

NIH Conference Held on C-Section Upon Maternal Request

In response to growing concern regarding the increase in cesarean deliveries (CD) performed on maternal request, the NIH convened a State-of-the-Science Conference from March 27 to 29. Overall, the CD rate reached 29.1 percent of births in the U.S. in 2004, of which it is estimated that 4 – 18 percent were performed upon request without medical necessity.

The impartial, independent panel reviewed the available literature in advance and then, during the first day and a half of the conference, heard presentations by expert researchers and practitioners that were further discussed in a public forum. The panel was charged with presenting a statement of its collective assessment of the evidence to answer four questions on the third day: 1) What is the trend and incidence of cesarean delivery over time in the U.S. and other countries? 2) What are the short-term (under one year) and long-term benefits and harms to mother and baby associated with CD by request versus attempted vaginal delivery? 3) What factors influence benefits and harms? 4) What future research directions need to be considered to get evidence for making appropriate decisions regarding cesarean on request or attempted vaginal delivery?

On the final day, the panel released a lengthy draft statement (available at <http://consensus.nih.gov>) that



included seven major conclusions: 1) There is limited evidence suggesting that the incidence of cesarean delivery on maternal request (CDMR) is

increasing in the U.S.; 2) There is insufficient evidence to fully evaluate the benefits and risks of CDMR as compared to planned vaginal delivery (PVD) and more research is needed; 3) Until quality evidence becomes available any decision to perform a CDMR should be carefully individualized and consistent with ethical principles; 4) Given that the risks of placenta previa and accreta rise with each CD, CDMR is not recommended for women desiring large families; 5) CDMR should not be performed prior to 39 weeks or without verification of lung maturity because of the significant danger of neonatal respiratory complications; 6) A request for CDMR should not be motivated by the unavailability of effective pain management with efforts made to assure availability of pain management services for all women; and 7) NICHD should establish and maintain a Web site to provide up-to-date information on the benefits and risks of all modes of delivery.

The panel's statement will be finalized in three weeks and published in the June issue of *Obstetrics & Gynecology*.

MFMU Network Project Scientist, Dr. Cathy Spong, one of the organizers of the conference, was invited to appear on the CBS

Early Show the day following the conference to talk about the results and implications from conference. Afterwards, she was interviewed by hosts of twelve different radio shows.

Network Re-competition Yields 14 Centers

The MFMU Network re-competed this year with 14 centers recommended for funding for the 2006-2011 cycle including two new centers. The two new centers are the University of Texas Medical Branch (UTMB) in Galveston and the Oregon Health and Sciences University (OHSU) in Portland.

Protocol and certification training for staff at the new centers is scheduled to take place at the BCC on Tuesday, April 24. Meanwhile, the new centers are working to acquire IRB approval for the CAPPs and GDM protocols. To get up to speed on Network procedures, UTMB staff have visited UNC and UAB. (Please see "People in the News" for staff bios.)

Karen Dorman, Chair of the Nurse Coordinators, has been advising the new coordinators on how to start a new Network center efficiently. All of the coordinators have contributed to a handbook on useful information and tips which will be shared with the new staff at their orientation.

New Chair of Steering Committee Appointed

NICHD has just announced that J. Peter Van Dorsten, MD, who is affiliated with the Medical University of South Carolina, will be the new Chair of the MFMU Network. Dr. Van Dorsten has a history with the Network going back to 1991, when he was a

Network PI, first at the Medical College of Virginia and then at the Medical University of South Carolina where he moved in 1992. He was a member of the Network's High Risk Aspirin Subcommittee. MUSC left the Network in 1996.



Dr. Van Dorsten has been very active in the profession, having served as President (*cont. pg. 2*)

(Van Dorsten cont.)

of the Society for Maternal-Fetal Medicine in 2000. He currently is Professor and Chairman of the Department of Obstetrics and Gynecology at MUSC with specialties in high risk pregnancy, breech presentation/external cephalic version and operative obstetrics.

