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# THE MFMU NETWORKER

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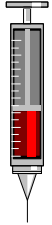
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## First Patients Randomized to Progesterone Trial



Delayed by manufacturing details and regulatory safety tests on the placebo, the progesterone study drugs were finally delivered to MFMU centers on February 23. Wayne State randomized the first patient to the trial on March 2, and then another on March 4, followed by Wake Forest on March 10. A number of prospective patients have received the trial run-in injection. As of March 18, three patients have been randomized.

This study, a double masked placebo controlled clinical, trial involves weekly intramuscular injections of 17  $\alpha$ -hydroxyprogesterone caproate or inert oil placebo in women who have had previous spontaneous preterm

deliveries. Women presenting between 16 and 20 weeks and meeting the inclusion criteria will be given a trial run-in injection to determine compliance.

The trial is expected to recruit 500 patients during the next 15 months. Ten centers have been certified so far.

An ancillary study to determine fatty acids and cortico releasing hormone levels in blood at time of randomization has been approved by the Steering Committee. The blood draws, which involve time-sensitive, complicated processing, will not begin until the details are worked out.

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### Surveys Conducted for Proposed Drug Studies

The Network is using a \$300,000 grant from the Office of Research and Women's Health to study the pharmaco-kinetics of drugs used during the last trimester of pregnancy. Surveys have been sent to centers to determine which drugs Network investigators are interested in studying and to assess the resources for pharmacological studies at individual centers. The drugs highlighted by investigators include prozac, nifedipine, labtalol, metronidazole, erythromycin and corbamazephrine.

As a result of these studies, the Network hopes to work with the FDA in changing drug labeling

to include recommended dosing levels during pregnancy.

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### BV Trial Ends Recruitment

Recruitment for the BV part of the BV/TV Trial ended January 31st, with 1953 patients randomized over the past two and two-third years. Data clean up has begun and the subcommittee hopes to have results presented at next year's SPO meeting. The fetal fibronectin ancillary study was stopped on February 12. The subcommittee, on a March 11 conference call, decided to recommend to the Steering Committee that Gram stain collection at screening be discontinued for the TV trial

(which continues to move ahead), though they still are collected at randomization and follow-up.

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### Terbutaline Trial Details Being Finalized

Negotiations with a supplier of study drugs for the terbutaline trial are expected to be finalized very soon. Meanwhile, the data forms are being programmed into the data entry software and certification procedures developed.

Discussions are being held with Adeza Biomedical about collection of baseline fetal fibronectin at the time of randomization.

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**Don't Confuse Me with the Facts** *Quotation of the Month:* "If the Network BV trial doesn't show a benefit, then there's something wrong with the trial." (by an eminent, although non-Network academician).

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## BEAM Trial Update

Recruitment in to the BEAM Trial is proceeding very well. As of March 18, 71 patients had been randomized, with both UTSW and Alabama in the lead with 13 patients each. All but 2 centers have been certified. As with any new study, minor questions about procedures and data entry have been raised, which will be addressed soon in an update by the BCC to the manual of operations.

Data forms for the follow-up exams are being finalized. A two day training session will be held in May or June for the pediatric examiners. There also will be training at a later date for those who will conduct the Bayley exam.

It appears that any potential conflict between the BEAM trial and the Canadian TIPP Trial (Treatment of Indomethacin Prophylaxis in Preterm Infants) soon will disappear, since the TIPP Trial is scheduled to end in April. The TIPP trial is treating 500-1000 gram preterm infants within six hours of birth with study drug and has similar outcomes as the BEAM Trial: death or neurosensory impairment, including CP. Only a few MFMU centers had a NICU involved in this study.

## Site Visits at Miami and San Antonio

Even tornadoes, torrential rains, flooding, and power outages couldn't keep NICHD and the BCC from conducting their site visit at the University of Miami on February 2! BCC staff were especially impressed with Miami's record keeping and organization. Each patient had a check list and all patient files had copies of prenatal charts and lab reports. Also included in their files were the printouts of the computer gestational wheel calculator and documentation of reasons for not being randomized, if so.

