



The MFMU Networker

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Two New Network Trials Being Fast-Tracked

Two new studies are being readied for implementation in the Network. One is a follow-up to the recently completed successful Progesterone Trial that found a significant reduction in the rate of preterm deliveries in women who had previously experienced a spontaneous preterm birth. Because of this positive effect, the NICHD is anxious to have the FDA approve the manufacture and marketing of progesterone for clinical use.

The FDA has requested that a follow-up study be done on the offspring born to mothers who participated in this trial. The Network's follow-up study

may meet this goal. It will involve re-contacting these mothers and getting their consent to allow their children to undergo a developmental assessment.

With the approval of the MFMU Steering Committee PIs, Drs. Mark Klebanoff and Cathy Spong are working with the BCC to develop the protocol, manual of operations and data forms. Nurse Coordinators Allison Northen and Missy Swain have been assigned to the subcommittee and are providing input to the design of the study.



The other new protocol will investigate whether Omega-3 (fatty fish oils), in combination with the progesterone, will have an effect on preventing preterm deliveries in women who have experienced a previous

preterm delivery. After working unsuccessfully for over a year to develop a nutritional supplement, the Steering Committee decided to use a currently available capsule containing Omega-3. A matching placebo is also available. Eminent Services, Inc. will be responsible for stability testing, packaging, labeling and distribution of the study medication. The NICHD is waiting to hear from the FDA whether this new study will require its own IND or whether it will be accepted under the existing IND for the STTARS trial.

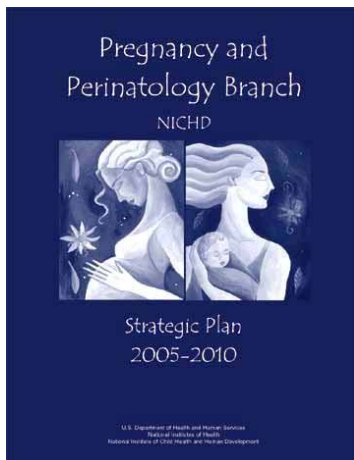
Coordinator training for both these trials will take place July 13-14, following the conclusion of the quarterly Steering Committee meeting. Following training, certification and IRB approval, it is hoped that both studies will begin in the Fall of 2004.

NICHD PPB Publishes Strategic Plan 2005-2010

In December 2002, the NICHD Pregnancy and Perinatology Branch (PPB) convened a two-day Planning Workshop to develop a research agenda that would guide Branch activities and priorities for the years 2005-2010. Fourteen eminent scientists participated and helped identify and prioritize scientific areas, research issues and the needs of the scientific community served by the PPB. The results of the workshop are reported in the NICHD publication, *Strategic Plan 2005-2010*.

One of the areas identified as having research gaps and needing increased investigation is prematurity. Despite research to reduce preterm delivery, approximately 10 percent of all births in the United States are still preterm and the rate is increasing. Preterm delivery accounts for 70 percent of perinatal mortality and for nearly half of the long-term neurologic morbidity of newborns. The underlying mechanisms of preterm birth are not understood; less than half of all preterm births have an identifiable risk factor.

New directions and approaches to addressing research gaps in prematurity are stated in the report and include investigating the etiology of preterm birth taking into consideration utero-placental insufficiency, fetal growth abnormalities and fetal stress. (Cont'd on page 2)



C-Section Findings Reported in *Child Magazine*

The June-July issue of *Child Magazine* featured an article, entitled *C-SECTION SURPRISE*, which reports to readers some of the findings from the MFMU NICHD Network's C-Section study that were presented at the 2004 SMFM meeting. The article points out that the research offers good news for women who have previously had a cesarean and are considering a vaginal birth. 73% of the women studied had successful vaginal births after a C-Section (VBACs), although the procedure involves slightly more risk than a repeat elective

cesarean. The overall rate of obstetric complications, such as endometritis or newborn brain injury, is one in 2,000 deliveries. Uterine rupture, the biggest concern, occurred in less than 1% of women.

Dr. Mark Landon, PI of the study, is quoted as stating that now that safety statistics are available, "women can ask their physicians whether they are good candidates for VBAC and be aware of the risks, albeit statistically small, so they can make an informed decision."

