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National Institutes of Health  
Bethesda, Maryland 20892  
[www.nih.gov](http://www.nih.gov)

The Honorable Jim McDermott  
U.S. House of Representatives  
Washington, DC 20515

Dear Representative McDermott:

Thank you for writing to the National Institutes of Health (NIH) about our research efforts on prematurity and stillbirth. I also appreciate your kind words about the lead role played by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). We agree with you and your colleagues about the public health importance of these issues in preventing both needless deaths and a range of morbidities associated with preterm birth. I am pleased to provide you with an overview of the NIH's current research activities in these areas.

By traditional definition, preterm infants are those born before 37 completed weeks of pregnancy; however, more recent research shows that 39 weeks of pregnancy should be the goal for most pregnancies. Infants born too soon who survive are at greater risk for a number of complications including respiratory distress syndrome, sleep apnea, brain hemorrhage, heart and vision problems, and necrotizing enterocolitis (a potentially dangerous or fatal intestinal problem). Preterm infants also face an increased risk of lasting disabilities such as intellectual and developmental disabilities, learning and behavioral problems, or cerebral palsy. The Centers for Disease Control and Prevention recently reported that following a long period of steady increases, the U.S. preterm birth rate declined to 12.3 percent in 2008, from 12.8 percent in 2006, the first two-year decline in nearly three decades. While this is encouraging progress, more needs to be done. For instance, a recent study (NEJM 2012; 366:1328-34) found that in 2008, 12 percent of all neonatal deaths worldwide were caused by complications from preterm birth.

The NICHD is strongly committed to reducing prematurity and stillbirth, to understanding the causes of both, and to identifying interventions for both mothers and premature babies that will optimize their health outcomes. The NICHD carries out these efforts through an extensive portfolio of investigator-initiated research and targeted clinical studies conducted by transdisciplinary networks of researchers.

#### *Preterm Birth*

The Genomics and Proteomics Network brought together experts in genomics and proteomics with clinicians, statisticians, and epidemiologists to apply advances related to other conditions (such as cardiovascular disease) in genomics and proteomics to the field of prematurity. This group has been studying the genetic and environmental causes and mechanisms of spontaneous preterm birth with the goal of identifying biomarkers of increased risk of preterm delivery, with the ultimate hope of designing effective prevention strategies. Large studies in this network include a genome-wide association study to analyze the DNA of premature infants. Another study is attempting to identify a common biomarker for prematurity in women who have had a previous preterm birth.



Realizing the advances that often come when a wide range of experts focus on an issue, the NICHD applies this transdisciplinary approach to its other long-standing research networks. The Maternal Fetal Medicine Units Network (MFMU) was established to perform clinical trials and conduct studies to improve pregnancy outcomes, with a special emphasis on reducing preterm birth. Many of the MFMU's Studies and trials include input from basic scientists, pathologists, clinicians, neurodevelopmental specialists, statisticians, epidemiologists, and researchers who specialize in conducting clinical trials. The MFMU has undertaken over 40 studies and clinical trials (please see <http://bsc.gwu.edu/mfmu/>), several of which have resulted in advances in prediction and prevention of preterm birth. For example, fetal fibronectin was identified as a diagnostic test for predicting prematurity. Progesterone was identified as a preventive therapy for one group of women at high risk of prematurity, those who had already experienced a previous preterm birth. However, treating asymptomatic women for bacterial vaginosis was shown not to prevent preterm birth or improve neonatal outcomes. Another study, a clinical trial of 10,000 pregnant women that evaluated whether vitamins C and E prevent preeclampsia (a substantial risk factor for preterm birth), found that these vitamins (which were being widely prescribed for pregnant women) did not prevent the condition.

The MFMU's research has contributed to improved management of women at risk for preterm birth. For women who experience premature rupture of membranes, broad spectrum antibiotics were shown to improve neonatal outcomes. In addition, the network conducted research showing that for women at risk of preterm delivery, treatment with magnesium sulfate reduces the risk of the child developing cerebral palsy by one-third.

The recently initiated "Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (NuMOM2b)" is evaluating the predictors and mechanisms of adverse pregnancy outcomes in 10,000 racially, ethnically, and geographically diverse women in their first pregnancies. The aim of this study is to determine factors in the first and early second trimester that can help identify women at the highest risk for preterm birth, preeclampsia, fetal growth restriction, and stillbirth and, ultimately, to create methods for early detection of these conditions. Over half of the needed participants have been recruited to date. (Please see attached Appendix for further details on these and other studies.)

