



The MFMU Networker

Volume IX Issue 1

March 2004



FOX Scampers On

March proved to be the highest recruiting month of the study with more than 255 patients randomized! The previous highest number was in September, 2003. Three centers, UT-Southwestern, the University of Utah and

the University of Alabama continue to provide the highest recruitment, having enrolled 44% of the total thus far.

Study-related documents for the FOX ancillary study on the relationship between intrapartum fetal oxygen saturation and the risk of meconium aspiration in pregnancies complicated by meconium-stained amniotic fluid are undergoing final review. This study, which is designed to complement the primary FOX trial, will study whether fetuses destined to develop meconium-aspiration syndrome, from very mild cases to severe disease, have lower intrapartum fetal oxygen saturation values during labor and delivery. Information also will be collected on other factors relevant to the prediction and development of meconium-aspiration syndrome, such as fetal heart rate patterns, obstetrical and pediatric interventions, and placental pathology findings.

The ancillary protocol is presented as an appendix to the trial protocol. The neonatal baseline form was modified to include a question about the presence of meconium and a new form was created to record information that will be used to assess meconium aspiration syndrome. The study will begin as each center receives IRB approval for the modified protocol and informed consent form.

STTARS Out and Shining

Following submission of the IND to the FDA on February 2 and the announcement of the IND number a few days later, the BCC and clinical centers were able to submit the STTARS protocol to their own IRBs for approval and begin work on certification. By the end of March, 5 centers were fully certified (Alabama, Drexel, Brown, Case Western and Northwestern) and study drugs sent. Centers already had patients waiting to be go on the compliance run-in and by April 2, the first patient had been randomized to the STTARS trial! To boot, this first patient, enrolled at Drexel, has triplets!

This trial is being conducted to evaluate the benefit of progesterone in women at high risk for preterm delivery because they have a multifetal pregnancy. In the recently

completed MFMU trial, progesterone was shown to substantially reduce the rate of preterm birth by 35% in women with a singleton pregnancy at high risk for preterm delivery because of a prior spontaneous pregnancy when compared with women receiving placebo. Six hundred women with a twin pregnancy and 120 women with a triplet pregnancy are expected to be randomized into STTARS over the next 48 months.



BEAM Recruitment Nears End

After a little more than 6 years, the BEAM trial will recruit its last patient as of May 31, likely exceeding the recruitment goal of 2220. The first year of the trial was conducted as a feasibility study, with the first patient randomized on December 1, 1997. In March 1999, a feasibility review organized by NINDS determined that the Network was executing the study well but that recruitment needed boosting. Three additional centers were certified to recruit for BEAM, two of which later became part of the Network in 2002 (Brown and St. Luke's Roosevelt). The third center, UTMB, remains outside the Network.

Infants will continue to be followed until 24-28 months of age to answer the research question of whether prophylactic magnesium sulfate given to women at risk for early delivery (less than 32 weeks gestation) reduces the risk of death or moderate to severe cerebral palsy in their children. More than half of the children already have completed the two-year follow-up exam. Thus, the results of the trial will be known sometime in late 2006.

Meanwhile, training for professionals involved in infant follow-up continues. Eighteen new and second time neurological examiners attended a two-day training at the Kennedy-Krieger Institute in Baltimore on March 15-16. In addition, two conference calls have been held with consultant Terri Leach and the Bayley examiners. A third conference call will be held for those who have not participated on a call. All Bayley examiners must submit a tape and the test score sheets to Terri by May 31. A memo has been sent with detailed instructions.

Can you guess the total number of patients enrolled in the 23 studies completed so far by the MFMU Network? Answer is near the bottom of page 2 in the right column.

Omega-3 Trial Back on Track

Carlson Laboratories, a nutritional supplement company near Chicago, has agreed to work with the Network by allowing their Super Omega-3 Fish Oils capsules and a matching placebo to be used as the study medication in the next Network study: A Randomized Trial of Omega-3 Fatty Acid Supplementation to Prevent Preterm Birth in High Risk Pregnancies. Paul Thadikonda, whose company, Eminent Services, provides study medications for other Network trials, will work with Carlson to prepare the IND that will be necessary for the FDA. Eminent Services will package the study medications, label and distribute them as for other studies.

