



The MFMU Networker

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January 1st Start for Cesarean Section Registry

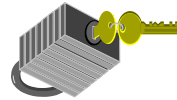
All MFMU Network centers will begin collecting data for the Cesarean Section Registry on the same day - January 1, 1999! This unusual procedure for study start up was planned so rates of deliveries can be assessed for each center over the same period of time. As of December 11, six centers had IRB approval and eleven centers had at least one certified nurse. Even if centers do not have IRB's by January 1, they will be required to enter the screening log, which records the number of daily C-Sections, VBACS, and non-VBAC vaginal deliveries. Centers will gather patient data on these deliveries once their IRB is approved. It is expected that about 1700 patients per month total will be enrolled.

The Steering Committee decided at the October meeting to add new form to collect data on Hypoxic Ischemic Encephalopathy. This data will evaluate whether infants suffer neurological damage. This form, along with other factors such as IRB approval have slightly delayed the study. Time was also spent on a capitation exercise to determine how long it takes to obtain data for study patients. As a result of the exercise, the capitation rate was increased to \$55.00 per enrolled patient.

BV Trial Data Lock / TV Trial Ends

With a December 2nd deadline looming for the BV trial data lock, research staff have been frantically completing outcomes for non-randomized patients in the fFN Ancillary, cleaning up the last of the edits and audits and, miraculously, finding delivery dates for presumed lost to follow-up patients! These efforts have decreased the lost to follow-up rate to 38 of 1953 patients (less than 2%). Dr. Ken Leveno at UTSW personally called hospitals in Dallas and had great success in obtaining outcome data for patients who were randomized at his center but did not deliver there.

Meanwhile, a last ditch effort to increase recruitment to the TV trial and suggested modifications by the subcommittee were not enough to dissuade the Data Safety and Monitoring Committee from recommending the trial be ended. Therefore, screening for the trial ended November 30. It is expected that eligible patients will be randomized through January, with final outcomes known by July.



SMFM Accepts All Network Abstracts & Selects BV Study for Plenary

For the seventh consecutive year a MFMU Network abstract has been selected for a Plenary Session at the annual meeting of the Society of Maternal Fetal Medicine. Only eight out of approximately 1000 submitted abstracts are accepted for the Plenary Session each year. This year, Dr. Mark Klebanoff will be presenting the results from the BV trial as the opening paper for the entire meeting, "*The effect of metronidazole on preventing preterm birth in asymptomatic women with bacterial vaginosis*". Besides the Plenary presentation, there will be three other orals, two given by Dr. Robert Goldenberg from the Preterm Prediction study and one by Dr. Alexander from the pPROM study, and six poster sessions. See the list of abstracts in the September issue of the *Networker* for titles.

S.C. Approves New Study of GDM

In October, the Steering Committee approved a new study, the Randomized Clinical Trial of Mild Gestational Diabetes Mellitus. This RCT will examine whether identification and treatment of mild GDM is associated with a lower risk for adverse perinatal outcome. The trial also includes four observational cohorts which will examine LGA and other data.

Reminder to Use Logo

Please use the Network logo on SMFM posters and slides! You can download it from the BCC web site at:

www.bsc.gwu.edu/~mfmuweb. Go to MFMU Network Study Documents and Reports and, after entering your password, click on MFMU Network Logo under Study Documents. Right click on the image with your mouse and choose "save as" to save the .gif file onto your hard drive where it may be edited.

BEAM Trial Feasibility to be Assessed.

A committee comprised of selected members of the DSMC and other reviewers chosen by NINDS will review BEAM data in mid-February. The focus will be on protocol adherence and success of the 6-month follow-up visit. Data will be collected on patients through December and then transmitted to the BCC and "cleaned up" during the first two weeks in January. It is important that all research staff respond to data queries as quickly as possible. As of December 9, 344 patients were randomized and 38 six month follow-up visits had been held.

Meanwhile, Dr. Dorothy Bulas of the Children's National Medical Center has done a preliminary assessment of head scans for quality and technique. Dr. Bulas was one of two reviewers for IVH in head scans from the High Risk Aspirin study. Most of BEAM scans were acceptable, and she has agreed to talk with the radiologists where improvement is needed.

There also was another training for eight new follow-up examiners in November at the Kennedy Krieger Institute at Johns Hopkins University, bringing the total number of trained examiners to 26. A conference call among follow-up coordinators was held December 15 to discuss techniques and strategies to ensure patients return for their follow-up visits. A patient from Center 18, UTSW was successfully tracked when she moved to Chicago where she was put in contact with Center 14, which was able to perform the infant's 6 month exam!

Formula for Placebo Steroid Drug is Waterlogged

The manufacture of the placebo drug for the Steroids Trial was delayed by the Hurricane that hit Puerto Rico in October! (Is this excuse the equivalent of "the dog ate my homework"?) Though details are unclear, apparently the facility used by Schering Drug, which has agreed to provide specifications for the formula, was damaged in the hurricane. Consequently, Schering was not able to forward the specs to Eminent Services, which has responsibility for its manufacture, until recently.

