NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

Volume 4 / Issue 3
March 2009

IN THIS ISSUE

NEONATOLOGY TODAY

Editorial and Subscription Offices
16 Cove Rd, Ste. 200
Westerly, RI 02891 USA
www.NeonatologyToday.net

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

Recruitment Ad on Pages: 2 and 11

Fetal Disseminated Candida Albicans Sepsis with Congenital Cutaneous Candidiasis Following Chorioamnionitis Associated with Premature Labor: Case Report

By Shay Barak, MD; Yuri Perlitz, MD; Amir Kushnir, MD; Anatoli Grinshpun, MD; Elena Chulsky, MD; Moshe Ben-Ami, Prof.

Abstract

We present a case of Candida Albicans chorioamnionitis associated with fetal Candida sepsis and Congenital Cutaneous Candidiasis (CCC) in an extremely premature infant. The delivery occurred at 25 gestational weeks following antibiotic and tocolytic treatment in a gravida who conceived with intra uterine device which was not removed.

Key words: Candida Albicans; Congenital Cutaneous Candidiasis; Candida sepsis; intrauterine contraceptive device; premature infant.

Introduction

Candida albicans vulvovaginitis during pregnancy has high prevalence and appears in up to 20-30% of pregnant women.[1,2] However, the incidence of Candida Albicans ascending infection causing chorioamnionitis is less than 1%.[3-5] But, when chorioamnionitis does happen, the consequences may be missed abortion, premature labor, intrauterine fetal death or Candida sepsis.[4,5,7-10] The diagnosis of chorioamnionitis in these cases is difficult, because of the absence of known risk factors and clinical and laboratory signs such as prolonged premature rupture of membranes, maternal fever and leukocytosis. Nearly one third of the reported cases of congenital Candida infection during pregnancy were associated with intrauterine contraceptive devices, the principle risk factor for Candida chorioamnionitis and fetal Candida sepsis.[4,7,8,15]

> ***"Candida albicans vulvovaginitis during pregnancy has high prevalence and appears in up to 20-30% of pregnant women. [1,2]"***

Case Report

A 32-year–old woman, gravida 2, para 2, was admitted to the delivery room at 24 weeks and 5 days gestation with lower abdominal

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"We suggest that in any case of preterm premature rupture of membrane in an IUCD carrier gravida, an amniocentesis should be performed. Early diagnosis of intrauterine Candidiasis can be treated by intrauterine infusion of Amphotericin B or by immediate delivery and prompt management of the neonate.[14]"

pain, suspected rupture of membranes and contractions.

Her obstetric history included two vaginal deliveries at term. Her medical history was uneventful except for recurrent Candida Albicans vulvovaginitis during index pregnancy, a detail that she did not provide during the first medical history taking, but only on the day after delivery. She conceived with intra uterine device (IUD) which was left in place and suffered from recurrent urinary tract infections during pregnancy and treated with antibiotics.

On admission, vital signs measurements (temperature, pulse, blood pressure) and general physical examination were normal. Uterine size was consistent with gestational age, no tenderness was observed on abdominal and uterine palpation. Leakage of greenish colored but not purulent or malodorous amniotic fluid was detected by sterile speculum examination. No cervical effacement or dilatation was observed. Complete blood count was normal. Ultrasonographic examination revealed a live fetus in vertex presentation, normal biometric measurements consistent with 24 weeks gestation and adequate amniotic fluid index. Fetal cardiac monitoring detected fetal tachycardia up to 180-190 beats per minute and regular uterine contractions.

No maternal symptoms or signs of chorioamnionitis were detected, but the leakage of green-brown meconium amniotic fluid was increased. A course of Bethametazone 12 mg, 2 doses, 24 hours apart was given. Smear from vagina for Gram stain and culture was performed and antibiotic therapy, which included Ampicillin and Erythromycin, was started.

At 25 weeks and 3 days gestation, the patient had started labor and was delivered by Cesarean section due to patient's request after detailed inform consent. Apgar scores were 2 and 6 at 1 and 5 minutes. Birth-weight was 680 grams, the 25th percentile for gestational age. Because of lack of spontaneous respirations and cyanosis the baby was intubated and ventilated in the delivery room and transferred to the Neonatal Intensive Care Unit (NICU). The first physical examination revealed a widespread squamous maculo-papular rash and, in a limited area, a pustulous rash ("red dots"). The rash covered the infant's trunk, extremities and the scalp, sparing the palms, soles and mucous membranes. No hepatosplenomegaly was noted. Umbilical arterial and venous catheters were placed.

Two different blood samples and smears from umbilical cord, placenta and skin were taken for culture for possible bacterial infection. Lumbar puncture and suprapubic aspiration were not done because of unstable condition at birth. The pathologic examination of the placenta revealed signs of acute chorioamnionitis.