#### *Caring for Preterm Infants*

Formed in 1986, the NICHD Neonatal Research Network (NRN) is a collaborative research network of 18 neonatal intensive care units across the U.S. This Network was established to conduct observational and interventional studies to improve health outcomes for newborns by bringing together experts in neurology, developmental pediatrics, genomics, pharmacology, surgery, and ophthalmology to conduct studies on newborn problems such as encephalopathy, bowel problems, blindness, and markers of disease. Focused on newborns, particularly extremely low birth weight (ELBW) infants, the NRN has completed, or is in the process of implementing, 18 observational studies and 31 interventional trials (details of which are available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and on the NRN website at [neonatal.rti.org](http://neonatal.rti.org)). For example, the *Surfactant Positive Airway Pressure and Pulse Oximetry Trial* (SUPPORT) study, which was co-funded by the National Heart, Lung, and Blood Institute, compared the use of continuous positive airway pressure (CPAP) initiated at birth with the early administration of surfactant in premature infants born at 24 to 27 weeks gestation. The trial found that higher oxygen saturation



targets improved preterm infants' survival but increased the risk of retinopathy of prematurity. The study also found that CPAP was as effective as the traditional ventilator/surfactant therapy in treating breathing difficulties in these infants, but that CPAP may result in fewer complications. Another study, the Necrotizing Enterocolitis Surgical Trial (NEST) currently is testing different treatment strategies to find which increase survival rates without neurodevelopmental impairment at 18-22 months adjusted age. (Please see the Appendix for a more detailed list of studies funded by the NICHD.)

To assist practitioners in caring for preterm newborns, the NICHD has also developed a web-based outcomes tool ([http://www.nichd.nih.gov/about/org/cdbpm/pp/prog\\_epbo](http://www.nichd.nih.gov/about/org/cdbpm/pp/prog_epbo)), which can be used to obtain survival and outcome information for infants at 22-25 weeks gestation.

### *Stillbirth*

The Stillbirth Collaborative Research Network (SCRN) conducted a multisite, population-based, case-control study to determine causes of and risk factors for stillbirths, and to better understand the scope and incidence of the problem. Participants underwent a standardized protocol including maternal interview, medical record abstraction, placental pathology, biospecimen testing and, in stillbirths, fetal autopsy. Results of this groundbreaking study were published in the *Journal of the American Medical Association (JAMA)*:

- Causes of death among stillbirths:
  - When a complete evaluation was performed, a possible or probable cause of death was found in 76.2% of stillbirths.
  - The distribution of causes of death was: obstetric conditions- 29.3%; placental abnormalities - 23.6%; fetal genetic/structural abnormalities- 13.7%; infection - 12.9%; umbilical cord abnormalities - 10.4%; hypertensive disorders - 9.2%; and other maternal medical conditions - 7.8%.
  - Fetal autopsy, placental histology, and karyotype (chromosome analysis) were the most useful tests for determining a cause of death.
- Association between stillbirth and risk factors known at pregnancy confirmation:
  - Prior pregnancy loss and first pregnancy were the strongest risk factors for stillbirth.
  - Other factors independently associated with an increased risk for stillbirth included: non-Hispanic black race/ethnicity; diabetes; maternal age  $\geq 40$  years; maternal AB blood type; history of drug addiction; smoking  $\geq 10$  cigarettes/day during the three months prior to pregnancy; obesity/overweight; not living with a partner; and multiple gestation.
  - Nonetheless, these risk factors known at the time of pregnancy confirmation accounted for only a small amount of the stillbirth risk.

Analyses of the data collected in the SCRN are ongoing to understand the role in stillbirth of: genetic and infectious causes, placental abnormalities, subclinical maternal disease (e.g., thyroid, diabetes, anticardiolipin antibodies), and exposure to stress. In addition, prediction models will be developed.



The Prenatal Alcohol and Sudden Infant Death Syndrome and Stillbirth (PASS) Network, a collaboration of the NICHD, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Deafness and Other Communication Disorders (NIDCD), is conducting community-linked studies to investigate the risks of prenatal alcohol exposure for sudden infant death syndrome (SIDS), stillbirth, and fetal alcohol syndrome (FAS), and how they may be inter-related within high-risk communities of the Northern Plains and Western Cape, South Africa. This transdisciplinary team includes fetal physiologists, pathologists, developmental biologists, pathologists, clinicians, geneticists, statisticians, and epidemiologists. The long-term goals are to decrease fetal and infant mortality, and to improve child health in these communities. This prospective study will enroll 12,000 pregnant women in early pregnancy and follow them and their surviving offspring through the first twelve months of life.

