline.com/conference](http://www.mproveonline.com/conference)

### 7<sup>th</sup> International Arab Neonatal Care Conference

*Sep. 29-Oct. 1, 2017; Dubai Festival City*  
<http://ancc2017.info>

### 8<sup>th</sup> Phoenix Fetal Cardiology Symposium

*Oct. 27-31, 2017; Phoenix, AZ USA*  
[www.fetalcardio.com](http://www.fetalcardio.com)

### 20<sup>th</sup> International Conference on Neonatology and Perinatology

*Dec. 4-6, 2017 Madrid, Spain*  
<http://neonatology.conferenceseries.com>

## NEONATOLOGY TODAY

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ISSN: 1932-7137 (digital).  
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# Physician Job Offers and Attorney Management

By Mike Hathaway

## Why Read This?

Physician recruiters often hear candidates talk about the “offers” they have, especially graduating residents and fellows. What’s been interesting to me over the years is how what is being called an “offer” is usually not really an offer at all. Often, the term is used synonymously with “lead,” and that’s all it is - they’ve heard about an opening somewhere but haven’t actually had a meaningful conversation with anyone about it yet. Although it’s becoming rarer, I’ve seen instances where a potential candidate will be given a “courtesy interview” even though there is no opening. This might be good interview practice for a candidate, but it should never be confused with an actual job opportunity. Too often, a candidate’s hopes are dashed when the “offer” they thought they had never actually materializes into a job. So, let’s look at what is an offer, what isn’t, and how to deal with a real one!

## What is an Offer?

To put it in the simplest terms, an offer is when you can say “yes” and have a job with a defined start date, compensation and benefits package, location, etc. Offers are also part of the negotiating process - this is where you and your potential employer will get into fine tuning one another’s expectations regarding those things. An initial offer may be verbal, but you will want it written as soon as possible.

Typically, an offer is extended verbally in a phone call AFTER at least one on-site interview. Increasingly, verbal offers are

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***“Too often, a candidate’s hopes are dashed when the “offer” they thought they had never actually materializes into a job. So, let’s look at what is an offer, what isn’t, and how to deal with a real one!”***

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reiterated by email, often to provide a record of your verbal acceptance in the phone call. Upon your acceptance of an offer, the employing entity will work on sending you a contract (sometimes simply an *Offer Letter*) that you can sign and return to solidify your position. Be patient here. Even the most efficient organizations will have an established process with several steps - it’s going to take a few days to get the contract to you. Larger practice management companies may even take a few weeks to physically deliver an executable contract - this is normal, be patient. This is a good time to shop for attorneys if you feel you need one, but don’t retain one just yet.

Once you have an executable contract/offer letter in hand, my advice is to sit down with some quiet time to read it carefully. Make notes of anything you have questions about. There may be some things that you will want an attorney to review, but have your notes ready before you spend the money. Plan on \$300 to \$500 for an attorney to review an employment contract.

## Attorney Management

Attorney management is a term I use to help candidates understand the relationship that they should have with the attorney they hire to review a contract. You’re smart enough to become a medical professional, so you’re smart enough to understand that your attorney works for you - not the other way around. You want to clearly define for them that their role is to help you understand the contract, and what it requires of you. I’ve seen too many people lose great opportunities because their attorney felt compelled to rewrite the contract, often with no meaningful changes other than language or with overly onerous conditions that couldn’t possibly be agreed to. Sometimes it seems that some attorneys feel that they must justify their fee by butchering your deal. Don’t let that happen. You want them to clarify the implications of the contract so that you can make an intelligent decision - period! That’s not to say that offered contracts are never subject to some final tweaking, they usually are - but a tweak is not a full rewrite.

You MUST specify to your attorney when you want the review to be complete. It should not take more than a week turnaround, even for a busy legal practice. There is an old saying in the recruiting business that “time

kills all deals” - and that can certainly be true if it takes too long to execute a contract that’s already taken a while to get out to you.

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***“IMPORTANT:  
For physicians and advanced practice clinicians working in hospital environments, an offer is always contingent on being successfully credentialed with the hospital(s).”***

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## What is NOT an Offer?

This is easy. Anything that is not an opportunity to commit and have a job secured is NOT a job offer. If you cannot say “yes” and be done, then you have only just begun.

NT



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# 99nicu

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Welcome to the **99nicu Meetup** in Stockholm! The exciting program includes lectures and workshops by neonatal staff with real expertise. Topics include:

- preventing infections,
- hypothermia,
- delivery room management,
- PDA controversies,
- ventilation,
- infant feeding,
- social media, and
- family-centered neonatal care
- and more....



Stefan Johansson, MD, PhD



Francesco Cardona, MD, MPH

***See you in Stockholm!***

**For detailed information on the programs and workshops,  
invited faculty, CME credits, poster sessions and sponsors, go to:  
<https://99nicu.org/meetup>**

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