During the NICU hospitalization, the infant suffered from Respiratory Distress Syndrome requiring surfactant administration and mechanical ventilation. Brain sonography at the age of 1 hour revealed bilateral grade IV intra-ventricular hemorrhage with ventricular dilatation. Additional complications included acute renal failure with anuria and severe cardiac arrhythmia. Significant hematological and electrolyte abnormalities were detected, including leucocytosis up to 56,000 with polymorphonuclear cells predominance and severe hyperkalemia up to 9 mmol/l. The infant's treatment included surfactant replacement (Curosurf), antibiotics (ampicilline and cefotaxime). Treatment of hyperkalemia and acute renal failure included fluid restriction, administration of diuretic (Furosemide), Insulin, Sodium Bicarbonate, Calcium Gluconate, Kayaxalate, inhalation of β-2 agonists (Salbutamol). Unfortunately, two days after birth the infant died. On the same day we received the results of cultures from the above samples, in which Candida albicans was detected in all samples, making the diagnosis of severe Candida albicans sepsis.

The parents refused to have an autopsy performed.

Discussion

Cervicovaginal candida infection has a high prevalence and occurs in one third of pregnancies.[1,2] Ascending infections in cases of vaginal infection is less than 1% and seldom cause chorioamnionitis.[3,4.5] Chorioamnionitis, in general, can be detected by clinical symptoms and signs, including a high temperature > 380C, C-reactive protein >20mg/L, leucocytosis>20,000cm3, premature labor, purulent malodorous amniotic fluid, uterine tenderness and maternal or fetal tachycardia. It is difficult to diagnose candida chorioamnionitis, because of its rarity and lack of sign and symptoms, such as prolong rupture of membranes and low incidence of maternal febrile morbidity. It may lead to early abortion, fetal demise premature labor and fetal candidiasis.[4,5,7,10,15] Disseminated congenital candidiasis, caused by invasion of the microorganisms from the vagina into the uterine cavity, results in chorioamnionitis with fetal infection of varying intensity. It may be limited to the skin and cause Congenital Cutaneous Candidiasis (CCC), which always is acquired in utero via ascending infection. This is a benign dermal disorder manifested as a diffuse maculopapular or papular rash followed by desquamation. On the other hand, organ-

isms may disseminate into the bloodstream and spread to many organs of the fetus and cause systemic disseminated candidiasis with very high mortality rate (39% - 94%). Unfortunately, in many cases only retrospective diagnosis is made from histopathologic or microbiologic findings in the placenta, fetal membranes or umbilical cord. Premature neonates are at increased risk of disseminated Candida infection due to immature cellular immunity and lack of the stiatum corneum in the skin and inadequate mucocutaneous barrier.

Another major risk factor for fetal Candida infection is pregnancy with intrauterine contraceptive device (IUCD).

We suggest that in any case of preterm premature rupture of membrane in an IUCD carrier gravida, an amniocentesis should be performed. Early diagnosis of intrauterine Candidiasis can be treated by intrauterine infusion of Amphotericin B or by immediate delivery and prompt management of the neonate.[14] Our patient had all of the risk factors (low birth weight, premature rupture of membranes, intrauterine contraceptive device) and developed Congenital cutaneous candidiasis with congenital candida sepsis. Unfortunately, in the presented case the accurate diagnosis was performed to late.

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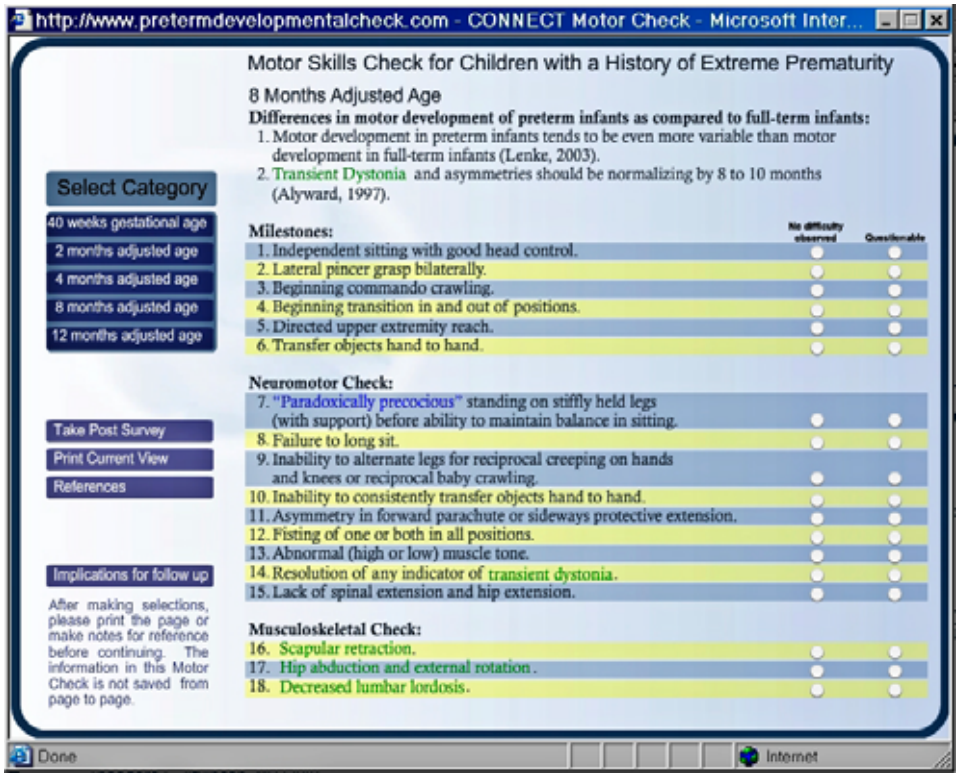
Monitoring Preterm Infant Motor Development: Web-Based Decision Support

