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Upcoming Medical Meetings

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Annual Neonatal Advanced Practice Nursing Forum

May 28, 2014; Washington, DC USA
www.chadkids.org/apnforum

Basic and Advanced Fetal Cardiology Symposium Workshop

Jun. 5-6, 2014; Chicago, IL USA
fetalcardiacsymposium.com

8th Annual Intensive Kangaroo Care (Skin-to-Skin Contact) Certification Course

Jun. 6-8, 2014; Cleveland, OH USA
www.kangaroo-careusa.org/events.html

XXII Parma International Echo Meeting

Jun. 16-18 2014; Parma, Italy
email: umbertosquarcia@gmail.com

World Symposium of Perinatal Medicine

Nov. 20-22, 2014; San Diego, CA USA
www.worldsymposium.net

Continuous Quality Improvement Pre-Conference at NEO

Feb. 18, 2015; Orlando, FL USA
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NEO: The Conference for Neonatology

Feb. 18, 2015; Orlando, FL USA
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Surgical Strategy for Thrombosed Unilateral Absence of a Pulmonary Artery

By Mark Cartoski, MD; Jessica M. Parson, BS; Alexander Ellis, MD; Elliot Tucker, MD; Felix W. Tsai, MD

Introduction

Unilateral Absence of a Pulmonary Artery (UAPA), first described by Frantzel in 1868, is a rare cardiac anomaly thought to develop from the persistence of the hilar components of the pulmonary artery to the distal sixth aortic arch with concurrent involution of the proximal portion of the same arch.^{1,2} It is a rare defect with an estimated prevalence in adult males of 1 in 200,000.¹ It is often associated with other cardiovascular anomalies such as Tetralogy of Fallot, pulmonary atresia, and Ventricular Septal Defect (VSD); however, UAPA may occur as an isolated finding.^{2,3} Left-sided defects, while UAPA is more often diagnosed with other cardiac defects while right-sided UAPA is more likely to be seen as a solitary finding.⁴ UAPA treatment strategies have mostly been limited to older presentations from single institution case reports; none have discussed neonatal presentations or strategies.^{1,4}

Case Description

A previously healthy two-day-old term female infant was referred to our center for evaluation of Congenital Heart Disease following an episode of desaturation to 80% at 16 hours of life. An echocardiogram demonstrated only a single left pulmonary artery with a small ipsilateral Patent Ductus Arteriosus (PDA) with bidirectional flow. Following transfer to our hospital,

“Unilateral absence of a pulmonary artery (UAPA), first described by Frantzel in 1868, is a rare cardiac anomaly thought to develop from the persistence of the hilar components of the pulmonary artery to the distal sixth aortic arch with concurrent involution of the proximal portion of the same arch.^{1,2}”

the infant was started on Prostaglandin E (PGE) infusion. After several hours of PGE infusion and clinical stability with oxygen saturations of 95%, a repeat echocardiography failed to show any discernible right pulmonary artery flow. No aortic collaterals were noted going to the right lung and no right-sided pulmonary venous flow could be seen. Right ventricular enlargement, PDA bidirectional flow, and interventricular septal flattening were all suggestive of elevated right heart pressures.

Prostaglandin therapy was continued. Computed tomographic arteriography was suggestive of a distal right pulmonary artery (RPA) that

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originated from an occluded right-sided PDA (Figure 1A and 1B). The lumen and size of the RPA could not be established as no contrast entered it. The right lung was otherwise well-developed with normal pulmonary venous return. Cardiac catheterization confirmed the diagnosis of anomalous origin of the RPA from the innominate artery via an occluded right sided ductus, as well as the presence of thrombus in the distal RPA (Figure 2A and 2B).

The next day, the patient was taken to the operating room to re-establish branch pulmonary artery continuity. The operation was performed through a median sternotomy without cardiopulmonary bypass. Upon opening the chest, the right lung was noted to be clearly paler than the left lung. A portion of the pericardium was harvested and formed into a 6 mm diameter tube using 7-0 Prolene suture. The patient was then systemically heparinized with 150 units/kilogram. In addition, PGE infusion was maintained and inhaled nitric oxide was started at 20 parts per million to avoid right ventricular failure during repair. Once snares were placed around the right-sided PDA, as well as the right upper and lower pulmonary artery branches, an incision was made in the right lower lobe branch. A Fogarty catheter was passed to remove all intraluminal clots within the RPA. The pericardial tube was then connected to the right pulmonary artery in an end-to-side fashion. The tube was clamped and the right-sided snares were released, allowing continuous blood flow to the right lung via the right PDA. The pericardial roll was placed behind the aorta, trimmed to the appropriate length, and sewn in an end-to-side fashion to the main pulmonary artery after placement of a side biting clamp. Both right and left ducti were then ligated, which did not significantly change systemic or pulmonary blood flow. The chest was closed and the patient was transferred to the Intensive Care Unit in stable condition. Her post-operative course was uneventful and she was discharged six days after the operation on daily furosemide and prophylactic aspirin.

