



The MFMU Networker

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NICHD Calls 2nd Steroids Consensus Conference

Six years ago, the NICHD held a consensus development conference on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. The ensuing recommendation was that women at risk of premature delivery receive antenatal corticosteroid therapy. However, the panel also identified areas of future research, including the short and long term benefits and risks of repetitive dosing. While there are no prospective trials to date, there are at least two ongoing randomized clinical trials in the U.S. (including the Network's trial of repetitive steroids dosing), and in the U.K, Australia and one poised to start in Canada.

At the May Steering Committee meeting, Dr. Duane Alexander, Director, NICHD, addressed NIH concerns about the Network's Steroids trial in light of recent research which reported no benefit and potential harm from additional doses of steroids. However, controversies and inconsistencies exist with the published data. He proposed that the original panel from the NICHD consensus development conference be reconvened to specifically address only the issue of repetitive dosing of steroids, which the Steering Committee felt to be reasonable and appropriate. In addition, the decision was made to continue recruitment to the Network's repetitive steroids trial.

The Conference will be held August 17-18, and has been given the following charges to answer:

- ◆ Is the research that has been done since 1994 sufficient to permit a consensus recommendation now on administration of repeat courses of antenatal corticosteroids?
- ◆ If so, what is the recommendation?
- ◆ If not, what additional information still needs to be obtained?

Recruitment Finished for fFN Trial

On May 31, the 715th patient was randomized to the fFN Trial, surpassing the goal of 700 patients in just under 4 years. While the 700th patient was randomized earlier in May, centers were allowed to continue screening patients for whom appointments had already been scheduled, and to randomize any fFN positive patients by May 31. The few additional patients will compensate for those who are lost to follow-up, though that number is outstandingly low for any multi-center trial and less than the average for a Network study.

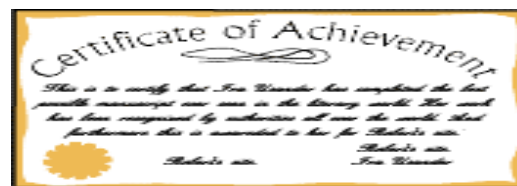
Nearly two hundred patients were randomized during the past year, 24 just in May. June 1998 was the highest recruiting month of the study, with 32 patients. Overall, the University of Texas Southwestern Medical Center randomized the most with 188 patients, followed by Alabama, Thomas Jefferson, Utah and Chicago. The last patient is expected to deliver by the end of September, with data collection and clean up to continue over the following weeks.

Three External Sites Recruited for BEAM Trial

Site visits were made to Women and Infants Hospital in Providence, RI, St Luke's-Roosevelt Hospital in NYC and the University of Texas Medical Branch in Galveston by NICHD, NINDS, BCC and U of Alabama representatives during April and May. These centers have been approved to begin recruiting for the BEAM trial by the end of June. JoAnn Tillinghast from Providence and Trista Christman from NY received a one day training session at the BCC in mid-May, and Elizabeth Martin from Galveston is scheduled for training soon.

The visiting team was impressed by how well each site had organized their BEAM research team, with whom they met, and the high degree of enthusiasm each had for participating in the trial. Though each of these centers has research experience, they do not currently have any competing intrapartum research projects. Of particular interest was the extensive transport system utilized by the Galveston hospital and its outlying clinics. A home away from home is less than two blocks from the hospital where high risk patients can live during the last part of their pregnancy. Vans are even available to help bring patients back to the hospital for their follow-up visits.

Meanwhile, Network centers have continued to randomize, with a total of 936 patients as of June 15. This past April was the highest recruiting month so far. The two year follow up exams are proceeding nicely with 22 done so far. A third ultrasound review is being scheduled with Drs. Bulas, DiPietro and Seibert for this summer.



Work Begins on Next Network Study

Two years ago, the Steering Committee approved a new prospective study to find ways to predict preeclampsia in pregnancy. The study, also funded by the Office of Women's Health, will address the hypothesis that changes in the concentrations of biochemical and/or biophysical markers, measured throughout gestation, can predict the development of preeclampsia. Resources are now available within the Network to begin finalizing the protocol and developing the data forms and manual of operation.

