

Record Number of Abstracts Submitted to SMFM

A record-breaking twenty one abstracts were submitted to SMFM for the 2009 annual meeting, surpassing the total of twenty submitted in 2005. Of these, only one was eliminated in the SMFM review process. About 70% of the abstracts are typically accepted overall. This year, 95% of MFMU Network abstracts were accepted.

Another record was broken when a total of eight abstracts were chosen for oral presentations - two of these for the oral plenary - almost 10% of all the orals being presented at the meeting. On average, 7% of submitted abstracts are selected for an oral and only 1.3% for one of the plenaries. The Network had 38% accepted for an oral and 14% for one of the plenaries. This is a great accomplishment given that the 1240 abstracts were submitted to SMFM this year.

The primary results of two major Network trials – CAPPS (Dr. James Roberts) and GDM (Dr. Mark Landon) - will be presented in the first oral plenary session, tying the last two years in which the results of two Network studies each were awarded a spot in the plenary session. Dr. Manuck's abstract, *Response to 17p vs PR-M from saliva DNA*, a secondary analysis of data from the Progesterone trial, was awarded an oral in the Fellows Plenary.

In addition, five other MFMU Network submissions were chosen as orals: Dr. Clark (BEARS), Dr. Hickman (CSEC), Dr. Rouse (FOX), Dr. Harper (Omega), and Dr. Durnwald (STTARS).

The remaining twelve abstracts will be posters reporting the results of secondary analyses of Network studies by: Dr. Rouse (BEAM), Dr. Mercer (BEAM), Dr. Gyamfi (Progesterone and two for

BEARS), Dr. Hashima (BEARS), Dr. Manuck (Factor V), Dr. Silver (Factor V), Dr. Harper (Omega), Drs. Horton/Gyamfi (STTARS), Dr. Simhan (STTARS) and Dr. Refuerzo (STTARS).

Following Network tradition, investigators will deliver a draft version of their SMFM oral presentation at the Steering Committee meeting in October. Suggestions regarding how to improve both the substance of the presentation and the visuals will be made by the group.

Investigators will present a revised version of their talk again at the January meeting and receive final suggestions to prepare them for the SMFM meeting in late January. Draft versions of the posters will be presented for review and comments at the January Steering Committee meeting also.

NIH Council Reviews Pregnancy and Perinatology Branch

Dr. Duane Alexander, Director of the NICHD, presided over the 136th meeting of the National Advisory Child Health and Human Development Council on September 11. The 14 members, NICHD staff and admitted guests heard a report from the Director and progress reports on several individual NICHD programs, including an update on the National Children's Study.

To help achieve the goals of the Institute, the National Advisory Child Health and Human Development Council is charged with the responsibility of advising, consulting with, and making recommendations to the Director, NICHD, on matters relating to the research and research support activities and functions of the Institute. The roles and responsibilities of the Council members include secondary review of grant applications, with a focus on NICHD scientific program priorities and program balance.

For the second time since Dr. Cathy Spong became Chief of the Pregnancy and Perinatology Branch, she delivered an extensive report about the Branch programs, including the MFMU Network at this Council meeting. Two presentations featuring representative Branch support research were given. Dr. Robert Silver highlighted the Stillbirth Collaborative Research Network which has completed its data collection, and Dr. Kathleen Caron from the University of North Carolina reported on the results of laboratory studies on adrenomedullin and its role in fetal growth.

Following these presentations, the attendees heard reviews from two of the Council members regarding their assessment of the Branch's activities. The comments were extremely favorable, with some recommendations for future areas of research. They did express regret that there is not enough funding to support all the research that should be done. There was open discussion from other Council members, echoing the strengths of the Branch, the Networks and the translation of the branch supported work to clinical practice.



Hurricane Ike Impacts Texas Network Centers

After a few scary days enduring the advance and retreat of Hurricane Ike, the two Network Centers, Houston and Galveston, are in very different circumstances. Kris Cannon reports that the clinics and medical school in Houston were closed for a few days after the hurricane passed but are now back up and running, while the hospital in Galveston remains closed for an undetermined period of time.

However, our indefatigable Joan Moss and staff from the Galveston center are working out of their regional clinics 100% and have screened 9 new SCAN patients and enrolled one with a short cervix! They have been busy finding their relocated patients from the Galveston clinic who are currently on the SCAN and TSH trials and conducting home visits to do study procedures.

They also have resumed screening for TSH at most of their other regional clinics and scheduling follow-up visits. The APEX study is on hold since the hospital is closed and they cannot get medical records for patients that delivered there prior to the hurricane and, of course, there are no patients currently delivering there.