Post-operative echocardiography showed persistent patency of the pericardial tube; however, she was lost to follow-up for several months. When she returned for care at 6 months, an echocardiogram revealed the interval development of some RPA stenosis. Cardiac catheterization revealed narrowing of the reconstructed RPA with the minimal diameter of 3-4 mm (Figure 3A). Initial RPA angioplasty with

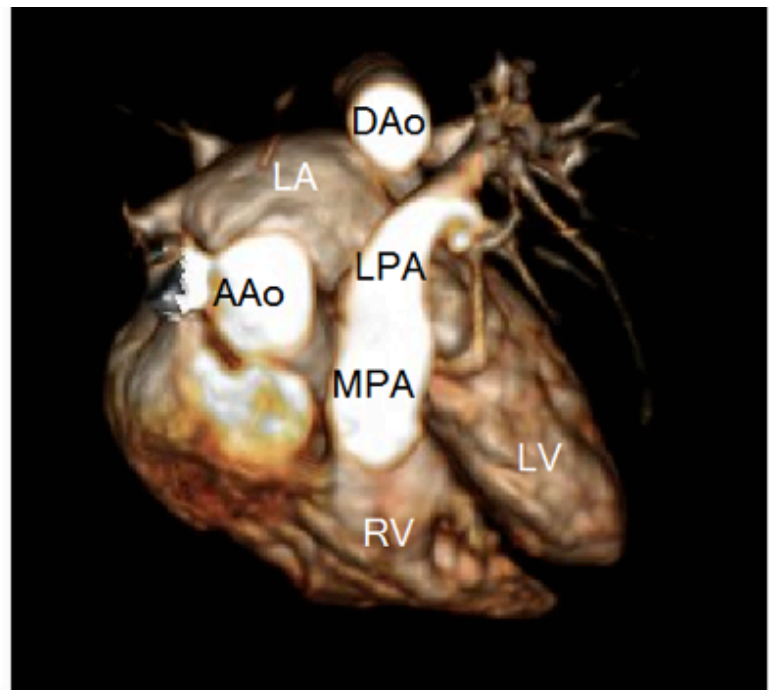
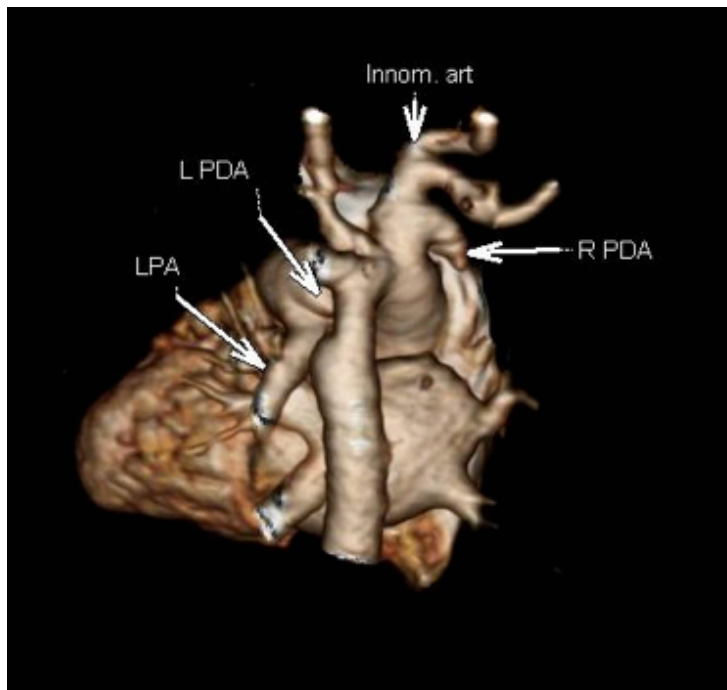
a 7 mm balloon resulted in a residual waist in the RPA. An 8 mm diameter, 18 mm length Valeo stent was placed. Initial dilation to 14 atmospheres of pressure resulted in residual stenosis. Subsequent dilatation with an 18 mm Conquest balloon taken to 23 mm atmospheres of pressure showed complete resolution of the waist, with angiographic equivalency of RPA and LPA flow. Prior to stent placement, right ventricular pressure was 27/5 mmHg and RPA pressure was 17/11 mmHg. Following angioplasty and stent placement, right ventricular pressure was 27/8 mmHg and RPA pressure was 20/8 mmHg. Repeat cardiac catheterization done 15 months postoperatively showed a widely patent RPA with a right ventricular pressure of 22/7 mmHg. She is doing well without clinical or echocardiographic evidence of recurrent RPA stenosis. She is off aspirin.