This study will enroll 2000 nulliparous women, who are at low risk for developing preeclampsia, during their first trimester of pregnancy. Various measurements, including blood pressure by sphygmomanometry, urine protein, body fat, BMI, CBC, hCG, genetic markers, doppler blood flows, plasma insulin, triglycerides, are expected to be collected at monthly visits during gestation.

The Co-PI for the study, Dr. Leslie Myatt, and Nancy Elder, Coordinator at the University of Cincinnati, will meet with BCC staff on June 29 to begin ironing out the details of the study. Dr. Menachem Miodovnik is the other Co-PI.

Spring Sees Start of Two New Studies

Since the Steroids Trial began in May, 15 patients have been randomized by eight centers. Thomas Jefferson recruited the first patient, quickly followed by Miami and Utah. The projected recruitment per month for this four year trial, with a sample size of 2400 patients, should average about 4-5 patients per center.

As with many Network studies when they first start, certain areas are identified which need further clarification or even revision. The Steering Committee voted at its May meeting to expand the eligibility criteria to include patients with placenta previa and chronic abruption. As a result of this and other refinements, revised study documents have been sent to the centers.

The Factor V Leiden study is also off to a good start. The eight centers that have been certified are aggressively recruiting, with more than 350 patients as of mid-June. Eventually 375 patients should be recruited each month to achieve a sample size of 5000 within 14 months. Of the 300 patients needed for the carrier/ control cohort, 21 already have been identified.

Coordinator's Corner



Millenium Movement

While only midway through the year, the Network has experienced a flurry of activity and novelty since the new millenium. Namely, we have experienced numerous changes to key NICHD & MFMU personnel. Moreover, pioneering areas of research during pregnancy have been proposed, including genetics, subclinical hypothyroidism, and smoking cessation studies. In short, a surge of creativity and innovative ideas have swept through the Network doors. As we look forward to the upcoming Network re-competition and the likelihood of new Network centers, the natural progression of the Network has created an ideal opportunity to improve and expand the scope of the Network.

For starters, it was agreed upon to resume P.I. meetings during Steering Committee meetings. The past two meetings have been quite productive and have proved to be an effective mechanism for communicating and trouble-shooting about Network issues. As a result of these discussions and the input of others, many exciting and hopefully positive changes are underway. Most significantly, it was decided to increase the amount of time spent on the development, presentation, and discussion of mini-protocols. Although this process is still in a trial stage, we hope to increase the efficiency of the entire protocol development process by allocating more time to this essential stage of development.

Secondly, it was decided to develop and discuss project budgets in greater detail. It is expected that developing more comprehensive budgets at the mini -protocol stage will circumvent potential study delays due to financial oversights and under budgeting. Additionally, this will allow a project's potential cost to have greater weight in the overall decision to advance and prioritize Network studies.

Finally, we have begun to revise and reiterate many Network policies, procedures, and guidelines that may facilitate the overall functioning of the Network. With the growth and shifting emphasis of the Network, many of the policies need a major overhaul! As always, we thank you for your input and commitment to ensuring the success of the Network.

Kimberly Howell, M.A, Network Coordinator

Calendar of Events

Steering Committee Meetings

July 17-18, Rockville, MD
October 16-17, Rockville, MD

Network RFA Due: July 11, 2000

Advisory Board Meetings

September 14, Rockville, MD
November 1, Rockville, MD

Steroids Consensus Development Conference

August, 17-18, Bethesda, MD

Hits Recorded on the Network's Web Site

Have you ever wondered how much the Network's web site is being used and by whom? The system has recently begun such reporting and shows some interesting statistics. There were 3595 "hits" within the Business Center during the month of April. Each click within the web site is counted, so not only are reading files included, but also hits on graphics such as directional buttons. Nevertheless, there were a substantial number of inquiries for data forms, especially the BEAM Trial, the February minutes of the Steering Committee meeting, the Rolodex and the MFMU Study Analysis Status. Though the server is not able to decode all the URLs which hit the system, the majority of the ones reported came from the NICHD, and various sites at the Universities of Texas, Ohio State, and Alabama.

During May, the Visitor's Center had 2498 hits, with projects, particularly the Postterm and PROM's placenta pathology studies, and newsletters being the most popular. The most frequent visitors were the NICHD, Alabama, Arizona, UNC, and Ohio Health. Interestingly, several search engines, including Google, Smartworld, and Fast-Search, made more than 30 hits this month.