BEAM Study Published in NEJM

Following its presentation as the number one plenary earlier this year at the Society of Maternal Fetal Medicine's annual meeting, the primary manuscript has been published in the August 28, 2008 New England Journal of Medicine. In a news article jointly released from the sponsors of the study, the National Institute of Child Health and Human Development and the National Institute of Neurological Disorders, NIH Director Elias A. Zerhouni, MD is quoted as saying "This study shows a significant reduction in cerebral palsy among preterm infants whose mothers were given magnesium sulfate."

In the study, the largest of its kind, 2,241 women at risk of delivering early – between 24 and 31 weeks – were randomly assigned to receive either magnesium sulfate or a placebo. Moderate or severe cerebral palsy was diagnosed in just 1.9 percent of the group treated with magnesium sulfate, compared with 3.5 percent in the placebo group. Dr. Dwight Rouse, lead author for the study, hypothesized that magnesium may "stabilize the vessels in the vulnerable preterm brain," protecting against damage from lack of oxygen, and guarding against injury caused by swelling and inflammation.

Dr. Catherine Spong, Chief of the NICHD's Pregnancy Branch and Project Scientist for the MFMU Network believes that the "results show that obstetricians can use magnesium sulfate, which they have experience prescribing, to reduce the risk of a devastating condition, cerebral palsy, in preterm infants."

Protocol Updates:

Study Drug Donated for ALPS

► *Schering Plough* generously has agreed to donate 2,000 vials of the active drug, betamethasone, for the new Network trial. They also provided the drug for the BEARS trial. Following approval of the late preterm birth and antenatal steroids protocol at the April Steering Committee meeting, BCC staff, and Drs. Cynthia Gyamfi, Ron Wapner and members of the subcommittee have ironed out many of the study details and have been working on the final protocol and data collection forms. The protocol and accompanying paperwork were submitted to the FDA, requesting a waiver of IND, in mid-September. The FDA has 30 days to respond.

A brief coordinator "training" will be held on October 22, the day before the Steering Committee begins its quarterly meeting to review changes and updates to the protocol and data forms since the meeting in July.

In this trial, women who present for imminent delivery between 34⁰ and 36⁶ weeks gestational age because of preterm labor, preterm PROM or planned delivery will be randomized to receive either a single course of corticosteroids or placebo. Women will be excluded if they have received prior steroids during the current pregnancy. The trial is designed to have two strata: singleton pregnancies, requiring a sample size of 2400 women and twin pregnancies requiring a sample size of 1400. The primary outcome is stillbirth, neonatal requirement for respiratory support or prenatal death less than 24 months of age.

CAPPS Data Still Being Collected

► The abstract reporting the outcome of the CAPPS trial was written without outcome data because at the time it was submitted in August not all of the study patients had yet delivered. Thus the primary outcome had not yet been determined! As of September 17, twenty-nine patients were still on study and there are still about 100 medical charts to be reviewed through the end of October.

This has been a massive trial, with over 10,000 patients randomized and approximately 3,200 charts reviewed for preeclampsia since July 2004.

A huge thankyou is owed to the following people who participated in the chart reviews: Dr. James Roberts, Dr. Ken Leveno, Dr. John Hauth, Dr. Les Myatt, Dr. Catherine Spong, Dr. Sean Blackwell, Dr. George Saade, Dr. John Thorp, Dr. Michael Varner, Dr. Matt Hoffman, Dr. Philip Samuels, Dr. Jay Iams, Ms. Stephanie

Fyffe, Ms. Peggy Cotroneo, Ms. Allison Northen, Ms. JoAnn Tillinghast, Ms. Sabine Bousleiman, Ms. Joan Moss, Ms. Karen Dorman, and Ms. Gail Mallett!

Rebecca Gernosvitz, PhD, & Trisha Boekhoudt, MPH, at the BCC collating and preparing the mailing of medical charts.

Thanks to a generous contribution of more than half of a million dollars from NHLBI, the CAPPS subcommittee is proceeding with initiating analyses of patient blood samples that were collected at six time points during pregnancy.

Hopefully using mostly Luminex multiplex panels, which require a very small sample, assays will be run on about nine analytes that measure vascular, placentation, hypoxia, and inflammation biomarkers.

Laboratory bids are being solicited and it is anticipated that the studies can begin in January.



GDM Data Clean-up Continues

► More than 55 maternal and infant charts have been requested from Network centers and reviewed for specific secondary outcome data. In addition, BCC staff are still plowing through more than 26,000 insulin readings recorded on patient meters. The readings are being compared to the patient diaries in order to determine whether the blood sample was taken before or after eating. Unfortunately, when the study started, the software on the meters did not have the capability of noting this information. It is anticipated that this activity will be concluded in time for Dr. Landon's plenary presentation at SMFM.

TSH Recruitment Proceeding

► The S Stratum of the TSH trial, which is now randomizing an average of about 20 patients each month, will complete recruitment by fall of 2009. Recruitment to the H Stratum has dropped off somewhat in the last few months, hopefully a temporary change. At the current rate, it is estimated to continue on for another year after S.