Discussion

The natural history of UAPA typically involves a progression of recurrent respiratory infections, hemoptysis due to congestion of collateral arterial circulation, and pulmonary hypertension. Signs and symptoms in infancy may include: murmur, failure to thrive, cyanosis, heart failure, and less commonly, respiratory distress or signs of pulmonary hypertension. As patients may remain asymptomatic or have vague symptoms, the diagnosis of UAPA can be difficult to make in infancy, which contributes to the later age at presentation with resultant difficulties in repair and effects on symptoms and outcomes.^{5,6}

Anatomic repair can be delayed by using a temporary modified Blalock-Taussig shunt to re-establish pulmonary perfusion.⁷ Previous case reports describe surgical palliation of UAPA utilizing artificial conduits such as Polytetrafluoroethylene (PTFE) initially or repair with native tissue, such as a main pulmonary artery flap or pericardium to augment the anterior wall.^{2,3} The present case differs in that we describe a single-stage surgical approach for repairing UAPA utilizing only an autologous pericardial tube.

An artificial graft in our patient would have been unable to grow with the patient, a critically important issue in the pediatric population. In a previous study, the diameters of PTFE grafts used in infant UAPA repairs measured 5 mm-8 mm, whereas the diameter of an adult right



Figures 1. Computed tomography angiogram illustrating complete absence of proximal RPA and presence of occluded right ductus arteriosus (R PDA). Left pulmonary artery (LPA), MPA (main pulmonary artery), AAo (ascending aorta), LA (left atrium), RV (right ventricle), LV (left ventricle).

or left pulmonary artery is at least 15 mm.³ Using a graft that does not enlarge over time requires a child to undergo subsequent staged operations to ensure they have a normally-sized PA and attendant adequate blood flow to the affected lung. An autologous pericardial tube, however, has the demonstrated potential to grow with the patient.⁸ In addition, although anatomic placement of the pericardial roll behind the aorta may result in external compression, pericardial

rolls have demonstrated enough compliance to withstand transcatheter ballooning and stenting as needed.⁸

Our patient presented with cyanosis and imaging evidence of an UAPA associated with acute distal RPA thrombus, and concerns for the subsequent development of an isolated right lung and pulmonary hypertension. Revascularization was achieved with thrombectomy and



Figures 2. Cardiac catheterization with anterior (Figure 2A) and non-simultaneous lateral (Figure 2B) views illustrating right ductus arteriosus off innominate artery giving rise to RPA with thrombus present in the right lower pulmonary artery. Figure 2A has right PDA opened with #3 French pigtail catheter.



Figures 3. Cardiac catheterization at nearly 7 months of life showing anterior views before (Figure 3A) and after (Figure 3B) stent placement. Figure 2A demonstrates 3-4 mm narrowing of the RPA prior to stent placement.

“As patients may remain asymptomatic or have vague symptoms, the diagnosis of UAPA can be difficult to make in infancy, which contributes to the later age at presentation with resultant difficulties in repair and effects on symptoms and outcomes.^{5,6}”

placement of a native pericardial tube to reconnect the main pulmonary artery and RPA. The Valeo stent placed is capable of dilatation to 18 mm, minimizing the need for future staged surgical intervention as our patient grows.

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- Comprehensive references are not required. We recommend that you provide only the most important and relevant references using the standard format.
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For the Love of Gracie: When Parent Support Goes Global

By Deb Discenza

When one thinks of supporting someone in a health situation, the vision is something akin to holding a hand, sitting by a bedside. Yet, with the Internet weaving its magical web across healthcare, it now also includes reaching out with keystrokes on a keyboard.

I know this all too well because I am a volunteer moderator on the free Inspire health network at www.Inspire.com. The forum I moderate is the “Preemie” forum at www.Inspire.com/preemie, and we have over 16,000 parents on there from around the world with more joining every day.

It was through my daily reviewing of discussion threads that I happened upon one from a parent with the user name “Dos” – an Australian mother of 25-week twin girls, Grace and Chelsea, but it was Gracie who was in grave danger. This mother, Donna O’Sullivan, reached out in earnest to our community of parents, some of whom have babies still in the Neonatal Intensive Care Unit (NICU), others with babies at home, and still others, like myself, with a child now in school. Her discussion thread entitled, “Desperately holding onto hope,” created a stir in our community ending up with 344 total responses to her plea for help and yes, for hope.

Gracie quickly became the battle cry of so many parents out there fighting to give their babies with Bronchopulmonary Dysplasia (BPD) a chance at life. It was as if our community was right there at Gracie’s bedside in the Pediatric Intensive Care Unit (PICU) working through the struggles and the joys. Collectively, we had an online celebration of Gracie’s first birthday, something Donna herself worried would not happen. It did, and we continued to rally around Donna and her sweet Gracie. Many of us threw out ideas and suggestions. I even reached out to my connections in the field of Neonatology here in the United States, and received their thoughts and advice as well. Never has compassion spanned across a parent/professional relationship as it did with this scenario. It has shown me the tightrope of emotions NICU professionals must walk on a daily basis when tending an infant that is so fragile. I was truly humbled by the professional struggles alongside the parent struggles.