In addition, the NICHD's intramural Perinatology Research Branch, which conducts clinical and laboratory research on maternal and fetal diseases responsible for infant mortality, has contributed substantially to our basic understanding of preterm birth, with a particular focus on the role of uterine infections and inflammation. The branch recently completed a multinational study that showed that the administration of vaginal progesterone (a natural hormone involved in pregnancy maintenance) to women with a short cervix reduced the rate of preterm birth by 45 percent, and reduced the rate of respiratory distress syndrome (RDS) by 61 percent. There was no evidence of adverse events in patients who received progesterone compared to those who received the placebo. Follow-up studies are currently being pursued in the U.S. and Europe. In addition to this line of investigation, the branch has identified a novel mechanism of disease responsible for late preterm birth, and is in the process of identifying biomarkers to identify the patient at risk and to select strategies for prevention.

The Perinatology Research Branch has several ongoing projects related to stillbirth. Currently, there is no effective screening test to identify a mother at risk for fetal death in the third trimester (stillbirth). Through several longitudinal studies, the Perinatology Research Branch has discovered biomarkers that would allow assessment of all pregnant mothers in the third trimester. In addition, the Branch has established a line of investigation to test an intervention to prevent stillbirth in patients identified to be at risk with the biomarkers indicated above.

Your letter correctly noted that other Institutes and Centers at the NIH are supporting research related to prematurity and its consequences according to their specific areas of expertise. These efforts are coordinated across the NIH through frequent communications among scientific program staff. Besides the collaborative efforts described above, other relevant research is supported by other Institutes and Centers, including those described below.

The *National Institute of Allergy and Infectious Diseases* (NIAID) is supporting research on microbial infections associated with poor birth outcomes, among them bacterial vaginosis (BV), a common vaginal condition. Women with BV are at substantially increased risk of preterm birth, as well as acquisition of sexually transmitted diseases including HIV.

Cytomegalovirus (CMV) is the most frequent cause of congenital infections in humans. Prematurity occurs in as many as 34 percent of infants with symptomatic congenital CMV infection, and prematurity is one sign that CMV infection may be present at birth. NIAID has



funded studies of the causes, detection, treatment, and prevention of congenital CMV for the past 30 years. Recent efforts include work to develop vaccines to prevent CMV infection and resulting premature birth.

A major concern in treating premature infants is that there are often no data on how they handle the drug of choice. As part of the HHS response to the 2009 H1N1 pandemic influenza, an NIAID-funded clinical pharmacology study assessed the use of oseltamivir (Tamiflu) in a neonatal intensive care unit. After a health care worker in the neonatal intensive care unit caring for 33 infants became ill with the 2009 H1N1 pandemic influenza, the hospital administered Tamiflu as prophylaxis to these infants. This study indicated that premature babies administered Tamiflu within a few weeks of birth have the ability and enzyme capacity to convert the pro-drug to the active metabolite at the doses that were administered.

Hepatitis E virus (HEV) is a major cause of hepatitis in much of the developing world and is increasingly identified as a cause of hepatitis in industrialized countries. Though most infections go undiagnosed and are self-limited, 10-25 percent fatality rates, increased risk of stillbirth, and other adverse pregnancy outcomes have been reported among HEV-infected pregnant women. An HEV vaccine developed by NIAID scientists in collaboration with GlaxoSmithKline (GSK) has proven safe and effective in field trials supported by the U.S. Army Medical Research and Materiel Command, NIAID, and GSK. If further developed, this could help prevent HEV infections and associated adverse pregnancy outcomes.

Malaria in pregnancy is associated with low birth weight, maternal anemia, and gestational hypertension, and both inflammation and the fetal response to infection may contribute to these poor outcomes. NIAID scientists are investigating factors associated with infection and disease in pregnant women in an effort to develop a pregnancy malaria vaccine.

The *National Institute of Nursing Research* (NINR) supports research to discover new ways to promote health and prevent disease to achieve long-term, positive outcomes in individuals across the lifespan. Consistent with this commitment to invest in health promotion and disease prevention, NINR supports science to elucidate the mechanisms underlying premature birth as well as interventions to improve birth outcomes across diverse populations. Current and recent research support in this area includes:

- Development of a predictive model of preterm birth in African American and Mexican American women that includes psychosocial, behavioral, and physiologic information with the goal of developing effective, culturally-tailored interventions to prevent pre-term birth in these populations.
- Examining the effect of acculturation of Hispanic women on preterm birth outcomes, using a biobehavioral approach, by exploring relationships between biomarkers, acculturation levels, and birth outcomes, with the goal of developing clinical interventions that account for level of acculturation in Hispanic populations.
- How socio-demographic stressors, including poverty, crime, and discrimination, relate to pre-term birth rates for African American women.