By T. E. Atkinson, MD; T. H. Daniels, M Ed; J. Prehn, PT, MS, PCS; V. Rachal, RN, PhD; and C. B. White, MD

Mississippi has the dubious distinction of leading the nation with the highest rate of preterm birth at 18.8% of live births.[1] Being a predominantly rural state with only one large university medical center, a large portion of the neonatal intensive care unit services for these infants are provided in community hospitals. After discharge from neonatal intensive care units, most of the families return to rural areas. The follow-up care to these often tiny and fragile infants is provided by primary care providers, in many cases family practice physicians, nurse practitioners or pediatricians.

In 2004, a group of organizations in the southern region of Mississippi recognized the need for better coordination of services to be provided to high-risk newborns and their families. These agencies included one acute care community hospital, a private practice neonatology group, a rural health organization, and pediatricians belonging to a large multi-specialty group and staff from a local university. The resulting partnership was awarded planning and implementation funding from the Agency on Healthcare Research and Quality to conduct CONNECT (Creating Online NICU Networks to Educate, Consult, and Team), a Health Information Technology research grant. Project CONNECT achieved four goals which developed: electronically-generated portable health records, an interoperable system between participating agencies with disparate electronic health record systems, training and bedside consultation via videoconferencing, and a Web-based clinical decision support system (CDSS).

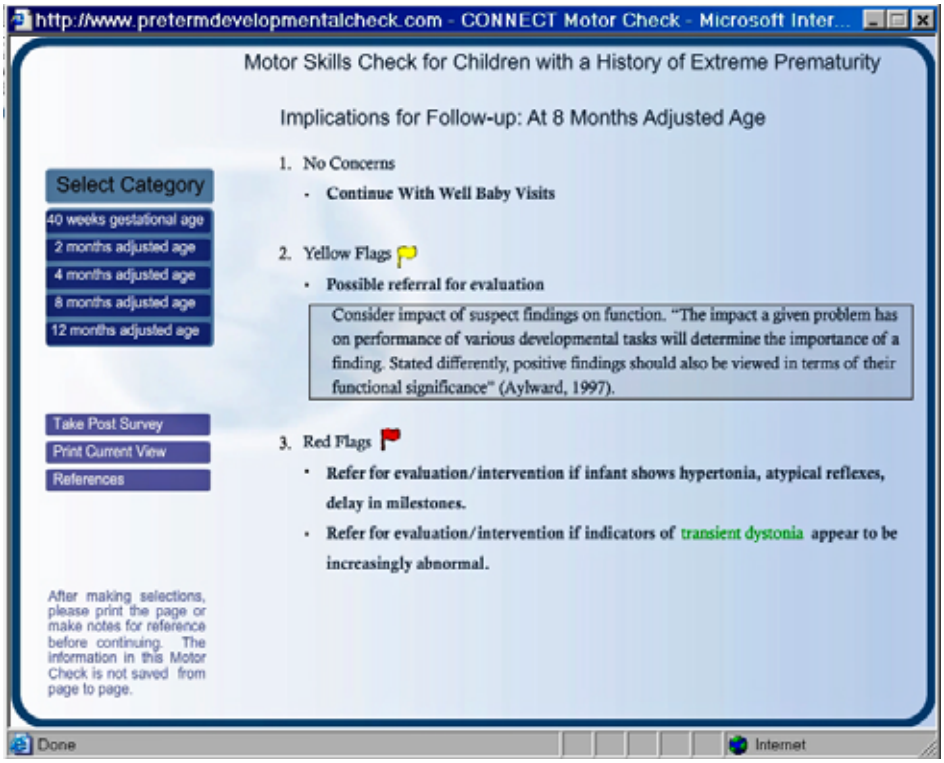
The foundational piece for the Web-based clinical decision support system is the *Preterm Motor Check* (available at www.pretermdevelopmentalcheck.com), which is designed for use during the first year of life (corrected age) for infants with a history of low birth weight or extreme prematurity. This initial component of the CDSS focuses on motor development and will be expanded to include infant interaction and feeding during the first year of life.



Screen shot from the Preterm Motor Check displaying the 8 month corrected age.