Study Updates

CAPPS Study Keeps Network Busy

The sheer volume of patients being recruited into the CAPPS trial has necessitated many housekeeping activities for Network staff. By the end of March more than 5,500 patients had been randomized to the trial with almost 700 of them also enrolled in the Observational Prediction cohort. In order to keep on top of data management, the BCC has requested that the centers respond to queries regarding lost-to-follow-up patients (159) and patients with overdue forms (88) by April 5. In reaction to several centers being able to recruit to the trial, but not enrolling many patients in the Prediction cohort, conference calls with participants from NICHD, NHLBI, BCC and Drs. Roberts and Myatt were held in March with four centers (UT-Southwestern, UT-Houston, Northwestern and Columbia) to discuss problems and strategies. In addition, the Subcommittee has reviewed 126 charts for the primary outcome during six conference calls since January.

The results of the UK's Vitamins in Pregnancy (VIP) trial were announced at the SGI annual meeting in March, followed by a manuscript in the *Lancet* and quickly picked up by the media. This trial studied whether the administration of vitamins C (1000 mg) and E (400 IU) to pregnant women who have preexisting risk factors for developing preeclampsia such as diabetes, preeclampsia in a previous pregnancy, hypertension requiring medication, chronic renal disease, multi-fetuses, reduced its occurrence. The trial had some unexpected results, including increasing the rate of babies born with a low birthweight in the diabetic group. The incidence of preeclampsia was similar in the treatment and placebo groups. The CAPPS trial, which is being conducted by the Network, is studying patients who do not have the above listed health problems and who are considered to be at low risk for developing preeclampsia.

The MFMU Network's DSMC reviewed the VIP data prior to its presentation and publication and determined that the CAPPS trial should continue without modification.

STTARS Trial Nears Completion

Recruitment into the twins stratum was completed at the end of February with a total of 661 patients randomized. The triplet stratum will continue to recruit, but only 18 remain to be enrolled as of the end of March. This twin stratum was completed in record time, with only three years between concept presentation to the Steering Committee and completion of enrollment. A chart review will be held at the April Steering Committee Meeting to review some specific outcomes including elective deliveries less than 35 weeks and coding for delivery indications.

Omega-3 Enrolling Patients Ahead of Schedule

Following in the footsteps of the STTARS trial, the Omega-3 trial is recruiting more quickly than estimated and probably will be finished recruiting before the end of this year. In response to a Subcommittee concern regarding patients being randomized who had a

planned cesarean delivery (mostly patients with a previous cesarean delivery with a classical incision), the January Steering Committee meeting voted to change the protocol and added an exclusion code for planned elective cesarean delivery before 37 weeks.

The application for the Certificate of Confidentiality has been completed and submitted to NICHD for approval. The BCC will let Centers know when it receives notification of official action.

BEARS Follow-up to End

While many of the infants born to the women participating in the repeat corticosteroids trial have completed the 24 month follow-up visit, the PI, Dr. Ron Wapner, is encouraging centers to contact the remaining patients to return for this visit. To request funds that are available to help with bringing patients back, please contact Dr. Ron Wapner or Ms. Michelle DiVito.

All follow-up visits must be completed by May 31, and all data entered by June 14. While the current follow-up rate is very good at 79 percent, Dr. Wapner's goal is 85 percent. As of earlier this year, 6 centers had accomplished a 90 percent or better follow-up rate (Magee, UAB, Wayne State, Utah, Drexel and Northwestern), while 2 centers had less than a 60 percent rate. To meet the 85 percent goal, only 31 more children need to have the follow-up exam.

Network's 20th Anniversary Celebrated in Miami

The 25th annual meeting of the Society for Maternal-Fetal Medicine specialists, held in Miami Beach this past February, was the setting for a dinner to celebrate the 20th anniversary of the NICHD MFMU

Network. More than 90 past and present members of the Network and honored guests attended the reception and buffet dinner at Shula's Steakhouse Restaurant on February 3.