Research supported by The **National Heart, Lung, and Blood Institute (NHLBI)** has found that although it has been thought that women return to normal health following pregnancies complicated by preeclampsia or gestational diabetes, epidemiologic studies indicate that they may have increased risk for subsequent hypertension, cardiovascular disease, and diabetes. In September 2010, the NHLBI, along with the NICHD and other stakeholders, held a workshop entitled *Bridging Preeclampsia and Future Cardiovascular Disease* (see: <http://www.nhlbi.nih.gov/meetings/workshops/bridging-pe.htm>) to provide recommendations regarding pregnancy complications including preeclampsia and gestational diabetes, and to consider their relationships to future maternal cardiovascular risk. The goal was to identify knowledge gaps and research opportunities that could facilitate the long-term prevention of cardiovascular disease outcomes. The NHLBI is planning to release a funding opportunity announcement later this year (see: <http://www.nhlbi.nih.gov/meetings/nhlbiac/oct11min.htm>) to address this important gap by performing a prospective cardiovascular risk assessment at approximately two years postpartum in women with and without adverse pregnancy outcomes including preterm birth, preeclampsia, and fetal growth restriction during their first pregnancy, by leveraging the existing NuMoM2b cohort study funded by the NICHD.

Prematurity increases the risk of long-term pulmonary disease, including bronchopulmonary dysplasia (BPD), asthma, pulmonary hypertension, and possibly chronic obstructive pulmonary disease. The lungs of premature newborns are not well developed and are particularly vulnerable to life-saving measures used to support breathing. The NHLBI initiated the Prematurity and Respiratory Outcomes Program (PROP), a collaborative study of potential molecular mechanisms and biomarkers that predict which premature infants are at increased risk of chronic pulmonary disease. The NHLBI also supports studies of the genetics associated with premature infants developing respiratory distress syndrome, pulmonary hypertension, and BPD. Several NHLBI clinical trials are now testing interventions during pregnancy to reduce the frequency and severity of lung disorders, e.g., “Vitamin C to Decrease Effects of Smoking in Pregnancy on Infant Lung Function.”

The **National Institute on Deafness and Other Communication Disorders (NIDCD)** conducts and supports biomedical and behavioral research and research training in the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language. The NIDCD is supporting a number of grants related to preterm birth and its consequences:

- NIDCD-supported scientists are collaborating with scientists in Brazil to study why some preterm infants develop hearing loss. Their study showed that the sensory cells that help amplify sound vibrations, called outer hair cells, are healthy but the sensory cells, the inner hair cells, which convert those vibrations to electrical signals that travel to the brain have been destroyed. This causes a condition known as auditory neuropathy and explains why other scientists have observed a higher incidence of auditory neuropathy in preterm babies.
- Feeding competency is a challenging hurdle facing many premature babies who have respiratory disease, brain injury, or certain genetic defects that impair oral development. NIDCD-supported scientists are testing a new medical device, known as the NTrainer, in a randomized trial among 240 tube-fed premature infants to determine if a novel synthetic oral stimulation therapy can accelerate development of suck and feeding skills,

enhance brain development, decrease the length of hospitalization, and improve speech-language and motor skills measured at three-years of age.

- Infant incubators are widely used in neonatal intensive care units for preterm babies, as they cannot cope with the environment without external help. However, excessive high levels of noise inside an infant incubator have been found to result in numerous adverse health effects, especially hearing impairments, on weak, premature infants. NIDCD-supported scientists are developing a new approach of noise reduction for infant incubators, using an active noise cancellation system and a carbon nanotube based transparent, thin film speaker. This research aims to prevent hearing loss to incubator residents by reducing the noise level inside these incubators.

I hope this provides you and your colleagues with a substantive overview of the NIH's research efforts. Dr. Alan Guttmacher, Director of the NICHD, would be pleased to further discuss these issues with you. He has led the NIH in these efforts, including partnerships with external organizations, and is helping to plan the July 2012 meeting in Seattle, Washington, which he will also attend. In addition, you will be pleased to know that in its recent "scientific visioning" process, the NICHD highlighted preterm birth and preterm infant outcomes as a priority research focus for the next decade.

Thank you again for writing to the NIH about these critical health issues.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "Francis S. Collins", with a stylized flourish at the end.