The *Preterm Motor Check* is derived from a synopsis of expert opinion on the neuromotor development of preterm and low birth weight infants, as well as common adverse sequelae of extended NICU stays. This CDSS includes optimal ages for screening neuromotor development and typically expected differences in the neuromotor developmental characteristics of infants with a history of prematurity as compared with infants born at full term. Also included are common expressions of adverse sequelae related to milestones, movement and posture. In addition to assisting the community-based primary care provider in decision making, this dynamic decision support includes photos and video clips of abnormal characteristics, and defines terms not routinely used by some health care providers.

Due to risk factors associated with preterm birth, neurodevelopmental and behavioral surveillance is warranted during the early



Screen shot from the Preterm Motor Check displaying implications for care for 8 months corrected age.

years of life through school age. While a variety of developmental screening tools are available for use in a physician's office, most are based on milestones or physical assessment. In addition, these tools are not illustrative of how actual questionable or abnormal findings may appear nor, do they take into account qualitative differences.

During the well-child visit, the *Preterm Motor Check* may be used to determine the infant's developmental status in terms of "Milestones," "Neuromotor Check," or "Musculoskeletal Check." After review and consideration of each item, the physician selects "No difficulty observed" or "Questionable." A "Questionable" finding prompts the display of a red or yellow "flag" indicating the level of concern for that finding. The primary care provider then clicks on "Implications for Follow-Up" which are intended as a decision support for the primary care provider and do not yield scores nor pass/fail status.

Based on the results of the *Check*, the primary care provider may determine that there are "No Concerns" and schedule the infant to return for a routine well-baby visit. "Yellow Flags" may indicate the need for possible referral for evaluation or for close monitoring of the infant's development. Findings with "Red Flags" indicate the need for evaluation/intervention. The type of referral for follow-up evaluation is subject to the clinical opinion of the primary care provider and could include, but is not limited to, neurology, developmental pediatrics, physical therapy, early intervention, etc.

Many challenges exist for the community-based primary care provider in monitoring development of a preterm infant. These challenges include the need to determine if a developmental difference exists, and if so, whether the difference is transient in nature or appears to be evolving into a more permanent delay or difference. A preterm infant's development may deviate from expected patterns; however, the finding may or may not be problematic. The *Preterm Motor Check* is designed to identify potential differences as they arise, despite the fact that a delay or problem may not be definitively expressed until later. This information could prove valuable to the many primary care providers, particularly those in rural areas, who are providing follow-up care for premature infants after discharge from the NICU.

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This project was supported by grant number 5 UC1 HS016147 from the Agency for Healthcare Research and Quality.

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Medical News, Products and Information

Innovative Center at UCSF Specializes in Treating the Infant Brain

UCSF Children's Hospital has opened an innovative new clinical unit focusing on the infant brain that is the first facility of its kind in the United States. The unit brings together specialized treatment for infants who show signs of brain damage at birth – and are at-risk for developing cerebral palsy, mental retardation and other cognitive disorders – with clinical research.

The new Neuro-Intensive Care Nursery http://vocuspr.vocus.com/VocusPR30/Url.aspx?517244x12868657x-13288521 (NICN) is a state-of-the-art newborn care unit designed to host clinical trials and bring the latest cutting-edge treatments to patients.

"My hope is that by bringing scientists and clinicians together in the NICN, we will be able to establish the root causes of brain damage in infants so that we can offer patients and their families real therapeutic options," Rowitch said.

A team of UCSF doctors specializing in newborn care, the pediatric brain, and pediatric brain imaging developed the NICN under the direction of David Rowitch, MD, PhD, Chief of Neonatology and a Howard Hughes Medical Institute investigator; Donna Ferriero, MD, Chief of Pediatric Neurology, and James Barkovich, MD, Chief of Pediatric Neuroradiology.

"Our highly skilled team of experts is well-equipped to address the critical need for improved care of the infant brain," said Sam Hawgood, MD, BS, Chair of the UCSF Department of Pediatrics. "By offering the most advanced treatments and hosting clinical trials, the new NICN is positioned to have a tremendous impact on care today and for years to come."

The type of specialized care for the infant brain that is offered at the NICN is already in high demand, Rowitch noted. Within the first month of the NICN opening in mid-summer, the number of patients referred to UCSF Children's Hospital for pediatric neurological care quadrupled.

What sets the NICN apart from other centers, according to Rowitch, is the integration of several components that means the best in patient care now and the ongoing development of promising new therapies, including a multidisciplinary team of doctors who represent all relevant medical specialties, a specialized nursing team, long-term follow-up of patients, and clinical trials funded by NIH and other sources.

Newborn brain damage is the leading cause of mental retardation, developmental delay and cerebral palsy in the US, according to Rowitch. Among all babies born very prematurely, five to 15 percent go on to develop cerebral palsy, and 25 to 50% develop cognitive disorders or a learning disability. The cost of treating cerebral palsy alone exceeds $35 billion annually, according to the March of Dimes Foundation.

"It must be remembered that a baby with a neurological disability will live decades after the insult with this burden," Ferriero said.

