



The MFMU Networker

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GDM Trial Poised to Go

More than 25 MFMU Network clinic coordinators and research nurses attended a one and a half day training session in May at the BCC for the newest trial being implemented in the Network. The Gestational Diabetes Mellitus (GDM) trial will investigate whether dietary treatment and exercise for mild gestational diabetes will reduce the frequency of neonatal morbidity associated with maternal carbohydrate intolerance. Four hundred fifty pregnant women with mild GDM (a glucose loading test between 135 and 200 mg/dl and follow-up OGTT < 95 mg/dl) will be randomized to one of two groups: 1) formal nutritional counseling and diet therapy (and insulin if required) or 2) no treatment. Another 950 women with an abnormal glucose loading test (GLT), but normal three hour glucose tolerance test (OGTT), will be enrolled in an observational cohort matched by race and body mass index to the no treatment group. The fourth group of 475 non-diabetic controls will be enrolled by centers to meet a BCC-assigned quota based on race and body mass index.

A central laboratory, Quest Diagnostics, will be responsible for running the OGT tests and will notify the BCC of results within 24 hours of the blood draws. The BCC will contact the center to verify patient eligibility after which they will notify the study nurse at the center of the patient's randomization assignment. Quest will also be processing the cord blood after delivery for C-peptide analysis. At the GDM

Next Network Trial Gets NHLBI Funding

The NHLBI has signed a \$12 million dollar memorandum of understanding with the NICHD to perform a trial of antioxidant and preeclampsia prediction studies over the next 4 years. In addition, a medical research group from Canada has floated a \$3 million proposal which would include a high-risk patient component and utilize 15 Canadian centers. Further discussions regarding inclusion of the Canadians are being held.

This study consists of two parts: a randomized, controlled, double masked trial of 12,500 high and low risk patients who are randomized to receive 1000 mg vitamin C and 400 IU of vitamin E or placebos. The objective is to determine the safety and efficacy of antioxidant therapy initiated prior to 16 weeks for reducing the frequency of perinatal mortality and morbidity. The primary outcome for the RCT is perinatal mortality and morbidity: 1) fetal or neonatal death, 2) weight less than the third (*cont'd p. 2*)



Michelle Divito demonstrates correct head measurement technique on Cora MacPherson's son, Jack, whose T shirt reads "I'm statistically significant"!

training Dawn Pisciotta, a representative from Quest Diagnostics, described the procedures for collecting and shipping the bloods for the OGTT and the C-peptides.

The One Touch Ultra glucose meters, along with the lancets and test strips, are being purchased from Lifescan, a subsidiary of Johnson and Johnson Pharmaceuticals. Donald Zettervall, a Lifescan consultant specializing in diabetic education, demonstrated to the nurses at the training how to use the glucose meter and download the data into a computer. He also shared a number of tips on how to teach and manage patients who will be using the meters for the first time. The remaining tests, infant bilirubin and glucose, will be assayed at each center's local lab.

A conference call with each center's nutritionist will be held in mid-July to standardize dietary guidelines for patients in the trial. The BCC is finalizing the manual of operations, the data entry software and the certification requirements. Most centers have submitted their materials for IRB approval. An initial supply of materials for the OGTT and C-peptide collection has been sent to each center by Quest Diagnostics. Ohio State and Brown have begun collecting 200 cord bloods for the c-peptide pilot study, which will establish a 95th percentile. Quest has already begun running the assays and sending the results to the BCC. Centers should start full recruitment by the first of August

NICHD Launches Management of Myelomeningocele Study (MOMS)

Over the past five years, several U.S. hospitals have begun performing hysterotomies to close the neural tube of fetuses diagnosed with myelomeningocele (spina bifida). Traditionally, the defect is closed soon after a (*cont'd p 2*)

MOMS Trial, *cont'd*

baby with spina bifida is born. In-utero surgery is being promoted because it is thought that the severity of neurologic damage increases throughout the pregnancy. Although preliminary results look good with some suggestion that neurologic function is improved over traditional surgery, and the need for a ventriculoperitoneal shunt which is used to control hydrocephalus is reduced, the NICHD has funded a multicenter trial to determine the safety and efficacy of this operation.