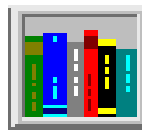


The aim of this trial is to determine whether Omega-3 fish oils will decrease the overall rate of preterm birth (less than 37 weeks) in high risk women. Eight hundred women will be randomized to either a daily dose of 4 soft gel capsules containing a total of 800 mg of DHA, 1200 mg of EPA and 40 IU of Vitamin E or a matching placebo. Since the Network found significant benefit for weekly injections of progesterone in women with a previous spontaneous preterm birth in a previous trial, the women in this trial will also receive progesterone injections as part of their treatment.

Two Network Papers Published in March

The results of the Network's randomized trial of inhaled beclomethasone dipropionate versus theophylline for moderate asthma during pregnancy was published in the March issue of the *American Journal of Obstetrics and Gynecology*. This prospective, double-blind, double placebo-controlled randomized clinical trial of 398 pregnant women with moderate asthma showed that treatment of moderate asthma with inhaled beclomethasone versus oral theophylline resulted in similar rates of asthma exacerbations and similar obstetric and perinatal outcomes. Since theophylline has the disadvantage of requiring serum levels, has more frequent side effects and because inhaled beclomethasone is equally efficacious when compared with theophylline, the authors conclude that the study results support NAEP recommendations that inhaled corticosteroids should be the therapy of choice for moderate asthma during pregnancy.

The second paper, published in the same edition of the journal, reported on women enrolled in the high risk aspirin trial who had pre-gestational diabetes. The purpose of this study was to determine whether the rate of preeclampsia in pregnant diabetic women is increased in those women with early-pregnancy proteinuria of 190mg to 499 mg/24 hours compared with women with proteinuria of <190 mg/24 hours. The authors did not find an increased rate of preeclampsia when the two groups were compared.



Results of Steroid Trial Announced

Dr. Ron Wapner, PI for the Randomized Placebo-Controlled Trial of Antenatal Corticosteroid Regimens, announced the study results at the first Oral Plenary Session of the Society for Maternal Fetal Medicine meeting on February 5 in New Orleans. The trial studied women who were at risk for spontaneous preterm delivery with intact membranes and pregnant one week after an initial course of corticosteroids and subsequently randomized to weekly courses of betamethasone or placebo. After 67 patients were recruited, the study course was limited to 4 weeks. The primary outcome was a composite of stillbirth/neonatal death, severe RDS, grade III-IV IVH, periventricular leukomalacia or chronic lung disease.



The initial sample size was 2200 but, after interim analysis, the Data Safety and Monitoring Committee recommended termination of the study because of safety concerns related to a trend of decreased birth weight without benefit. At that point 492 patients (591) infants were available for analysis. In the final analysis, no difference was found in the primary outcome between multiple courses and placebo. However, for those delivering less than 32 weeks, there was a trend towards reduction in the primary outcome after repeat steroids. In the entire group improvement was seen in secondary outcomes related to lung function. Multiple courses were associated with a decrease in birth weight, adjusted for gestational age. In infants exposed to four courses or more, there was a significant decrease in birth weight but no difference in head circumference.

In conclusion, the trial demonstrated that four or more weekly courses of antenatal steroids significantly reduce birth weight. However, repeated courses may reduce infant morbidity, especially when delivery occurs before 32 weeks. Dr. Wapner noted that further investigation of rescue steroid administration to women at high risk for early preterm birth is warranted.

The total number of patients enrolled in completed MF MU studies is 10,694

■ Have you noticed that the format of the **BCC monthly reports and capitation reports** has changed? In addition to being easier to read, the new format will allow the BCC to email these reports to you in the very near future, speeding the process and saving expense!

■ **Final reports for the BV and TV** trials and the **Varicella** study have been distributed.

■ **Correction:** The correct email address for the new grants manager, Margaret Young is: youngmar@mail.nih.gov

■ The **Network DSMC** met for 10 long hours on March 12 to discuss each of the Network's trials. Cathy Spong will report their recommendations at the April Steering Committee. The BCC is preparing a report for the IRBs.

People in the NEWS



We sadly bid farewell at the end of March to **Kevin Pinder**, Executive Coordinator at the BCC. Kevin moved to Florida with his wife who had accepted a fabulous new job there. We welcome Karla Lawrence as his replacement. Karla has worked at the Biostatistics Center

for over a year as the Executive Aide on another research project. She received her undergraduate degree in education and taught for a year before coming to the BCC. She is enrolled in a masters program in community counseling at GWU. While work and school do not leave much free time, Karla enjoys going to museums, poetry readings, listening to music and making crafts.