CAPPS Study Revised to Ease RN Workload

Both the RCT and Prediction protocols of the CAPPS study have been changed to help alleviate some of the research nurses' workload required by the multitude of required procedures. Instead of patients being seen by research nurses at each of the scheduled prenatal visits, they will be seen monthly to assess compliance and collect biological fluids. In addition, weight and blood pressure measurements will be recorded from the patient's same-day prenatal visit, as long as the clinical staff taking the patient's blood pressure are trained in BP techniques used by the Network.

In another change, the exclusion criterion addressing the use of antioxidants prior to randomization, as found in usual prenatal vitamins, was increased to permit up to 150 mg for vitamin C and 75 IU for vitamin E per day. Both of these changes require IRB approval and most of the sites are in the process of getting the approval, thus a positive effect on recruitment is still anticipated.

The centers were also notified that capitation has been substantially increased to allow for the hiring of additional staff to cover recruitment and follow-up of patients at outlying clinics.

Screening & Randomization Dates Widened for GDM Trial

The Steering Committee approved several modifications to the GDM trial at its April meeting to enhance recruitment. Screening eligibility was widened from 29 weeks 6 days to 30 weeks 6 days. Gestational age at enrollment was changed from 30 weeks 6 days to 31 weeks 6 days. Patients in Group II will be notified that they are assigned to Group II by the study nurse using a standardized script.

In addition it was decided that initial breast feeding does not impact neonatal glucose and therefore is allowed before doing the heel stick. However, glucose measurement by heel stick *must* be done before the *first non-breastfed* feeding and it must be analyzed by a lab, not a glucose meter. A question was also added to the maternal delivery form (MG10) to capture data on perineal lacerations.

Capitation also has been increased to encourage more screening and OGTT testing of patients. According to data received during the first part of June, these changes may be having a positive effect on recruitment.

MFMU - NICU Joint Network Meeting Deemed An Important Milestone

The Steering Committees for the Maternal Fetal Medicine Unit and the Neonatal Research Networks were brought together in a joint meeting last April for the first time in several years. Dr. Duane Alexander, Director of NICHD, who attended the morning session, noted the importance of having the two Networks share a collaborative research effort.

Principal Investigators from both Networks briefly presented recently completed, ongoing and upcoming studies that were followed by audience discussion. The afternoon session allowed time for discussion of "Hot Topics", including viability, genetics, pharmaceuticals and nosocomial infection.

Following the meeting, a survey of participants' evaluation was conducted. The results from 45 respondents are as follow:



Survey Results

Topic	Ranking (1 – 10)*
Scientific information presented at the meeting	8.0
Information regarding trials in both networks	8.4
Potential for research collaboration between networks	7.3
Meeting Frequency	Percent
Twice a year	2 %
Once a year	42%
Every two years	56%

*1=very poor, 10=excellent

(Strategic Plan cont'd)

Research also should focus on individualized growth assessment, early pregnancy and pre-pregnancy periods including the role of the cervix and variability in host responses, strategies for the prediction of preterm birth, methods of differentiating between women who are and are not in true labor, and studies to determine the role of tocolytics. Categorization of preterm birth should be improved and studies should focus on the cases with highest mortality and morbidity and not be diluted by including preterm births close to term which are clinically less relevant. Clinically applicable methods also would be useful for identifying pregnancies in which delaying delivery is futile or detrimental.

The report recognizes that many of the proposed studies require access to a large and diverse patient population as well as to representative tissue samples and, thus, recommends that a consortium of centers be involved together in preterm labor research and that tissue and data banks be included in the design of studies. NICHD also recognizes that consolidation, coordination and collaboration between the various groups involved in this area of research, including neonatology, would be more efficient than the present system.