Following recommendations from the October meeting of the Data Safety and Monitoring Committee, modifications to the protocol have been made. The inclusion criteria have been changed to include patients with a short cervix or funneling by ultrasound and a previous spontaneous preterm delivery. The primary outcome was also changed so that only severe, rather than any, RDS will be included. This decision will increase the sample size by 400 to 2,400.

Dr. Ron Wapner and Coordinator Michelle DiVito spent December 18 at the BCC working with BCC staff on the manual and data forms.

Asthma Studies Enrollment Slows

Like fund raising, the last few patients seem to be the hardest to recruit. Perhaps our Centers have found the cure for asthma in pregnancy, or perhaps La Nina is responsible! Only 15 patients need to be enrolled in the mild cohort to complete the Observational Cohort Study. The other cohorts were closed in August. The Universities of Alabama, Cincinnati and Chicago were the high recruiting centers.

Though the eligibility criteria were tightened for the randomized trial which has made recruitment more difficult, capitation was increased to \$2,000 per patient. As of December 9, only 68 more patients are needed. So far, recruitment has improved in December.

Centers are reminded to send their IRB approvals to NICHD for the Maternal and Cord Plasma Levels of Inhaled Corticosteroids Ancillary Study and are urged to increase recruitment. Remember, this study is funded by an outside source.

A one day Asthma Protocol Subcommittee meeting is being planned for early Spring with consultants selected by NIH/LBI. They will discuss ideas for follow-up studies on women who participated in these asthma studies, and plan analyses of the observational data..

Development of New MFMU Study Underway

The next protocol in line for implementation in the Network is an observational study evaluating obstetric outcome in women with the factor V Leiden mutation. Women with the factor V Leiden have an increased risk for deep vein thrombosis (DVT), which is the number one cause of maternal mortality in pregnancy. Women will be enrolled and genetically screened to see if they are positive for this mutation and, if so, followed for thromboembolism and obstetric outcome.

The objective is to determine the proportion of women with the factor V Leiden mutation who have DVT.

Based on certain assumptions, 3,350 women need to be screened prior to 22 weeks gestation for the mutation to identify 67 individuals as being factor V Leiden mutation positive. The neonates of the positive women will also be tested for the mutation. This study may lead to a trial of heparin therapy.

BCC Y2K Compliance Status

In the event anyone is wondering what the BCC is doing to ensure that the Network software and hardware don't crash or a zillion data queries aren't generated because the year of birth or EDC isn't read correctly at the turn of the millennium, here's the scoop.

Like many other institutions, The George Washington University has outlined a number of steps and procedures that each department must go through. The BCC sent letters to all subcontractors and clinical centers this month requesting that they report to us on their efforts to meet compliance. The BCC also submitted a report to NICHD on the progress of our efforts to meet

compliance. Appropriate changes are already being made to production, edit and audit programs. Fortunately, women's pregnancies do not last more than 100 years so the programming changes are not difficult, though testing is still required! Watch for future updates on the Network's Y2K status.

Network to Participate in MSCIDA Study

For the past year and a half, Cynthia Shellhaas of OSU, who received NICHD's first Medical Specialized Clinical Investigator Development Award, has been developing a research protocol as part of her Fellowship. Her project, Cervical Length in Women with Preterm Prematurely Ruptured Membranes, is planned to begin in January. The objective of the study is to determine if cervical length is an independent predictor of the length of the latent phase between time of rupture and time of delivery. Two different subsets of patients, early and late pPROM, separated on the basis of gestational age, will be looked at. The sample size is 245 women.

Fellows at ten other Network centers besides OSU will participate by screening and enrolling patients, and collecting and sending data to OSU where data analysis will be done. On December 9-10, Cynthia consulted with BCC staff and Dr. McNellis to finalize protocol and data collection details.

1998 Sees Proliferation of MFMU Network Publications

In addition to the following eight journal articles which were published in 1998, three others have been accepted and nine additional ones have been submitted! This *has* been a busy year!