Congratulations to **Kristine Lain**, Co-PI from Magee-Womens, who gave birth to her fourth child, a third son, Samuel Markham Lain. Samuel was born March 16, 2004 and weighed in at 8 pounds, 2 ounces. Kristine will miss the April Steering Committee meeting but plans to be back to work very shortly.

We welcome to **Carmen Tekwe**, the newest statistician to join the BCC staff. Carmen received her undergraduate and masters degrees in math and statistics at the University of Florida. Though she grew up in Florida she was born in the West African country of Nigeria and her parents are from the Republic of Benin.

For the past year and a half, Carmen worked at Johns Hopkins as a biostatistician on epidemiology studies on aging. She is the statistician for the upcoming Omega-3 trial and is excited about working with the BCC and MFMU Network. Carmen hopes to begin classes for her PhD in Statistics at GWU this summer and still find time to continue cross country running and reading for pleasure.

Congratulations to our Project Scientist and fearless leader, **Dr. Cathy Spong**, who received a President's Award at the Annual SMFM Meeting in February for her research and oral presentation on the use of novel peptides as postnatal therapy to prevent alcohol-induced learning abnormalities in fetal alcohol syndrome.

Publications Policy Undergoes Revisions



The NICHD MFMU staff and the BCC, along with the Publications Committee, have been working on updating the Publications Policy for the Network for almost a year. The original policy was brought up to date in 2001 when the MFMU Network Policy Manual was developed for the newly constituted Network convening that Spring. Since then, the complexity and quantity of data, the availability of resources, the need to disseminate the results of the research and to accord appropriate academic recognition to participants who make significant contributions to Network research necessitated close scrutiny of Network policy. The result is a more in-depth document (about 22 pages vs. 7!) which describes among other things types of studies and analyses, timetables for analysis proposals, procedures for submission, review and prioritization of secondary analysis requests, review and approval process for manuscripts, and guidelines for authorship.

On March 22, all PIs and coordinators and were sent a final draft of the new publications policy for review and comments. These will be discussed at the April Steering Committee meeting. After final modifications, the new publication policy will be distributed. Work also has begun to update other sections of the Policy Manual to include information on certification, IRB and informed consent form language and study close-out. The Publications Committee also has concentrated over the past year on cleaning up outstanding proposals for analyses and manuscripts.

In October, the Steering Committee approved a policy requiring authors to affirm their intent to write a manuscript when submitting an analysis request. The protocol subcommittee will consider publication potential of the proposed analysis during their review process. Authors will prepare and submit to the appropriate protocol subcommittee their manuscript for review before presenting their analyses at a professional meeting. If the author has not completed the manuscript and passed it through the appropriate protocol subcommittee or declared the manuscript unfeasible by the time the analysis is presented at the professional meeting, the author forfeits the right to submit further analysis requests, concepts or ancillary protocols until the issue is resolved. Following are the deadlines for processing analyses requests for the 2005 SMFM and SGI annual meetings.

2004 Analysis Submission & Prioritization Deadlines for SMFM & SGI 2005 Annual Meetings

	<u>SMFM</u>	<u>SGI</u>
SMFM Analysis Requests:	April 15	June 15
Protocol Subcommittee Prioritization	By April 30	By June 30
Subcommittee Results to Pubs Committee	April 30	June 30
Pubs Committee Prioritization Call	May 10	July 9
Pubs Committee Abstract Approval Call	August 3	About October 26
Meeting Deadline for Abstract Submission	August 6	About October 29
Deadline for manuscript submission to Pubs Committee	December 15	February 15



MFMU CALENDAR



Steering Committee Meetings

April 15 - 16, 2004 (overlap with Neonatal Research Network)
July 12 - 13, 2004
October 21 - 22, 2004
January 27 - 28, 2005
April 21 - 22, 2005
July 21 - 22, 2005
October 27 - 28, 2005

Training

New RN/Coordinator Training: April 14, 2004

Ultrasound Reviews

May 6- 7, 2004

Site Visits

University of Utah: May 17 - 19, 2004

Professional Meetings

SMFM: Reno, NV; February 7 - 12, 2005
SGI Los Angeles, CA; March 23 - 26, 2005

02-00 050-050 050 50