Pregnancy and Perinatology Branch

NICHD

Report to the NACHHD Council
June 2004U.S. Department of Health and Human Services
National Institutes of Health
National Institute of Child Health and Human Development

PPB Branch Presents at NACHHD Council

The National Advisory Child Health and Human Development (NACHHD) Council of the NICHD convenes two-day meetings three times annually for the review, discussion, and evaluation of grant applications and related information. The Council meeting is open to the public on the first day for general Council business, presentation of new initiatives, Congressional issues, and a presentation from one of the NICHD Branches. On a rotating cycle, the extramural Branches undergo a review by Council for approval for continuation. For this review, the Branch prepares a report of what it has accomplished since the last review and highlights research advances. Commonly, two or three speakers present their work that was funded by the branch. The second day is closed to the public for their secondary review of the Institute's grant applications.

For the June meeting of the NACHHD Council, the Pregnancy and Perinatology Branch was up for review, covering the period from January 2000 to June 2004. Dr. Cathy Spong opened with a presentation of activities by the Pregnancy and Perinatology Branch. As one of the featured presentations, Dr. Jay Iams, MFMU Principal Investigator from Ohio State University, and Dr. Alan Jobe, Chair of the NICHD's Neonatal Research (NRN) presented work performed

by the MFMU and NRN Networks. They provided an overview of the Networks' history, organization, mechanisms, growth, trials, and goals.

BEAM Trial Ends Recruitment

After six years, the BEAM trial ended recruitment on May 31, 2004, with a total of 2240 patients randomized - about 20 patients over the recruitment goal. All infants require a two-year follow-up exam so the results of the trial (whether prophylactic magnesium sulfate given to women at risk for early delivery reduces the risk of death or moderate to severe cerebral palsy in their children) will not be known until sometime in late 2006.

The BCC has just issued new data entry software for the BEAM follow-up forms in the Visual FoxPro format that is being used for the newer Network studies. Directions for installation and use have been detailed to the Center personnel.

Two Ancillary Studies Added to STTARS Trial

Two ancillaries are being developed for the STTARS trial - one is a single center ancillary to be conducted by Magee-Womens, the other is a multi-center ancillary and involves blood collection, and a cervical exam at randomization and again at 26 weeks. Collection of fetal fibronectin also is being considered. The purpose of these ancillary studies is to evaluate the steady state pharmacokinetics of 17P, and the pharmacodynamic impact of 17P on biomarkers of progesterational activity. These biomarkers were selected because they are accessible and also are recognized as determinants of risk for preterm birth. Training on the STTARS outcome forms and the new STTARS ancillary studies will take place at the July training session.

Though the study began recruiting just a few months ago, the rate of randomization is encouraging! Coordinators have found that practitioners outside their MFM are enthusiastic about the trial and are referring patients to them. Thanks to the efforts of research nurse, Donna Allard at Brown University, a mother of triplets and member of the Triplet Connection, the STTARS trial is featured as a special interest article in its recently issued quarterly magazine. A summary of the Network's successful progesterone trial is given along with

details of the STTARS trial, a list of Network centers and a website link for further information at www.tripletconnection.org

Cochrane Neonatal Reviews On NICHD Webpage

The NICHD has been funding, in part, the Cochrane Neonatal Review Group to provide Neonatal Reviews for posting on the NICHD website. Through this web-link, anyone in the United States using the Internet can access the full-length neonatal reviews without having to go through a medical library.



To read these reviews, visit the NICHD website (<http://www.nichd.nih.gov>). Link to the *Sitemap* and scroll down to *Research Resources* and find the Cochrane page. There is an introductory section on systematic reviews, an alphabetical listing of 169 full-length reviews that lead to the full manuscript, and instructions for searching. If you wish to suggest topics for future reviews, or carry out reviews, please contact: Dr. Tonse Raju, MD, Medical Officer, PPB/CDBPM/NICHD: E-mail: rajut@mail.nih.gov (Phone: 301-402-1872).