The opening of the NICN comes at an important time, as the last few decades have seen an increase in the number of infants who show signs of brain damage shortly after birth. This increase is primarily due to a corresponding increase in the survival rate of extremely premature infants – known to be much more susceptible to brain damage than full-term infants.

Although advanced neonatal care has enabled doctors to keep preterm infants alive, there is currently a lack of therapies that prevent or diminish brain damage in these cases. Rowitch says he hopes that the work done at the NICN will play an instrumental role in the development of new therapies for premature babies at high risk for brain damage.

"We currently lack neuro-protective therapies for these tiny babies," he said. "They face a rough road and unfortunately many of them develop significant brain injury. It is clear that we must be able to deliver a better standard of care in the future to reduce the impact of neurological injury in this very fragile patient population."

One treatment now used by the NICN team is hypothermia, which involves cooling a newborn's brain and body by a few degrees immediately after birth. Research has shown that hypothermia treatment within the first six hours of an infant's life can help prevent or minimize the long-term consequences of brain damage caused by a loss of oxygen during birth. Hypothermia treatments, however, have only been tested in full-term infants.

"Current research suggests that we can diminish the mortality and severe disability with the use of hypothermia in some newborns," Ferriero explained. "However, the protection is not complete, so we must continue searching for additional therapies that aid the newborn brain in its ability to repair itself.

Another key component of the new NICN is the use of an advanced neonatal brain monitoring system, called cerebral function monitoring or amplitude integrated electroencephalography (aEEG), which provides a window into the brain activity of newborns. According to Yao Sun, MD, PhD, Director of Neonatal Clinical Programs at UCSF, this type of intensive monitoring is a routine part of the clinical care in the NICN, while most other nurseries use it only when an infant shows signs of seizure.

"By monitoring the electrical function of the newborn brain under various conditions of illness and stress, we will gain a better understanding of how our treatments affect brain function and the risk of injury. This, in turn, will lead to better treatments to optimize neurological outcome," Sun explained.

The nursery also uses an MRI-compatible incubator, which Barkovich developed in order to photograph the brain anatomy in extremely premature babies who need a carefully controlled environment. Researchers at the NICN are using the information gathered from both the incubator MRI and the cerebral function monitoring system to learn more about brain development in preterm babies.

The NICN is the main clinical branch of the Newborn Brain Research Institute (NBRI), founded at UCSF in 2006. The goal of both the NBRI and the NICN is to discover the root causes of brain damage in infants and to develop and test new treatments, using translational research that integrates the work of basic scientists and clinicians. In one of the initial steps of this research, Rowitch and Arturo Alvarez-Buylla, PhD, of the UCSF Institute for Regeneration Medicine http://vocuspr.vocus.com/VocusPR30/Url.aspx?517244x12868656x-419936, are investigating the key attributes of stem cells in the developing brain.

The NICN is supported through private donations and the UCSF Medical Center. Clinical and basic research is supported by the National Institute of Neurological Disorders and Stroke, the National Institute of Child Health and Development and the Howard Hughes Medical Institute.

One of the nation's top children's hospitals, UCSF Children's Hospital creates an environment where children and their families find compassionate care at the healing edge of scientific discovery, with more than 150 experts in 50 medical specialties serving patients throughout Northern California and beyond. The hospital admits about 5,000 children each year, including 2,000 babies born in the hospital. For further information, visit www.ucsf.edu.

Mothers Exposed to Hair Spray on the Job More Likely to Have Sons with Hypospadias

Newswise — Maternal on-the-job exposure to hair sprays, some of which contain chemicals known as phthalates, has been linked to hypospadias in newborn boys, according to a study accepted for publication today by the peer-reviewed journal, *Environmental Health Perspectives* (EHP). Hypospadias is a birth defect of the male urethra that results in an abnormally placed urinary opening. It is one of the most common urogenital congenital anomalies among baby boys.

Phthalates, predominantly diethyl phthalate (DEP) and dibutyl phthalate (DBP) are present in many cosmetics including deodorants, fragrances, and nail and hair products. Studies have linked the phthalates or their metabolites, including monoethyl phthalate (MEP) and mono-n-butyl phthalate (MBP), with androgen-lowering activities, abnormal Leydig cell function, a decrease in anogenital distance in male infants, and reproductive tract malformations including hypospadias.

The case–control study included 471 hypospadias cases referred to surgeons, and 490 randomly selected birth controls, born over a 21-month period in South East England. Sons of women working in industries where there is exposure to phthalates—including hairdressers, beauty therapists, research chemists, line operators, pharmaceutical operators, electrical assemblers, and factory assistants—had a 2- to 3-times greater risk for hypospadias. The results add to growing evidence that endocrine-disrupting chemicals (EDCs) such as phthalates may play a role in hypospadias.

However, folate supplementation in the first three months of pregnancy was associated with a 36% reduction in risk of hypospadias. Additionally, there was no observed association between hypospadias risk and eating a vegetarian or vegan diet, contrary to the findings of earlier studies.