The San Antonio site visit is being held March 16-18.

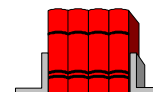
## Aspirin Trial is Lead Article in NEJM

The primary manuscript from the high risk aspirin trial, *Low-dose aspirin to prevent preeclampsia in women at high risk*, appeared as the lead article in the March 12 issue of the *New England Journal of Medicine*. The study concluded that low-dose aspirin does not reduce the risk of preeclampsia in women with pregestational insulin-treated diabetes mellitus, chronic hypertension, multifetal gestations, or a history of preeclampsia. It also does not significantly reduce the incidence of perinatal death, preterm birth or small-for-gestational-age infants. Though aspirin does not affect mothers or neonates adversely, the authors believe, therefore, routine use of aspirin prophylaxis is not justified.

An editorial by Dr. William Barth, Jr., in the same NEJM issue, claims that the question is still unresolved. Dr. Barth points out that the MFMU study relied on available clinical information to define high-risk women, and that other screening tests might identify women with different physiological bases of diseases who could benefit from aspirin, perhaps at a different stage of gestation. According to a recent study, there may also be a circadian response to aspirin. He also cited the study with not presenting data comparing the proportions of women in the four groups who delivered at specific times before term. The CLASP study showed that preeclampsia was less likely to contribute to preterm birth at earlier gestational ages than other causes.

## Another Preterm Prediction Study Published

The February issue of the *American Journal of Public Health* published another paper from the Preterm Prediction study: *The Preterm Prediction Study: The Value of New vs Standard Risk Factors in Predicting Early and All Spontaneous Preterm Births*, RL Goldenberg, Iams, Mercer, et al. The "pathways" paper examined the relationship between fetal fibronectin, short cervix, bacterial vaginosis, other traditional risk factors and spontaneous birth. The paper concluded that fetal fibronectin and a short cervix are stronger predictors of spontaneous preterm birth than traditional risk factors. Bacterial vaginosis was found more often in Black than in non-Black women and accounted for 40% of the attributable risk for spontaneous preterm birth at less than 32 weeks.



## Logo Contest Revived

Within the next couple of weeks, centers will receive a packet with copies of proposed logos that have been submitted to the BCC by various MFMU Networkers. Each center will be asked to rank the logos in order of preference. The winner will be the new NICHD MFMU Network logo (pending Steering Committee approval)!

## Dr. Steven Gabbe to Chair Next S. C. Meeting

Dr. Steven Gabbe has been chosen to chair the April steering committee meeting because Dr. Jim Roberts has an unavoidable conflict. Dr. Gabbe has been the Department Chairman at the University of Washington (Seattle) since July 1996, following nine years as the Chairman of the OB/GYN Department and Director of the residency training program at Ohio State University. He is world renowned in the area of diabetes in pregnancy and is the senior editor of *Obstetrics: Normal and Problem Pregnancies*, a major textbook of obstetrics. He also is the Associate Editor of the *American Journal of Obstetrics and Gynecology*.



While on the cruise, Cora MacPherson hands Dr. Mark Landon a candlelit appetizer as Carmen Alfonso and Dr. Don McNellis wish him happy birthday.

## Network Piggybacks S.C. Meeting with SPO

In the interest of time and economy, the Steering Committee held its first quarter meeting of the year prior to the annual meeting of SPO. While Miami, Florida sounded enticing for the winter meeting, the weather was wild and affected some travel plans. However, the weather cleared in time for the attendees to enjoy a cruise around Miami's harbor.

All nineteen of the abstracts submitted by the Network were accepted by SPO. Dr. Jay Iams overcame a balky projector to deliver a well received presentation on the HUAM study, *Prediction of preterm birth with ambulatory measurement of uterine contraction frequency*, at the plenary session. Dr. Baha Sibai's report from the aspirin study, *Risk factors for adverse pregnancy*

*outcome in women with chronic hypertension*, was delivered during the last session, but won the prize for best paper in Oral Concurrent F. It is the second time he has received an award at SPO for a Network study.