Giving her daughter every possible chance at life, Donna herself continued to seek answers, reaching out to the stem cell research community directly for help. She got back responses and things were starting to look promising on that front despite the research being experimental at best. Unfortunately, Gracie had set-



back after setback due to very common illnesses that her body could just not fight.

All the while, the community checked in on Donna’s discussion thread, hoping there was news. Many posted that they were thinking about her and hoping “today was a good day for Gracie.” There were days of struggle and then there were days of triumph.

Eventually, Donna, her family and her medical team came to understand that Gracie was growing continually weaker and the unthinkable came to be a reality. Gracie was being prepared to be taken off life support and to be kept comfortable in her mother’s arms as she died. With this new reality coming forward, Donna and her family reached out to the community again for suggestions on poems to read to Grace during her final moments. Responses came back in fast and furious with lists of poems, as well as words of strength, resources for grieving and more for Donna and the family. A couple of days later Donna posted again with the news that Gracie had passed away peacefully in her arms with the poems being read to her one by one. Donna’s eulogy a few days later wove many of the Inspire discussion thread sentiments about her daughter through the text.

Our community had lifted up Gracie and her family at a time when the world doesn’t know what to say when a baby is so sick and might die. We spoke to her and we supported her. And even in death, we continue to support Donna in the most important ways – with our presence online and even more so. One of our community members, Jenny Reyes of Santa Ana, CA, reached out to me about sending the discussion thread posters’ requests for sending Donna sympathy cards, one day at a time. In the end we had 28 cards going out in the mail to Australia from all over the world. As the holidays approach, Donna will once again be supported by our community as we send her supportive holiday messages as well. For our families, Inspire is not just an online forum – it is an extension of our families. And for many of us, it replaces families that often do not understand the traumatic experience behind a premature



birth and the ongoing needs should the baby make it home from the NICU.

Gracie’s book of life is not truly closed. Many families would pull back from such a traumatic time to look inward and not outward. Yet with incredible selflessness Donna and her family have put a face, and a name to fundraising for stem cell research: Gracie, as the face to promote the Ritchie Centre at the Monash Institute of Medical Research, an Australian group of researchers looking to use placental stem cells as a treatment for BPD. Like so many babies on our Inspire board, Grace symbolizes the ongoing need for research to help save lives. For more information or to spread the word about this effort go to: <http://bit.ly/LoveGracie>.

“We can do no great things, only small things with great love.” ~ Mother Teresa

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INDICATION

SURFAXIN[®] (lucinactant) Intratracheal Suspension is approved by the FDA for the prevention of respiratory distress syndrome (RDS) in premature infants at high risk for RDS.

IMPORTANT SAFETY INFORMATION

SURFAXIN (lucinactant) Intratracheal Suspension is intended for intratracheal use only. The administration of exogenous surfactants, including SURFAXIN, can rapidly affect oxygenation and lung compliance. SURFAXIN should be administered only by clinicians trained and experienced with intubation, ventilator management, and general care of premature infants in a highly supervised clinical setting. Infants receiving SURFAXIN should receive frequent clinical assessments so that oxygen and ventilatory support can be modified to respond to changes in respiratory status.

Most common adverse reactions associated with the use of SURFAXIN are endotracheal tube reflux, pallor, endotracheal tube obstruction, and need for dose interruption. During SURFAXIN administration, if bradycardia, oxygen desaturation, endotracheal tube reflux, or airway obstruction occurs, administration should be interrupted and the infant's clinical condition assessed and stabilized. Overall the incidence of administration-related adverse events did not appear to be associated with an increased incidence of serious complications or mortality relative to the comparator surfactants.

SURFAXIN is not indicated for use in acute respiratory distress syndrome (ARDS).

For more information about SURFAXIN, please visit www.SURFAXIN.com and see accompanying brief summary on the next page.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please see package insert for full prescribing information.

INDICATIONS AND USAGE

SURFAXIN® is indicated for the prevention of respiratory distress syndrome (RDS) in premature infants at high risk for RDS.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Acute Changes in Lung Compliance

Administration of exogenous surfactants, including SURFAXIN, can rapidly affect lung compliance and oxygenation. SURFAXIN should be administered only by clinicians trained and experienced in the resuscitation, intubation, stabilization, and ventilatory management of premature infants in a clinical setting with the capacity to care for critically ill neonates. Infants receiving SURFAXIN should receive frequent clinical assessments so that oxygen and ventilatory support can be modified to respond to changes in respiratory status.

Administration-Related Adverse Reactions

Frequently occurring adverse reactions related to the administration of SURFAXIN include bradycardia, oxygen desaturation, reflux of drug into the endotracheal tube (ETT), and airway/ETT obstruction.