About half of the Network centers have obtained IRB approval for the ancillary regarding patient mood. Centers are encouraged to begin this ancillary as soon as possible, since the S stratum will be ending shortly and a total of 300 patients are needed for the sample size.

Plans for conducting training for the 24-month Bayley III evaluation are being discussed. The training will most likely take place next spring. It is anticipated that examiners will need to be identified and training conducted for the DAS II exam, which is administered at 36-months of age, by the end of 2009.

APEX – A Part of Network Daily Life

► *The APEX* study is well underway at all of the Network centers and data gathering seems to have become routine, although it continues to require a monumental effort. Among the entered AP01 forms, 51.2% were entered within two weeks of delivery.

As of September 29, there have been a total of 1549 days of data collection among all of the 25 participating hospitals, resulting in 21,812 enrolled patients. Charts from 15,927 of these have been abstracted and entered into the web data base.

The data base is being carefully edited and audited and the BCC software staff are working on the release of more web reports that will help the nurses keep track of missing data forms. Centers should notify the BCC staff if they notice that their computer

performance drops while using the MIDAS system, which could be the result of large databases.

In Memoriam



Robert C. Cefalo, MD, PhD, professor emeritus of obstetrics and gynecology in the UNC School of Medicine, director of the medical residency and fellowship programs at UNC Hospitals for 25 years, and the first Chair of the NICHD MFMU Network Steering Committee, died April 22 at the age of 74.

A native of Boston, MA, Dr. Cefalo earned his undergraduate degree at Tufts University, and his PhD from Georgetown University. He entered the US Navy Medical Corps where he received his advanced medical training in 1956 and served until he joined the UNC faculty in 1979.

During his tenure as the Steering Committee Chair from 1986 – 1991, he was also head of the UNC physician training programs (1981-2006), served as assistant dean for graduate medical education, and was director of maternal fetal-medicine (1979 – 1997). While he was Chair, the Network initiated four research trials: Induction vs Expectant Management in Postterm Pregnancy, Low-Dose Aspirin as a Preventative of Preeclampsia, Adjunctive Antibiotic Treatment in Preterm Labor with Intact Membranes and Low-Dose Aspiring Aspirin to Prevent Preeclampsia in High Risk Women.

Dr. Cefalo served terms as president and chair of the American Board of Obstetrics and Gynecology and as president of the North Carolina Obstetrical and Gynecological Society where he was also honored by the North Carolina Governor's Commission on Reduction of Infant Mortality for contributions to the improvement of maternal and infant health.

Advisory Board to Review 7 Proposed Protocols

The Network's Advisory Board is being convened on two separate conference calls – October 15 and November 5 – to review protocols that are in the Network's queue for implementation. Those serving on the Advisory Board are: Drs. Larry Gilstrap, Roger Newman, Martin Keszler, Margaret Harper and Raymond Bain. In addition to the ALPS trial, which should be starting soon, the Board will review six additional approved protocols and rate them according to a) importance for MFMU to undertake, b) scientific priority, c) clinical relevance and d) potential impact. Following the Board's review and comments, the Network's Protocol Prioritization Committee will determine which study will be undertaken next.

Following are the six Network approved protocols being reviewed by the Advisory Board:

- Antenatal late preterm steroids (ALPS) – already in progress
- Maternal hyperimmune globulin prophylaxis to prevent congenital CMV infection
- Cord gas values and neurodevelopment
- 17 alpha hydroxyprogesterone caproate as adjunct therapy for preterm labor
- MFMU rare events surveillance system
- Randomized, placebo controlled trial of vitamin C and E supplementation to prevent recurrent preterm premature rupture of the membranes
- Perinatal transmission of hepatitis C – disease prevalence, risk factors and clearance rate

Winner of "An age Problem"

Leonardo Pereira, ultrasonographer at OHSU, was the first to enter the correct answer to the June Networker puzzle.
Yes - Mary is also 90 years old!

Solve the following puzzle and be the first to submit the solution to Lucy_L@bsc.gwu.edu to win recognition in the next newsletter.

AN UNUSUAL YEAR

The year 1961 had the rare property of reading the same upside-down (assuming the ones are written as vertical strokes).

1. Of how many years (A.D.) has this been true so far?
2. When is the next year for which this will be true?



MFMU CALENDAR

Remaining 2008 Network Meeting dates
October 23 – 24

2009 Network Meeting dates
January 8 – 9
April 23 – 24
July 9 – 10
October 22 – 23

SMFM 29th Annual Meeting: January 26-31, San Diego

Society for Gynecological Investigation (SGI)

- Abstracts due to mfmuprop@biostat.bsc.gwu.edu by noon October 13
- Publications conference call October 17
- Abstract Submission: October 21, 11:59 CDT
- Annual Meeting: March 18-21, Glasgow, U.K.