1. Mercer BM, Das A. **Reply to: Premature Rupture of Membranes, Antibiotics, and Amnioitis.** *JAMA*, 279(1):22, 1998.
2. Mercer BM, Thom EA, Goldenberg RL. **Reply to: Antibiotic Therapy for Premature Rupture of Membranes to Prevent Respiratory Distress Syndrome.** *JAMA*, 279(10):749, 1998.
3. Goldenberg R, Iams J, Mercer B, Meis P, Moawad A, Copper R, Das A, Thom E, Johnson F, McNellis D, Miodovnik M, VanDorsten JP, Caritis S, Thurnau G, Bottoms S for the NICHD Maternal Fetal Medicine Units Network. **The Preterm Prediction Study: The value of new vs standard risk factors in predicting early and all spontaneous preterm birth.** *Am J Public Health*, 88(2):233-238, 1998.
4. Meis P, Goldenberg R, Mercer B, Iams J, Moawad A, Miodovnik M, Menard MK, Caritis S, Thurnau G, Bottoms S, Das A, McNellis D for the NICHD Maternal Fetal Medicine Units Network. **The Preterm Prediction Study: Risk factors for indicated preterm births.** *Am J Obstet Gynecol*, 178:562-567, 1998.
5. Iams J, Goldenberg R, Mercer B, Moawad A, Thom E, Meis P, McNellis D, Caritis S, Miodovnik M, Menard MK, Thurnau G, Bottoms S, Roberts J and the NICHD Maternal Fetal Medicine Units Network. **The Preterm Prediction Study: Recurrence risk of spontaneous preterm birth.** *Am J Obstet Gynecol*, 178(5): 1035-40, 1998.
6. Caritis S, Sibai B, Hauth J, Lindheimer M, Klebanoff M, Thom E, VanDorsten P, Landon M, Paul R, Miodovnik M, Meis P, Thurnau G, Bottoms S, McNellis D, and Roberts J for the NICHD Maternal Fetal Medicine Units Network. **Low dose aspirin to prevent preeclampsia in women at high risk.** *N Eng J Med*, 338(11):701-705, 1998.
7. Caritis S, Sibai B, Hauth J, Lindheimer M, Klebanoff M, Thom E, VanDorsten P, Landon M, Paul R, Miodovnik M, Meis P, Thurnau G, Dombrowski M, McNellis D, Roberts J and the NICHD Maternal Fetal Medicine Units Network. **Predictors of preeclampsia in high risk women.** *Am J Obstet Gynecol*, 179(4):946-951, 1998.
8. Sibai B, Lindheimer M, Hauth J, Caritis S, Klebanoff M, MacPherson C, VanDorsten P, Landon M, Paul R, Miodovnik M, Meis P, Dombrowski M, Thurnau G, Roberts J, McNellis D and the NICHD Maternal Fetal Medicine Units Network. **Risk factors for preeclampsia, abruptio, adverse neonatal outcome in women with chronic hypertension.** *N Eng J Med*, 1998;339:667-671.

People in the News

◆ It was with sadness that we said a fond farewell to **Molly Fischer**, MFMU Network Coordinator in November. Molly left to take a position at the FDA working on projects that are being developed because of the Food and Drug Modernization Act (FDAMA). Her main project will be working with review divisions to review protocols and submissions for off label drug use and quality of life claims. She will also be working on the Pregnancy Labeling Task Force and in the area of managed care outcomes and pharmacoconomics. Sounds like she is going to be very busy! NICHD is working to create a government position for her replacement.

◆ Our appreciation also goes to **Carmen Alfonso**, Coordinator at the University of Miami, for her efforts in the Network over the past few years. Carmen took a position at another research center at the University. **JoNell Potter**, Director of OB/GYN Research, is taking over the position until a permanent candidate is found. JoNell, who is a nurse practitioner and a doctoral candidate in nursing at the University of Miami expecting to receive her degree in May, has been in research for 15 years. She currently oversees all the OB/GYN clinical trials at Miami including AIDS Clinical Trials Group and the Women's Health Initiative. She has two children, four and six years, and is the head of the Miami-Dade chapter of AWHONN, the Association of Womens Health, Obstetrics and Neonatal Nurses.

◆ **Jenny Mark** has joined the BCC as a research assistant on the Cesarean Section Registry. She majored in psychology at James Madison University and worked at the Chemical Manufacturer's Association in the area of public health outreach. Her one year old son Alexander keeps her busy, but she finds time for needlepoint and reading and plans to attend graduate classes at GWU.

◆ **Kevin Pinder** has taken over **Lynne Haverty's** duties as secretary for the BCC. He came to the Center through a temporary agency and found the job interesting and the environment enjoyable enough to stay! He is close

to finishing his degree in biology and looks forward to continuing his education at GWU. His interests include reading, especially philosophy and politics, medical science and hiking. He expects to announce his engagement soon!

◆ Our congratulations to **Dr. Sean Daly** who has been appointed Master of the Coombe Womens Medical Hospital in Dublin. The hospital is one of the largest womens health care centers in Ireland and the position is equivalent to being appointed CEO. Dr. Daly has been a Fellow at Thomas Jefferson and working on research, especially folic acid in the prevention of neural tube defects. We anticipate a continuation of an international research collaboration and to hear about his continued success in the future.

◆ Staff changes have also taken place at Tennessee where both research nurses, **Mary Peterson** and **Jennifer Doss**, left. We thank them for the hard work and dedication over the past years. We welcome nurses **Rhonda Carrasquilla**, **Donna Forge** and **Alison Kirk** who are working hard to get up to speed on Network protocols.

Calendar of Events



Steering Committee Meetings:

- February 11-12, 1999
- May 10-11, 1999