Increased Serious Adverse Reactions in Adults with Acute Respiratory Distress Syndrome (ARDS)

Adults with ARDS who received lucinactant via segmental bronchoscopic lavage had an increased incidence of death, multi-organ failure, sepsis, anoxic encephalopathy, renal failure, hypoxia, pneumothorax, hypotension, and pulmonary embolism. SURFAXIN is not indicated for use in ARDS.

Clinical Trials Experience

The efficacy and safety of SURFAXIN for the prevention of RDS in premature infants was demonstrated in a single randomized, double-blind, multicenter, active-controlled, multi-dose study involving 1294 premature infants (Study 1). Infants weighed between 600 g and 1250 g at birth and were 32 weeks or less in gestational age. Infants were randomized to received 1 of 3 surfactants, SURFAXIN (N = 524), colfosceril palmitate (N = 506), or beractant (N = 258). Co-primary endpoints were the incidence of RDS (defined as having a chest x-ray consistent with RDS and an FiO₂ ≥ 0.30) at 24 hours and RDS-related mortality at 14 days. The primary comparison of interest was between SURFAXIN and colfosceril palmitate with the intent of demonstrating superiority. Beractant served as an additional active comparator. Compared to colfosceril palmitate, SURFAXIN demonstrated a statistically significant improvement in both RDS at 24 hours and RDS-related mortality through Day 14. A second multicenter, double-blind, active-controlled study involving 252 premature infants was also conducted to support the safety of SURFAXIN (Study 2). Infants weighed between 600 g and 1250 g and were less than 29 weeks in gestational age. Infants received 1 of 2 surfactants, SURFAXIN (N = 119) or poractant alfa (N = 124).

The safety data described below reflect exposure to SURFAXIN administered intratracheally to infants at a dose of 5.8 mL per kg (up to 4 doses) in either 4 aliquots (Study 1) or 2 aliquots (Study 2) in 643 premature infants.

Comparator surfactants colfosceril palmitate and beractant were administered at the recommended doses (5.0 and 4.0 mL per kg, respectively) while the first dose of poractant alfa administered (2.2 mL per kg) was less than the recommended dose of 2.5 mL per kg. Any subsequent doses of poractant alfa were at the recommended 1.25 mL per kg dose.

Overall, the incidence of administration-related adverse reactions was higher in infants who received SURFAXIN compared to other surfactants (Table 1) and resulted in a greater proportion of infants treated with SURFAXIN who experienced administration-related oxygen desaturation and bradycardia. For Study 1, oxygen desaturation was reported in 17%, 9%, and 13% and bradycardia for 5%, 2%, and 3% of infants treated with SURFAXIN, colfosceril palmitate, and beractant, respectively. For Study 2, oxygen desaturation was reported in 8% and 2% and bradycardia in 3% and 2% of infants treated with SURFAXIN and poractant alfa, respectively. These adverse reactions did not appear to be associated with an increased incidence of serious complications or mortality relative to the comparator surfactants (Table 2).

Table 1. Administration-Related Adverse Reactions in SURFAXIN Controlled Clinical Studies^a

	Study 1 ^b			Study 2 ^c	
	SURFAXIN (N = 524)	Colfosceril palmitate (N = 506)	Beractant (N = 258)	SURFAXIN (N = 119)	Poractant alfa (N = 124)
Total Doses Administered	994	1038	444	174	160
Total Number of Events (Events per 100 Doses)					
ETT Reflux	183 (18)	161 (16)	67 (15)	47 (27)	31 (19)
Pallor	88 (9)	46 (4)	38 (9)	18 (10)	7 (4)
Dose Interruption	87 (9)	46 (4)	30 (7)	7 (4)	2 (1)
ETT Obstruction	55 (6)	21 (2)	19 (4)	27 (16)	1 (1)

^a Table includes only infants who received study treatment.

^b Study 1 doses were administered in 4 aliquots.

^c Study 2 doses were administered in 2 aliquots.

Table 2. Common Serious Complications Associated with Prematurity and RDS in SURFAXIN Controlled Clinical Studies Through 36-Weeks Post-Conceptual Age (PCA)

	Study 1			Study 2	
	SURFAXIN (N = 527) %	Colfosceril palmitate (N = 509) %	Beractant (N = 258) %	SURFAXIN (N = 119) %	Poractant alfa (N = 124) %
Apnea	52	52	46	66	75
Intraventricular hemorrhage, all grades	52	57	54	39	38
-Grade 3/4	19	18	21	13	8
Periventricular leukomalacia	10	10	12	4	9
Acquired sepsis	44	44	44	45	52
Patent ductus arteriosus	37	35	37	43	44
Retinopathy of prematurity, all grades	27	26	25	32	31
-Grade 3/4	6	7	6	5	9
Necrotizing enterocolitis, all grades	17	17	19	13	15
-Grade 2/3	6	8	14	8	8
Pulmonary air leak through Day 7, all types	15	17	14	9	7
-Pulmonary interstitial emphysema	9	10	10	3	5
-Pneumothorax	3	4	2	4	1
Pulmonary hemorrhage	10	12	14	6	9

All-cause mortality through 36-weeks PCA was similar regardless of which exogenous surfactant was administered.