There were fewer inquiries to the Business Center in May, with 2268 hits. The Rolodex was the most popular site, followed by BEAM and Factor V Leiden data forms and other study documents. Ohio State's Medical Center was the heaviest user, followed by the NICHD, Thomas Jefferson and Chicago.

It appears evident that the Network is increasingly using electronic technology as a means to promote quick and interactive communication among Network members and the public. Using the Internet to maintain up to date study documents is more efficient, and keeping paperless files and documentation are a reality. The BCC is continuing to investigate useful ways to exploit the Internet, such as reporting and even data entry.

Data Review Visit Made to Utah

An exhaustive, two and a half day site review was conducted at the University of Utah in April by Liz Thom, Steve Weiner, Anita Das and Lisa Mele. While much of the time was spent reviewing charts, which yielded helpful information for data checks, visits were also made to three of the four hospitals comprising the Utah Network center.

The visiting team was even present for the opening celebration of the newly renovated L&D unit at the University Hospital. The team was particularly impressed with how well the four hospital sites have coordinated their data collection and entry system. During the visit, the BCC staff was treated to a delicious, fun dinner at a restaurant in a canyon outside Salt Lake City.

MFMU Network Research Staff at the U. of Utah

From left: Elaine Taggart, Lisa Fullmer, Cathy Miller, Kristi Nelson, Lori Williams, Melanie Fuller, Kathy Jolley, Diane Ercanbrack, Anna Guzman, Iris Hourvitz



People in the News

√ Two new alternate PIs have been approved by the NICHD. **Dr. William Mabie** will represent the University of Tennessee and **Dr. Judith Hibbard** will represent the University of Chicago.

√ A speedy recovery is wished **Dr. Charlotte Catz**, who broke her hip during a fall at the end of May. Surgery was required to insert a pin, but she returned home on June 6 and is

reported to be in good spirits. She will be undergoing about six weeks of rehab before reporting back to her office.

√ Congratulations to **Anita Das** for completing her fourth AIDS ride, this time doing a 7-day, 580 mile ride from San Francisco to Los Angeles. More than 2800 riders participated, raising \$11.3 million for AIDS research.

People in the News, cont.

√ Congratulations and best wishes to **Dr. Sumner Yaffe**, who was named Special Assistant to the Director of NICHD. He will be especially involved in the area of pharmacology and pregnancy. **Dr. Owen Rennert**, who was previously Chair of Pediatrics at Georgetown University, has been named the new Acting Director of the Center for Research on Mothers and Children, effective June 19.

√ Two new research assistants have started work at the BCC. **Kevin Kiger** started in May, taking on responsibility for the C Section registry. He has an extensive background in large multi-center studies, from both the coordinating center and the clinic perspective, having served as a study manager for the AIDS Clinical Trials unit at his alma mater, Case Western Reserve University, and also the study manager for the

International Multi-center Hemophilia Cohort Study at NCI. Kevin has lived in D.C. for six years and is a MPH candidate at GWU. He volunteers at the Whitman Walker Clinic and, for his fifth year working on with DC AIDS Ride, will take on the task of assistant crew manager managing the 600 crew members serving over 2000 riders. In June, **Claudine Tiffault** started as the RA for the Progesterone Trial. A native of Maryland, she attended the University of Maryland, Baltimore Campus, majoring in psychology and is currently finishing her masters degree in psychology at American University. She has worked on several drug studies at Johns Hopkins University. Claudine enjoys outdoor activities, such as hiking and biking, reading, and her dog Geronimo

Six Statistical Suggestions for Surgeons

Rule 1: Never P alone.

Always state the statistical test used to obtain the reported *P* value.

Rule 2: Too many P's in the pod.

"As the number of significant differences arises, the significance of the differences falls." Beware of multiple analyses. The reported significance level is probably much too small.

Rule 3: Do the N's justify the means?

A difference, to be a difference must make a difference. Significance depends on sample size.

Rule 4: Absence of proof does not prove absence.

Failure to disprove the null hypothesis does not prove the null hypothesis.

Rule 5: Ignorance of assumption leads to assumption of ignorance.

There are many assumptions underlying statistical techniques that should not be assumed to hold.

Rule 6: Don't break the scale.

Different kinds of data require different types of analysis.

(Reproduced from Neurosurgery, 1981, Vol. 9, pp.414-418, by Stephen J. Haines, M.D.)