The University of California at San Francisco, Vanderbilt University Medical Center and

Children's Hospital of Philadelphia, along with the GWU Biostatistical Coordinating Center (BCC), will cooperate in this study of 200 women carrying a fetus with spina bifida. Women will be screened by Dr. Catherine Shaer, Program Manager at the BCC, and, if qualified, will be sent to one of the three MOMS Centers. If still qualified after extensive medical and psychological evaluation, they will be randomized to prenatal or postnatal surgical repair of their fetus' spina bifida defect.

The status of the mothers and children will be followed for 30 months. The two primary outcomes

are death or the need for a ventricular decompressive surgery by one year of age, and a composite outcome of two measures: the Bayley Scales of Infant Development and the level of motor and sensory function.

The trial will start this summer with extensive publicity to the medical community to enhance recruitment, including a web site. If you know of a patient to refer to the study, please call Dr. Elizabeth Thom or Dr. Catherine Shaer at the Biostatistics Center (301-881-9260). Further information will be detailed in the next issue of the *Networker*.



Thoughts for the Day

- To steal ideas from one person is plagiarism, to steal from many is research.
- A conclusion is the place where you got to when tired of thinking.
- We can't solve problems by using the same kind of thinking we used when we created them!

Courtesy of Albert Einstein

Next Trial, *cont'd*

centile for gestational age, and 3) birth at or before 32 weeks gestation.

The other component of the study is a prospective observational study of biophysical and biochemical markers performed at specified intervals throughout gestation on a subset (5000 low risk and 1000 high

risk subjects) of the 12,500 women included in the antioxidant trial. The subjects in this component who receive placebo will provide information on possible predictors and early pathophysiological changes of preeclampsia. Those who receive the antioxidants may identify subsets of

women who are likely or unlikely to benefit from this therapy and indicate the impact of the therapy on the pathophysiology of preeclampsia.

It is planned to fast-track this study to start around the end of this year.

Infant Follow-up To Begin for BEARS Trial



The infants of the first patients randomized to the BEARS Trial in June 2002, are now due for their 24 months corrected age follow-up examination. The first 500 infants born in the BEARS trial will also receive a follow-up exam at three years.

Many of the procedures and lessons learned from the BEAM trial will be used. In fact, the follow-up coordinators and examiners will be the same for both studies at most centers. Though data collected will be similar to BEAM, pediatric examiners and developmental psychologists will be looking at other factors related to the use of antenatal steroids.

The BCC is finalizing the data collection forms and developing the software data entry and production programs. A training conference call with coordinators who are immediately involved with patient follow-up is also being scheduled.



NEWS?



FOX Finally Randomizing

After holdups caused by Nellcor's delay in validating their 2000 software update for the N400 and then problems caused by the new software's ultrasensitivity in detecting oxygen levels, the first patient was randomized on May 6 at the University of Alabama. As of June 19, 50 patients were reported as randomized. Four centers have been certified and are actively recruiting: U. of Alabama (20), UT Southwestern (19), U of Utah (8), U of Houston (3). The University of North Carolina, Case Western and Brown have also completed certification. Several others have completed their Nellcor training and are diligently working on the remaining certification requirements. By the end of June, all centers will have completed Nellcor's perinatal training.

Other than the N400 problems and a few center-specific glitches, mostly due to connecting to central monitoring systems, the study unit is performing as required. Data from the forms are being transmitted, uploaded on the mainframe at the BCC, and edited. Data from the study unit are also being successfully collected via the laptop computer and transmitted to the BCC where it is being examined and archived.