Study author Gillian Ormond, of the Department of Epidemiology and Public Health, Imperial College London wrote, "Measurements of exposure to phthalates and/or biomonitoring may help to understand possible pathways of exposure and toxicology, and provide quantitative estimates."

EHP Editor-in-Chief, Hugh A. Tilson, PhD, said, "The findings in this study are the first showing an association between occupational exposure to endocrine-disrupting chemicals in hair sprays and the risk of birth defects in newborn babies."

Other authors include: Mark J Nieuwenhuijsen, Paul Nelson, Mireille B Toledano, Nina Iszatt, Sara Geneletti, and Paul Elliott.

The article will be available free of charge at www.ehponline.org.

EHP is published by the National Institute of Environmental Health Sciences (NIEHS), part of the U.S. Department of Health and Human Services. EHP is an Open Access journal.

NIH/National Library of Medicine Scientists Identify New Congenital Neutropenia Syndrome and Causative Gene Mutation

A team of scientists has discovered a new syndrome associated with severe congenital neutropenia (SCN), a rare disorder in which children lack sufficient infection-fighting white cells, and identified the genetic cause of the syndrome: mutations in the gene Glucose-6-phosphatase, catalytic subunit 3 (G6PC3). The findings, which are published in the Jan. 1, 2009 issue of The New England Journal of Medicine, were made by an international team of scientists, composed of 14 researchers from the Medical School of Hannover in Germany and 12 from other research institutions, including the National Center for Biotechnology Information at the National Library of Medicine, National Institutes of Health.

"Our discovery will help facilitate genetic diagnosis in this newly defined group of severe congenital neutropenia patients," said Christoph Klein, MD, PhD, Hannover

Medical School, the principal investigator of the study. "Knowledge about the underlying genetic defect is an important first step in developing a targeted therapy."

The research also identified a novel pathway that is critical in controlling the life and death of immune cells. "This may eventually open new horizons for the development of drugs interfering with that pathway, which is important not only for patients with SCN, but potentially also for patients with other blood disorders," said Kaan Boztug, MD, Hannover Medical School, lead author of the study.

Severe Congenital Neutropenia (SCN) is a rare disorder, with an incidence of less than one in 200,000 births. The disorder is characterized by insufficient quantity of neutrophils, a type of white blood cell important in fighting infection. Children born with SCN suffer from frequent bacterial infections, and until the introduction of treatment with recombinant human granulocyte colony-stimulating factor (GCSF) in the 1990s, about three-fourths of affected children would die before 3 years of age. Treatment with GCSF usually reduces the duration and severity of neutropenia and results in improved clinical outcome and survival. However, SCN patients eventually may develop myelodysplasia or acute myelogenous leukemia.

In recent years, significant progress has been made in identifying the genetic defects that cause SCN, but in many patients, the underlying genetic cause remains unknown. The most common cause of inherited SCN is a heterozygous mutation (where one copy of the gene is mutated and the other is not) in the neutrophil elastase (ELA2) gene. In 2007, Klein's lab identified another causative mutation in a subgroup of SCN patients: homozygous mutations (where the defect is present in both copies of the gene) in the HAX1 gene.

To conduct the current study, the researchers focused on five children of Turkish descent, four of whom were known to be related; the children did not have identified mutations but had recessive SCN (i.e., the children inherited mutations from both of their parents, who each carried one mutated gene but were themselves unaffected). The children were identified for the study using the SCN International Registry.

A researcher from NCBI analyzed data on the children to look for suspect genes, and determined that the gene of interest was among 258 on chromosome 17. Further positional analysis at NCBI reduced the number of suspect genes to 36. A big break in the research came in early 2007 when a team headed by Janice Chou, PhD, at NIH's National Institute of Child Health and Human Development, published research showing impaired neutrophil activity and increased susceptibility to bacterial infection in mice lacking the protein glucose-6-phosphatase, catalytic subunit 3 (also known as G6PC3). The G6PC3 gene happened to be among the 36 genes Klein's team was examining, and DNA analysis indeed showed that all five study patients had the same mutations in this gene.

The researchers then sequenced the DNA of 104 additional patients from the SCN International Registry with unknown mutations and found G6PC3 mutations in seven. These seven children had different types of G6PC3 mutations than the original five study subjects, but they shared a constellation of clinical symptoms. Eleven of the 12 patients had heart defects or urogenital malformations, and 10 had unusually prominent subcutaneous veins. This grouping of clinical characteristics has not previously been described with SCN and defines a new syndrome associated with G6PC3 mutation.

The study also clarifies the importance of maintaining adequate glucose levels in keeping neutrophils alive and ensuring an adequate immune response to infections. The researchers found that insufficient supply of glucose causes neutrophils to undergo stress, and if the body's stress response is not adequate, the neutrophils will die. This connection between insufficient glucose and cellular stress response may be relevant to other more common diseases, especially those related to glucose disorders and glycogen-storage disorders.