Attendees were presented with a 37 page booklet describing the last 20 years of work performed by the Network. They also were encouraged to participate in a history quiz. Most participants were stumped by the quiz which consisted of twelve questions regarding Network personalities, trials and publications. The prize (a bottle of wine!) went to Karen Dorman, UNC coordinator. Extra copies of the booklet are being distributed by the BCC. If you would like a copy, please contact Karla Lawrence at the BCC.



FOX Trial Results Announced; Wins Main Award at SMFM

Dr. Steve Bloom's published abstract and oral presentation regarding the results of the MFMU Network's FOX trial was the lead presentation in the first plenary session at the Society of Fetal-Maternal Medicine's 2006 annual meeting, and subsequently received the award for best presentation.

The objective of the Network's trial was to measure whether knowledge of fetal oxygen saturation, as an adjunct to continuous electronic fetal monitoring, is: 1) associated with a significant change in the overall rate of cesarean delivery, including those performed specifically for non-reassuring fetal heart rate pattern and dystocia, and 2) related to infant condition at birth. 5341 nulliparous women in early labor at term were randomly assigned to "open" (fetal oxygen saturation values displayed) or to "masked" fetal pulse oximetry (values hidden but recorded by computer).

The trial was stopped before the final sample size of 10,000 because the overall cesarean rate in the masked arm was higher than expected. The investigators have concluded that knowledge of fetal oxygen saturation is not associated with a reduction in the rate of cesarean delivery or improvement in the newborn condition. The final manuscript has been submitted to a major medical journal for consideration. Numerous secondary analyses of the data are expected to follow.

Trial of Thyroid in Pregnancy Nears Start-up

Following the recommendation of the MFMU Network's Data and Safety Monitoring Committee and with the approval of the Network's Steering Committee, the Subcommittee has revised the protocol to include an additional group of pregnant women who are considered hypothyroxinemic (low free T4 and normal TSH hormones). This group, in addition to the original group of pregnant women with subclinical hypothyroidism (normal free T4 and elevated TSH hormones), will be studied to see if the administration of thyroxine is effective in improving the intellectual ability of their offspring at five years of age.

Eligible women with a singleton pregnancy between eight and twenty-one weeks gestation will be randomized to receive thyroxine supplements or placebo. Dose adjustments will be made based on the results of monthly blood tests for thyroid hormone levels. It is estimated that 120,000 women must be screened to yield the 1,000 randomized patients needed for the trial (500 per group).

The primary outcome will be the IQ score at five years of age as based on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III). Infants will have yearly examinations until 5 years old that will test their intellectual development. Mothers will have follow-up blood draws at one and five years postpartum to test for thyroiditis or the development of overt hypothyroidism.

Proposals have been solicited for a central laboratory that will do all of the thyroid testing. Discussions are underway with the drug supply and distributing company for the study medications and preparation of the IND for the FDA. Training for nurse coordinators is scheduled for April 26 at the BCC.

Next Network Trial Selected

After a ranking of existing approved protocols by the Network's Steering Committee, which was followed by a discussion of results by the Prioritization Committee, the vote was cast to implement a trial of *Progesterone for Prevention of Preterm Birth in Nulliparous Women with a Shortened Cervix in the Second Trimester*. The protocol subcommittee chair is Dr. Bill Grobman of Northwestern University.

This study will enroll about 750 patients between 16 and 22 weeks gestation who have a cervical length less than 30mm, as measured by transvaginal or transabdominal ultrasound. After an initial compliance run-in, consenting patients will be randomized to receive 17 α -hydroxyprogesterone caproate or placebo. It is estimated that approximately 7,000 patients will be screened for the trial.

Typical U.S. Pregnancy Now is Only 39 Weeks

According to a new analysis by the March of Dimes, published in the March 2005 special supplement of *Seminars in Perinatology*, the average length of pregnancy in the United States is now 39 weeks, a week shorter than the traditional definition of a full-term pregnancy. The paper was presented at a July 2005 symposium sponsored by NICHD.