In general, medical staff and patients are receptive to participating in the trial. Of the 74 patients approached for consent in May, more patients were randomized than refused. The main reason patients were ineligible (again fewer than randomized) was their cervical dilation was greater than 5 cm. Once centers get their second study unit operational, recruitment is expected to increase.

New Data Entry System Implemented for the Network

More than a year and a half ago, the BCC embarked on a mission to revamp its distributed data entry system for the MFMU Network and generated interest on the part of staff working on other research projects at the GWU Biostatistics Center in this endeavor. After investigating a number of possibilities, Visual Fox Pro (VFP) was selected and programmer, Amarjot Singh, was hired to develop a more efficient and user friendly data entry system. It was decided that the MFMU FOX trial would be the guinea pig and that the existing protocols would remain in the old data entry system.

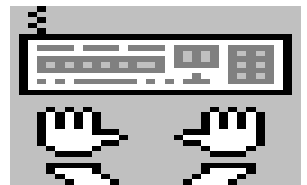
The software programmers who designed and maintained the original system (Julia Zachary, Alysia Jones and Brendan Broderick from the MFMU) were also key in developing the new system and ensuring it met the Network's data entry and reporting requirements. In addition, Ralph Kova brought his expertise in object-oriented programming (OOP) to the task. Besides providing a better screen and other options for keyers, the VFP system has also changed the way software programmers and research assistants assign variables, create data dictionaries and interfield checks, and run production on the PC and mainframe computers at the BCC. The fact that the Network programmers didn't need to bring any new protocols on line during the last couple of years made it possible to implement the new system so quickly for the FOX protocol.

By last October, the VFP system was ready to be previewed by the coordinators for their input and comments, at which time several coordinators requested that the BCC hold training sessions for their data entry staff. While not required for certification, six data entry people attended one of two sessions held in April and May. Three others have completed their certification by entering test forms, printing the forms and submitting them to the BCC along with the forms inventory report for review. Certification is required before data entry staff enter randomization data for the FOX trial.

Rachel Cavaness from Utah, who attended one of the sessions, raves about the new system and feels it is much more intuitive and helpful. Though she has experience entering Network forms for a year and a half, she said the BCC training was valuable and taught her little tricks that she might not have discovered. She loves the new Smart Skip option and believes it will really cut down on edits and audits caused by typos. She also says the new screen format is much easier to read and she likes being able to see on the screen what forms have been entered for patients.

Andrea Castille, an experienced data entry person from UTSW, did not attend the training but said she finds the new system self explanatory and easy to maneuver. The most difficult adjustment for her is getting used to the mouse. She also gives the Smart Skip an A+ and, in addition, likes the new use of the wild cards.

The VFP system has now been implemented for some BCC in-house keying of data forms and will be used for the new GDM trial and all other studies. Other NIH research studies within the GWU Biostatistics Center are now also using versions of the system beta-tested by the MFMU Network.



People in the News

- "We are FA-MI-LY"...and welcome **Chris Talucci** who is working at the BCC this summer. Chris is the son of **Mary Talucci**, a research nurse at MCP Hahnemann, and attends Tulane University in New Orleans where he is a junior majoring in computer science and math. Chris will be helping out the BCC with some computer programming and data entry.



A reminder... All biological fluids collected for the Progesterone trial should remain at your site until further notice. This includes the estriol and progesterone saliva samples, as well as the blood samples. All remaining Progesterone study drug will be shipped back later this summer after all patients deliver and you are notified.

M F M U Network Calendar

Steering Committee Meetings

- July 29-30, 2002
- November 18-19, 2002
- February 20-21, 2003
- May 5-6, 2003
- July 14-15, 2003
- October 23-24, 2003

SMFM

Abstracts due to Dr. P. Meis: August 2, 2002
Annual Meeting: February 3-8, 2003

ACOG Annual Meeting

April 28-30, 2003

AGOS Annual Meeting

September 18-19, 2003