"The study's findings are important for the care of patients with SCN, and for building an understanding of the diverse genetic causes of this disease," said David Dale, MD, University of Washington, who wrote an accompanying editorial on the study in The New England Journal of Medicine. "We do not know yet if patients with mutations in the G6PC pathway are at risk of developing leukemia and if they will need as frequent blood tests as other SCN patients. Knowledge of G6PC3 mutations will also alert physicians to look for cardiac defects in children with severe neutropenia as a clue to making this specific diagnosis."

Promising New Drug Being Evaluated as Possible Treatment Option for Fragile X Syndrome

(Chicago) – A pilot trial of an oral drug therapy called fenobam has shown promising initial results and could be a potential new treatment option for adult patients with Fragile X Syndrome (FXS). Findings of the open label, single-dose study by researchers at Rush University Medical Center and the University of California, Davis, Medical Center were published in the January issue of the *Journal of Medical Genetics.*

Results of an initial evaluation of the safety of fenobam, which is an mGluR5 antagonist, in adult males and females with Fragile X Syndrome showed there were no adverse side effects from the medication.

"This is the first study assessing the safety and pharmokinetic metabolism of an mGluR5 antagonist in humans with Fragile X Syndrome," said Dr. Elizabeth Berry-Kravis, pediatric neurologist at Rush and principal investigator of the study. "Also, some patients showed calmed behavior and rapid reduction in hyperactivity and anxiety, similar to effects of the drug in mouse models."

Fragile X Syndrome is the most common inherited cause of mental impairment and the most common known cause of autism.

Fragile X affects 1 in 4000 males and 1 in 6000 females of all races and ethnic groups (source: Centers for Disease Control- www.cdc.gov/genomics/hugenet/factsheets/FS_FragileX.htm). About 1 in 259 women carry Fragile X and could pass it to their children. About 1 in 800 men carry fragile X; their daughters will also be carriers. Symptoms of Fragile X Syndrome include mental impairment such as: learning disabilities, attention deficit, hyperactivity, autistic-like behaviors, and anxiety and unstable mood.

Fragile X Syndrome is caused by lack of activity of the FMR1 gene, which is responsible for a protein called FMRP. Without FMRP, activation of cell pathways by a brain receptor protein called mGluR5 goes unchecked, and it has been theorized that this plays an important part in Fragile X Syndrome.

To test this theory, past researchers have used laboratory mice without an active FMR1 gene, like in Fragile X Syndrome, but with a reduced amount of mGluR5 protein. The mice showed an improvement in their brain structure and function, in their brains' ability to make key proteins, and in memory and body growth. This shows that the over-activation of mGluR5 is very important in Fragile X Syndrome, and suggests a path for drug development to treat the syndrome.

In the current study, twelve participants recruited by Rush and the University of California, Davis received a single oral dose of 50-to-150 mg of fenobam. Prepulse inhibition (PPI) and continuous performance test (CPT) were obtained before and after dosing to explore the effects of fenobam on measures of sensory gating, attention and inhibition. In six of the 12 individuals there was a 20% improvement.

“Currently, there are no therapies on the market to treat cognitive deficits associated with Fragile X Syndrome," said Berry-Kravis. “This pilot study has identified the potential beneficial clinical effects of fenobam, but further research is needed.”

The Fragile X Syndrome clinic at Rush is dedicated to the care of children with Fragile X Syndrome, an X-chromosome-linked condition that is the most common inherited cause of mental retardation. The clinic is the only one of its kind in Chicago and one of few in the Midwest.

Perinatal Strategies Workshop: “The Light Bulb Moment: Embedding Innovation in Practice”

Pointe Hilton Squaw Peak Resort – Phoenix, AZ || April 3 – 5, 2009

Over the past 5 years, the Perinatal Workshop has focused on topics related to organizational structure and evaluation methods applicable to the NICU. As many meetings provide the clinical and research evidence upon which we base clinical decisions, this forum focuses on the transitions from theory to actual practice. This process requires communication at many levels, people skills, fiscal expertise and leadership. This year’s Workshop will include some perspectives on what the future may hold and how practices can plan for anticipated change. Highlights of the meeting include:

- The L. Joseph Butterfield Lecture and Keynote Address - John Kattwinkel, MD, the 2008 Virginia Apgar Award winner, will discuss “Building on the Efforts of Others: A Critical Element of Leadership.”
- Presentations on “Quality, Safety, and Innovation,” “Maintenance of Certification” and “The Irresistible Force and the Immovable Object: Life vs. Work.”
- Small group and workshop sessions will address a diverse topic list, including interpreting financial data, use of regional outcome data, beyond coding, quality and competency in neonatal resuscitation, innovation and technology assessment and your NICU, and getting involved in global health.
- The Section on Perinatal Pediatrics and Committee on the Fetus and Newborn will present and discuss priority activities and upcoming statements and guidelines.