Adverse reactions reported in the controlled clinical studies through 36-weeks PCA occurring in at least 10% of infants were anemia, jaundice, metabolic acidosis, oxygen desaturation, hyperglycemia, pneumonia, hyponatremia, hypotension, respiratory acidosis, and bradycardia. These reactions occurred at rates similar to the comparator surfactants.

No assessments for immunogenicity to SURFAXIN were performed in these clinical studies.

Follow-up Evaluations

Twelve-month corrected-age follow-up of 1546 infants enrolled in the 2 controlled clinical studies demonstrated no significant differences in mortality or gross neurologic findings between infants treated with SURFAXIN and those treated with the comparator surfactants (colfosceril palmitate, beractant, or poractant alfa).

OVERDOSAGE

There have been no reports of overdose following the administration of SURFAXIN.

HOW SUPPLIED/STORAGE AND HANDLING

SURFAXIN (lucinactant) Intratracheal Suspension is supplied sterile in single-use, rubber-stoppered, clear glass vials containing 8.5 mL of white suspension (NDC 68628-500-31). One vial per carton.

Store SURFAXIN in a refrigerator at 2° to 8°C (36° to 46°F) and protect from light until ready for use. Do not freeze. Vials are for single use only. Discard any unused portion of SURFAXIN. Discard warmed vials of SURFAXIN if not used within 2 hours of warming.

To report SUSPECTED ADVERSE REACTIONS, contact Discovery Laboratories, Inc. at 1-877-SURFAXN (877-787-3296) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Medical News, Products & Information

Parental Exposure to Marijuana Linked to Drug Addiction and Compulsive Behavior in Unexposed Progeny

Newswise - Exposing adolescent rats to THC (tetrahydrocannabinol), the primary psychoactive ingredient in marijuana—can lead to molecular and behavioral alterations in the next generation of offspring, even though progeny were not directly exposed to the drug, researchers at the Icahn School of Medicine at Mount Sinai have found. Male offspring showed stronger motivation to self-administer heroin during their adulthood and molecular changes in the glutamatergic system, which is the most important excitatory pathway for neurotransmission in the brain. Damage in the glutamate pathway, which regulates synaptic plasticity, has been linked to disturbances in goal-directed behavior and habit formation.

The study was published online Jan. 22nd in *Neuropsychopharmacology*.

“Our study emphasizes that cannabis [marijuana] affects not just those exposed, but has adverse effects on future generations,” said Yasmin Hurd, PhD, the study’s senior author, and Professor of Psychiatry and Neuroscience at the Icahn School of Medicine at Mount Sinai. “Finding increased vulnerability to drug addiction and compulsive behavior in generations not directly exposed is an important consideration for legislators considering legalizing marijuana.”

In the study, Dr. Hurd and colleagues gave adolescent male rats 1.5 mg/kg of THC, similar to about one joint in human use. None of the rats had been exposed to THC before, but their parents were exposed to THC as teens and then mated later in life. THC-exposed offspring worked harder to self-administer heroin by pressing a lever multiple times to get heroin infusion.

Although marijuana use and safety tends to be discussed in terms of its impact on the individual during the lifetime, few studies have addressed adverse effects in future generations. “What this opens up are many questions regarding the epigenetic mechanisms that mediate cross-generational brain effects,” said Dr. Hurd.

Future studies are now being explored to determine whether THC effects continue to be transmitted to even the subsequent grandchildren and great-grandchildren generations. Another important question relates to potential treatment interventions in order to reverse the cross-generational THC effects. Such insights could also have implications for novel treatment opportunities for related psychiatric illnesses.

Henrietta Szutorisz, PhD; Jennifer A. DiNieri, PhD; Eric Sweet, PhD; Gabor Egervari, MD, Michael Michaelides, PhD, Jenna Carter, PhD; Yanhua Ren, PhD; Michael Miller; and Robert D. Blitzer, PhD, all from the Icahn School of Medicine at Mount Sinai also contributed to this study, which was supported by the National Institutes of Health grants DA030359 and DA033660. For more information, visit www.mountsinai.org.

Preterm Birth is Associated with Increased Risk of Asthma and Wheezing Disorders

Children who are born preterm have an increased risk of developing asthma and wheezing disorders during childhood according to new research published in *PLOS Medicine*.

The research by Jasper Been, from the Maastricht University Medical Centre (Netherlands) and The University of Edinburgh (UK), and colleagues at Harvard Medical School (US) is a systematic review and meta-analysis of 30 unique studies that collectively involved approxi-

mately 1.5 million children. The authors found that children born preterm (before 37 weeks of gestation) were about 46% more likely to develop asthma or a wheezing disorder during childhood, than babies at full term (≥ 37 weeks of gestation). The authors also found that children born very preterm (<32 weeks of gestation) were at even higher risk of developing asthma or a wheezing disorder, almost three times as likely as children born at full term. The authors estimate that if no preterm births had occurred, there would have been more than a 3.1% reduction in childhood wheezing disorders.