Nurse Coordinators Asked for More Input to Network Studies

At the April 2004 Steering Committee meeting, the nurse coordinators were asked to discuss the current state of the Network and to suggest further directions. As a result of their recommendations, nurse coordinators will be seated surrounding the main meeting table to allow closer proximity to the PIs and to facilitate their input. In addition, it was suggested that for each new concept approved by the Steering Committee, a subcommittee of three nurse coordinators, one of whom will be the coordinator working with the proposing PI, would be established. This subcommittee would submit a formal analysis of each protocol to the proposing PI for consideration prior to his/her next presentation to the Steering Committee of the concept at the miniprotocol phase

NICHD RFA to Establish New Network

The NICHD PPB Branch has announced the release of a new RFA that will establish a Genomic and Proteomic Network for Premature Birth Research (RFA-HD-04-002). The Letter of Intent must be received by July 20, 2004, and the application must be received by August 20, 2004. The application can be found at

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-HD-04-002.html> or through the NIH Guide (<http://grants.nih.gov/grants/guide/rfa-files/index.html>). Scroll down to [RFA-HD-04-002: Genomic And Proteomic Network For Premature Birth Research](#)

The purpose of this solicitation is to create a network for premature birth research. The aim of the network is to

accelerate the pace of premature birth research by focusing on global genomic and proteomic strategies and the dissemination of genomic and proteomic data to the scientific community.

Specifically, the network will: 1) design and implement hypothesis-driven, mechanistic studies based on large-scale, high-output genomic and proteomic approaches, and 2) provide a public, web-based, genomic and proteomic database for data mining and data deposition by the research community. It is anticipated that the creation of this network will hasten a deeper understanding of the pathophysiology of premature birth, discover novel target molecules and diagnostic biomarkers, and ultimately aid in formulating more effective interventions to prevent premature birth.

People in the NEWS

◆ Congratulations to **Stephanie Lege-Humbert**, BEAM follow-up coordinator at UT-Houston who had a baby on April 19. He was 21 inches long and 9 pounds and his name is James Tyson Humbert. According to Mary-Clare Day, mom, dad and baby are all doing great.

◆ Get well wishes continue for **Kris Anderson**, Coordinator at Utah, who required surgery on her shoulder after an accident at the April Steering Committee meeting. Two weeks after *that* surgery she had carpal tunnel surgery on the same arm. Not really a glutton for punishment, Kris figured that if her arm was out of use for awhile, she might as well have her carpal tunnel problem fixed! She is undergoing physical therapy but still intends to attend the July Steering Committee meeting

MFMU CALENDAR



Steering Committee Meetings

July 12 - 13, 2004
October 21 - 22, 2004
January 27 - 28, 2005
March 17-18, 2005
July 21 - 22, 2005
October 27 - 28, 2005

Protocol Training (Omega-3, Follow-Up, STARS Ancillary)

July 13-14, 2004

Professional Meetings

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

2004-5 Analysis Submission & Prioritization Deadlines for SMFM & SGI 2005 Annual Meetings

	<u>SMFM</u>	<u>SGI</u>
Analysis Requests:	April 15	June 15, 2004
Protocol Subcommittee Prioritization	By April 30	By June 30
Subcommittee Results to Pubs Committee	April 30	June 30, 2004
Pubs Committee Prioritization Mtg	May 10	July 12, 2004
Pubs Committee Abstract Approval Call	August 3	About October 26, 2004
Meeting Deadline for Abstract Submission	August 6	About October 29, 2004
Deadline for manuscript to Pubs Committee	December 15	February 15

On the Light Side: Brain Teaser Contest

Below are 3 brain teaser questions. The first person to submit the correct answer to all 3 will receive special recognition. Please submit to Lucy_Leuchtenburg@biostat.bsc.gwu.edu. Good Luck!

- 1) Ann, Barb, Cath and Deb went out to dinner. Cath sat opposite Ann. Deb sat at Ann's right, opposite Barb. Barb and Deb ordered spaghetti. Cath ordered lasagna. Ann ordered like this: "Unless the woman at the left of the woman opposite the woman who ordered lasagna is not having what the woman across from the woman at the right of the woman at my left is having, then I'll have what the woman across from the woman at the right of the woman opposite me ordered. Otherwise, I'll have a pizza." If "right" and "left" are from the perspective of the diner, what did the waiter bring Ann? _____
- 2) I start with the letter e; I end with the letter e; I contain only one letter; yet I am not the letter e! What am I? _____
- 3) You have two hourglasses: one a 4-minute time and one a 7-minute timer. How can you measure 9 minutes? _____