The Workshop provides ample opportunity for attendees to meet old colleagues, develop new friendships, and exchange ideas. It also provides an opportunity for all in attendance to meet the leadership of our Perinatal Section and of the Committee on the Fetus and Newborn. Both of these groups seek your guidance on the priority concerns of your practice, be it academic, hospital-based, or private.

This conference focuses on how to manage neonatology - its practice, personnel, and environment. It is a great way to get a little “outside of the box”- and the Arizona sun won’t hurt either! Register online at www.pedialink.org/cmefinder or call toll-free 800-433-9016, option 3.

Chair, Perinatal Workshop Planning Group:
Mark Mammel, MD, FAAP

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

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ANNUAL NEONATAL PRACTICES CONFERENCE RETURNS TO CHICAGO IN JUNE 2009

The Sixth Annual Evidence vs Experience in Neonatal Practices® CME conference is scheduled for June 19-20 in Chicago

In the fast evolving field of neonatology, this annual conference has become a widely anticipated and well attended event, attracting an international faculty and a large audience for an up-to-date perspective on current research and clinical management of preterm infants. A distinguished faculty of 15 thought leaders in neonatology will provide in-depth presentations on important and urgent issues, with the goal of improving treatments and outcomes in patient care.

During this two-day conference, the topics will range from areas such as nutrition and infection, to ventilation and brain injury. Participants will be able to expand and test their knowledge in areas most applicable to their own day-to-day practices and research.

EVIDENCE vs EXPERIENCE IN NEONATAL PRACTICES®

SIXTH ANNUAL CME CONFERENCE

Presentations will include:

- Changing Spectrum of Neonatal Infectious Disease
- Medical Management of Short Gut Syndrome
- PDA: Treat or Not Treat?
- Advances in Hemodynamic Monitoring in Neonatology
- Nasal Ventilation: Its Time Has Come!
- Utilizing EEG in the Neurological Assessment of Term and Preterm Neonates
- Cooling to Prevent HIE: A Metanalysis

In 40-minute-long presentations, the faculty will examine the far-reaching effects of chorioamnionitis, and explore the question of why oxygen is still being used to resuscitate term infants. They will discuss iatrogenic complications in the NICU, and whether there is a hemodynamic basis for cerebrovascular injury in premature infants. Neil N. Finer, MD, of the University of California, San Diego, will present the keynote address on the subject, "Art and Science of Neonatal Resuscitation in the ELBW Infant."

Jatinder Bhatia, MBBS, of the Medical College of Georgia, will serve as Chair of this important conference. In addition to Dr. Bhatia, the Organizing Committee is composed of Rangasamy Ramanathan, MD, FAAP (Keck School of Medicine of USC and Women's & Children's Hospital in Los Angeles), Kris Sekar, MD, FAAP (The University of Oklahoma Health Sciences Center and The Children's Hospital in Oklahoma City), and Istvan Seri, MD, PhD (Keck School of Medicine of USC and Childrens Hospital Los Angeles). The program's faculty members will include neonatologists from the United States, Norway, and the Netherlands.

The target audience for this important conference includes physicians, nurse practitioners, nurses and other clinicians caring for preterm infants. The faculty will encourage the audience to participate fully in the program, interacting with not only the speakers but also with one another, and offering their own insights and perspectives into recent research and patient care in neonatal medicine.

This annual conference will be jointly sponsored by the Annenberg Center for Health Sciences at Eisenhower and the Keck School of Medicine of USC and supported by an independent educational grant from DEY, L.P.

To register online for ***Evidence vs Experience in Neonatal Practices®***, or for additional conference information including the complete program agenda, visit the conference Web site at **www.5StarMedEd.org/neonatal**

Questions about this event can be addressed to the Annenberg Center for Health Sciences at Eisenhower by calling Nina Pratt at 800-321-3690 (toll-free) or 760-773-4500 (8 am to 5 pm Pacific time).

Introduction

In 2006, there were more than half a million preterm births in the US (an increase to about 12.8% of live births). The percentage of low birthweight infants also rose in 2006 to 8.3% of live births. The problems encountered by a premature infant are related to the immaturity of the organ systems. The infant requires specialized care until his or her organ systems have developed enough to sustain life without specialized support. Depending on the extent of prematurity, this may take weeks to months. This conference will continue the examination of newly developing treatment options for these problems, while reviewing current evidence for treatment protocols. International thought leaders in the field will help clarify desired and efficacious treatment options.

Learning Objectives

Upon completion of this activity, participants should be able to:

- Rapidly diagnose and effectively treat hemodynamic issues in preterm and low birthweight infants
- Diagnose and treat neurological issues in neonates
- Provide appropriate ventilatory strategies to enhance the health of neonates
- Apply evidence-based treatments for infections in neonates

Nursing Learning Objectives

Upon completion of this activity, participants should be able to:

- Provide optimal care of preterm and low birthweight neonates as part of the treatment team.

This activity will address professional practice gaps in knowledge and competence.

Accreditation and Certification

The Annenberg Center for Health Sciences at Eisenhower is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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