The findings are important because increasing numbers of preterm babies survive today thanks to improvements in the management of prematurity, with approximately 11% of children now being born preterm. However, accumulating evidence suggests that early life events are involved in the subsequent development of non-communicable diseases. Given the increasing burden of preterm birth, a better understanding of the long-term effects of preterm birth is essential.

The authors say, “[t]he current findings do not support prior suggestions that the association between preterm birth and wheezing disorders becomes less prominent with increasing age [...] Instead, the strength of the association was similar across age groups [up to 18 years], suggesting that the pulmonary consequences of preterm birth tend to persist throughout the life course.”

They conclude, “[t]here is compelling evidence that preterm birth—particularly very preterm birth—increases the risk of asthma. Given the projected global increases in children surviving preterm births, research now needs to focus on understanding underlying mechanisms, and then to translate these insights into the development of preventive interventions.”

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Children’s National’s Husband-Wife Neuro Team Uses Novel MRI Technology to Identify Early Fetal Brain Development

A husband-and-wife team at Children’s National Health System focuses on identifying the earliest signs of impaired fetal brain development in high-risk pregnancies in order to develop the safest management plans for pregnancy and the earliest hours and days after birth. The hospital uses innovative imaging technologies to evaluate the fetus and the newborn using biomarkers that until now have been unavailable to most clinicians aiming to deliver the best possible care during these critical life phases.

Adre J. du Plessis, MBChB, MPH, Chief, Division of Fetal and Transitional Medicine, and Catherine Limperopoulos, PhD, Director of the Advanced Pediatric Brain Imaging Research Laboratory, have targeted

fetal brain growth trajectories to establish the earliest indications that a fetal brain is in jeopardy of disturbed development. The ultimate goal is to pinpoint the at-risk fetal brain before irreversible injury occurs.

“During a fetal brain insult there comes a point where a cascade of biochemical processes is unleashed. Beyond this point, containing brain injury becomes like putting out a forest fire. Our goal is to identify the problem before that critical time point is reached,” du Plessis says.

“The fundamental point of departure for our work is identification of the fetus and the newborn at risk for brain injury before that injury happens,” says du Plessis. “Of all the organs, the brain is the least forgiving when it comes to injury. There is currently no cure for brain injury. Our entire focus is on identifying insult before it becomes irreversible injury. As such we are in pursuit of truly preventive neuroprotection strategies rather than rescue or salvage.”

Limperopoulos says advanced fetal magnetic resonance imaging (MRI) is becoming an important clinical tool to measure brain development in healthy fetuses during the second and third trimesters of pregnancy. The researchers are engaging in novel MRI techniques that will provide vital information to healthcare providers to counsel patients effectively and base rational decisions regarding potential medical and surgical procedures.

“We want a safe birth,” says Limperopoulos. “We are capturing signs and symptoms that will identify the fetus or newborn en route to a significant brain insult before she or he suffers irreversible injury. Until now we haven’t had the technology to identify signs of trouble with enough warning to reliably do something about it,” she adds. One major area of concern is failure of oxygen and nutrient supply to the fetal brain in pregnancies complicated by conditions such as Complex Congenital Heart Disease or placental failure. In large studies of pregnancies complicated by congenital heart disease, these researchers’ imaging techniques have identified very early signs of failing brain development, signs that currently go undetected by conventional techniques.

Du Plessis, Limperopoulos and the team at Children’s National are unique in their focus on the potentially hazardous transition from fetal to neonatal life. With the aid of these innovative brain imaging techniques, the future coordination of informed, rational, and effective care of the immature brain appears within reach.

Women & Infants Unveils New England’s First March of Dimes® NICU Family Support Bright Space® for Siblings

Families of babies being seen in Women & Infants Hospital’s Neonatal Follow-Up Clinic now have an educational and developmentally appropriate space to promote self-healing through play, thanks to an innovative partnership with the March of Dimes and the Bright Horizons Foundation for Children.

Rhode Island’s first March of Dimes NICU Family Support® Bright Space® for Siblings was unveiled to a crowd that included current and former neonatal intensive care unit (NICU) families, administrators, physicians, nurses and community representatives. This Bright Space for NICU Siblings is the first to open in a developmental follow-up clinic in the U.S. in partnership with the March of Dimes.

“Women & Infants Hospital is delighted to partner with the Bright Horizons Foundation for Children and continue our longstanding partnership with the March of Dimes,” said Mark Marcantano, acting President of Women & Infants Hospital. “As a patient and family-centered hospital, we are excited to create an enriching learning and play facility for NICU graduates and the siblings and families of some of our most fragile newborn patients.”