According to the report, 25 percent of all singleton babies were born full term at 39 weeks in 2002. Between 1992 and 2002, births at or after 40 weeks declined by nearly 21 percent while births occurring between 34 and 36 weeks increased 12 percent.

About one in eight babies is born prematurely and 70 percent of these are "late preterm", accounting for more than 355,000 births a year. Late preterm babies can suffer complications of respiratory distress, hypoglycemia, temperature instability, jaundice and reduced brain development. The amount of time these babies spend in the intensive care unit has a significant impact on public health care because the total hospital cost is about the same as it is for the extremely preterm babies since there are more of them.

The March of Dimes analysis suggests that increasing rates of Cesarean section deliveries and induced labor, as women become more focused on controlling their delivery dates, have probably contributed to, but do not completely explain these shifts in deliveries. They encourage all women who have a singleton, uncomplicated pregnancy to go to term.

People in the News

Joining the MFMU Network from the *University of Texas Medical Branch (UTMB)* are:

- MFMU Network PI, **George Saade, MD**, Professor of Obstetrics and Gynecology, and currently Director of the Chairman's Research Group. He received his medical degree from the American University of Beirut Medical School and was a resident in OB/GYN at Union Memorial Hospital in Baltimore. Prior to affiliating with UTMB in 1995, Dr Saade was a MFM Fellow at Baylor College of Medicine



where he conducted extensive laboratory and basic science. He has continued his research at UTMB in the areas of maternal and fetal medicine including preeclampsia, preterm labor and fetal physiology and therapy, garnering numerous awards and authoring hundreds of research articles. He holds several editorial positions on professional journals and served as Program Chair for the SMFM 2006 annual meeting. He and his wife, Yomna, an Endocrinologist in private

practice, are the parents of 9 and 13-year old girls. He is an opera buff and lives for snow skiing!

- Nurse Coordinator, **Joan Moss, MSN, WHCNP**, who received her Master's of Science in Nursing – Women's Health Nurse Practitioner Program at UTMB in 2004, and is the Senior Research Nurse Coordinator in the Department of OB/GYN Division of MFM. She co-manages high risk pregnancies with MFM faculty in the outlying UTMB regional maternal child health clinics. She has experience recruiting and enrolling subjects for various ongoing research studies within the department of obstetrics. Prior to enrolling in graduate school, Joan practiced obstetrical nursing for 20 years, including conducting childbirth, breastfeeding and gestational diabetes classes. Her hobbies are long distance cycling, surfing, reading and traveling with her family.

Staff from the Oregon Health and Science University will be profiled in the next issue of the Networker.

On the Light Side: Return of the Brain Teaser Contest

The first person to submit the correct answer will receive special recognition. Please submit to: Lucy_L@biostat.bsc.gwu.edu.

My coffee shop has just raised the prices, but hasn't yet printed a new menu. I will learn the new prices by observing the cashier.

The first customer buys 1 sandwich, 3 danish and 7 coffees (to go) for \$14. The second buys 1 sandwich, 4 danish and 10 coffees for \$17.

- 1) How much will I pay for a sandwich, a danish and a coffee?
- 2) If I wanted to buy 2 sandwiches, 3 danish and 5 coffees, how much would I pay?



MUFMU CALENDAR

2006 – 2007 Steering Committee Meetings

April 27-28, 2006
 July 20-21, 2006
 October 19-20, 2006
 January 18-19, 2007
 April 26-27, 2007
 July 12-13, 2007
 October 11-12, 2007

2007 Professional Meetings

SMFM.....February 5-10, San Francisco, CA
 SGI..... March 14-17, Reno, Nevada

2006 Publications Deadlines

April 15 – Proposed analyses to Subcommittee Chairs
 April 30 – Subcomm.-approved analyses to Pubs Comm.
 June 15 – SGI proposed analyses to Subcomm. chairs
 June 30 – Subcomm.-approved analyses to Pubs Comm.
 August 11 – Abstracts due at SMFM
 December 15 – Manuscripts due (if to be included in the SMFM issue)