## Recruitment Continues for Cervical U/S

Three centers have been certified for the Cervical Ultrasound study since December: Tennessee, San Antonio and Thomas Jefferson. UTSW is in the process of obtaining their certification. Though recruitment has improved, centers need to work on increasing enrollment. Fifty out of 235 patients thus far have been randomized.

## Software Release Planned for End of March

Clinical centers soon will receive a new release of the MF MU software which includes biologic fluids catalogs for the BEAM and Progesterone Trials. Data entry for the Progesterone catalog will differ from other biologic fluids catalogs in that it will more resemble a screening log because it records salivary estriol samples, which are not aliquoted like blood and urine. The release will also include some minor dictionary changes for MF MU studies.

## Two Abstracts Submitted & Accepted by SGI

Two investigators from the Network will be presenting MF MU study results at the Society for Gynecological Investigation on March 18.

- **Varicella zoster in pregnancy: risk factors of varicella pneumonia** (oral presentation) - Dr. Mac Ernest, Wake Forest
- **Antenatal markers of neonatal sepsis following preterm premature rupture of membranes** (poster) - Dr. B. Rosenn, the U. of Cincinnati

**Upcoming Steering Committee Meetings:** April 27-28, 1998 - Bethesda, MD  
 July 13-14, 1998 - Bethesda, MD  
 October 22-23, 1998 - Bethesda, MD

**R e m i n d e r s**

- Please focus on collecting maternal blood and cord vein blood for patients enrolled in the Asthma Observational study who are eligible (i.e., have received inhaled Beclomethasone dipropionate (BDP) or Triamcinolone acetonide (TAA) for at least 30 days). This ancillary study is supported by non-Network funds.
- Please complete and enter outcome data (MB01D) for patients in the BV/TV FFN Ancillary study . There are more than 2,733 forms outstanding for patients whose EDC was two months ago.
- Please enroll any pregnant kidney transplant patients who are at your center in the Pregnancy Renal Registry (215-955-2849).

## PEOPLE IN THE NEWS

◆ Congratulations to **Dr. Mark Klebanoff**, who has been appointed Acting Director of the Division of Epidemiology, Statistics and Prevention Research. He replaces Dr. Berendes who has stepped down as Division Director. In between putting out fires and attending lots of meetings, Mark hopes to be able to implement some of his own research.

◆ We are pleased to welcome **April Burton**, the new NICHD secretary for the MFMU Network. In addition to full time employment, she is the mother of two girls, ages 9 and 6, and a boy almost 2, and also attends college. Last December, she was inducted into Psi Beta, the psychology honor society. April plans to transfer this fall to the University of Maryland and hopes to become a psychologist or therapist. She says that her extended family of relatives are a big help!

◆ Best wishes to **Terry Schwartz**, research nurse at Magee Womens, who became Terry Kamon when she married Joseph Kamon on December 27. The new family, including 11 year old stepson Joseph, is busy looking for new living quarters.

◆ We will miss the good work of **Joyce Fricke**, research nurse at the University of Tennessee. Joyce

moved to North Carolina in February to be near her significant other.

◆ Congratulations, bon voyage and good luck to **Sheryl Nicholson**, coordinator at San Antonio, as she begins new life directions. Having been ordained as a Minister of the Gospel in December 1997, she joins 9 other pastors on a 3 week crusade to Poona, India. Feeling that the ministry is her calling, Sheryl is resigning as coordinator. Marriage plans are also in Sheryl's future. We wish her well in her new endeavors and hope the snakes aren't too ferocious in India!!

◆ More kudos for **Dr. Jay Iams** at OSU from a reader writing to the editors of *Good Housekeeping* about their Top Doctors article. Nancy Rinehart of Chicago wanted to share her personal experience with the "winning" doctor, Jay Iams. She wrote to say her husband died while she was pregnant with her second child and she had to tell Dr. Iams that paying her medical bills might be a problem. Dr. Iams assured her that she would receive the required care regardless and, though she will never be able to repay him, she wanted to publicly recognize and thank him for being such a caring, competent doctor.