Bright Spaces®, the signature program of the Bright Horizons Foundation for Children,

creates warm, enriching playrooms in organizations that give children and families a special place to gather, relax and have fun. David Lissy, CEO of Bright Horizons Family Solutions, said, “We hope that this space will help maintain a sense of normalcy for siblings and families of babies in the neonatal intensive care unit.”

In addition to providing a gathering place for families, the Bright Space at Women & Infants will offer hope and inspiration. It will have vintage toys and art work, a library, interactive and developmentally appropriate toys, and an art cart.

“Bright Spaces bring hope and comfort to families and children during an especially difficult time – when a baby is in need of neonatal intensive care,” said Betsy Akin, Director of the March of Dimes Rhode Island Chapter. “This Bright Space in the developmental follow-up clinic will offer a place where moms and dads can talk, NICU graduates and siblings can play, and where families can simply be together.”

The March of Dimes chose Women & Infants Hospital as one of the eight Bright Spaces for NICU Siblings sites in the U.S. because of their longstanding relationship. March of Dimes NICU Family Support was established at Women & Infants in 2002. It is built on a family-centered philosophy and addresses the needs of parents, siblings and extended family throughout the baby’s hospitalization, during the transition home, and in the event of a newborn death.



Adults pictured from left to right are: Nichole Aguiar, March of Dimes Rhode Island; Dr. Edward McCabe, Senior Vice President and Chief Medical Officer, March of Dimes National Office; Dr. Betty Vohr, Medical Director, Neonatal Follow-Up Clinic, Women & Infants Hospital; Mary Ann Tocio, Chief Operating Officer, Bright Horizons Family Solutions; Jennifer Cardullo, Neonatal Follow-Up Clinic, Women & Infants Hospital; and Andrea Halbrook, Neonatal Follow-Up Clinic, Women & Infants Hospital. They are pictured with Isabella, Katie and Sophia Silva – Katie spent three weeks in the Carter Family Neonatal Intensive Care Unit at Women & Infants Hospital in August 2009.

Researchers Stress the Need to Strengthen Pediatric Clinical Trials Infrastructure

Strengthening the infrastructure required to conduct pediatric research is essential for obtaining information needed for the medical care and treatment of children, wrote Children's National Health System's Director of the Office of Innovation Development, Edward M. Connor, MD, MBE, the lead author of the article "Meeting the Demand for Pediatric Clinical Trials," published in the journal *Science Translational Medicine*.

In recent years, legislation and regulations around the need for high-quality data on medications used in pediatric patients have gotten stronger, increasing the demand for pediatric clinical trials. To meet this demand, the authors, who include researchers from the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA), highlight the need for an improved and standardized research infrastructure to better guide treatment and care for children.

"Many drugs used in children have not been adequately studied in this population," says Dr. Connor. "While this situation is improving there is still a lot of work to do to fill the knowledge gap, particularly in newborn infants and young children."

The authors suggest that collaboration among the public and private sectors is needed to ensure that the proper expertise and infrastructure are in place.

"In the past, the required trials networks were created as the need arose then dismantled when it waned," says Dr. Connor. "The increasing demand for data that meet regulatory standards for labeling means that we need to find ways to sustain infrastructure for pediatric trials. The pediatric research community, federal agencies, advocates, and industry are all making progress but a comprehensive and urgent solution is needed."

According to Dr. Connor, pediatric trials that are used for drug labeling demand a level of quality standard that is higher than the average study. Having a network of experts in pediatric clinical trials and an enhanced infrastructure in place would ensure consistent, high-quality data are produced to

guide therapeutic decisions in pediatric clinical practice.

"Establishing such an enhanced infrastructure has been a major goal of the child health platform within the Clinical and Translational Science Award (CTSA) National Consortium," says Lisa Guay-Woodford, MD, Director of the CTSA program, a partnership between Children's National and George Washington University. "This report provides a clear roadmap for our continued efforts."

"There is a need for high-quality, compliant pediatric clinical trials infrastructure," said study co-author Steven Hirschfeld, MD, PhD, Associate Director for Clinical Research at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). "The NICHD's Pediatric Trials Network provides needed infrastructure for evaluating drugs commonly prescribed off label for the express purpose of obtaining information needed for pediatric labeling."

Co-authors of the article were William E. Smoyer, MD, Nationwide Children's Hospital; Jonathan M. Davis, MD, Tufts Medical Center; Anne Zajicek, MD, PharmD and Steven Hirschfeld, MD, PhD, the Eunice Kennedy Shriver National Institute of Child Health and Human Development; Linda Ulrich, MD, Office of Orphan Products Development at the FDA; and Mary Purucker, MD, PhD, the National Center for Advancing Translational Sciences at the NIH.

For more information, visit <http://ChildrensNational.org>.

Letters to the Editor

Neonatology Today welcomes and encourages Letters to the Editor. If you have comments or topics you would like to address, please send an email to: LTE@Neonate.biz and let us know if you would like your comment published or not.

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