Francis S. Collins, M.D., Ph.D.  
Director



### *Appendix*

#### *Preterm Birth and Stillbirth – NICHD Maternal-Fetal Medicine Units Network*

*(<http://www.bsc.gwu.edu/mfm/>)*

The MFMU Network is composed of 14 sites across the U.S. and a data center. The network started a new cycle in April 2011 with three new sites. Ongoing trials related to preterm birth include:

- *SCAN (Short Cervix and Nulliparity): Randomized Trial of Progesterone for prevention of preterm delivery in women with short cervix.* This placebo-controlled trial was aimed at determining whether 17alpha hydroxyprogesterone prevents preterm birth in nulliparous women with short cervix, finding that the treatment in this subpopulation of women was not effective. Results will be published shortly.
- *ALPS (Antenatal Late Preterm Corticosteroids):* This placebo-controlled trial is a study of pregnant women in late preterm period (34-37 weeks) who present with a threatened premature delivery, testing whether treatment with the steroid betamethasone (versus placebo) will improve the infant's breathing after birth. The study is currently recruiting participants.
- *TRIO (Translating Research in Obstetrics):* This study was aimed at understanding how to translate clinical research efficiently into practice in the obstetrical setting, particularly the factors associated with the implementation of evidence-based practices. The three treatments to be evaluated are: Antenatal maternal corticosteroids for fetal lung maturity, Progesterone for prevention of preterm birth, and Magnesium sulfate for cerebral palsy prevention. The project has been completed and results will be published.
- *STAN (ST segment monitor):* This is a large clinical trial to test whether fetal EKG tests improve infant health outcomes e.g. stillbirth, low Apgar scores, or the need for intubation at delivery. Nearly 4,000 of the target of 11,000 women have been recruited.
- *CMV Trial (Cytomegalovirus):* A randomized controlled multi-center clinical trial to evaluate if maternal administration of hyperimmune CMV globulin can prevent fetal loss or lower the rate of congenital CMV infection among the offspring of women who have been diagnosed with primary CMV infection during early pregnancy (before 23 weeks' gestation). This study is underway.

#### *Complications following preterm birth – NICHD Neonatal Research Network*

*(<http://www.neonatal.rti.org/>)*

- *Generic Database of Very Low Birth Weight Infants (GDB):* The GDB is a registry of very low birth weight infants born alive in NRN centers. Centers collect data on both mothers and infants, the therapies they received, and infant outcomes at time of hospital discharge. Data are analyzed to find associations and trends among baseline information, treatments, and infant outcome, and to develop future NRN trials. Since its inception, the NRN has registered 70,407 infants in this database.
- *Moderate Preterm Registry:* Started in March 2012, NRN is collecting similar data for a one year period on moderately preterm infants (born between 29 and 33 weeks



gestational age). The purpose is to estimate the frequency of maternal and perinatal health events, morbidities, and in-hospital outcomes to permit testing hypotheses in observational studies and to guide the design of randomized controlled trials.

- *Follow-up Study of High Risk Infants*: Launched in 1998, the NRN's Follow-Up Study is a cohort of surviving extremely low birth-weight infants who participate in neurodevelopmental, neurosensory, and functional assessments at 18 to 22 months corrected age (that is, 18 to 22 months after original due date for the pregnancy). The goal is to identify maternal and neonatal risk and protective factors for neurodevelopmental outcome. Currently, the NRN has followed 12,330 children.
- *Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT)*: This study, co-funded by the National Heart, Lung, and Blood Institute, compared the use of continuous positive airway pressure (CPAP) initiated at birth with the early administration of surfactant in premature infants born at 24 to 27 weeks gestation. The trial found that ensuring higher oxygen levels (independent of CPAP) improved preterm infants' survival, but increased the risk of retinopathy of prematurity. The study also found that CPAP was as effective as the traditional ventilator/surfactant therapy in treating breathing difficulties in these infants, but CPAP may result in fewer complications.
- *Cerebral Function Monitoring in Premature Infants*: This pilot study tested the feasibility of enrolling subjects and obtaining an electroencephalogram (aEEG) within the first 72 hours of life, a second aEEG recording between 72-168 hours of life, and weekly thereafter up to 36 weeks post-menstrual age. It enrolled 102 infants between 401-1,000 grams birth weight or between 23 and 28 weeks gestational age.
- *Early Blood Pressure Management in Extremely Premature Infants*: This study tested the feasibility of enrolling extremely preterm infants in a randomized, double-blinded trial of blood pressure management. The randomized trial showed that blood pressure increases spontaneously over the first 24 hours of life, similar to that in more mature infants, with no difference in the rate of increase for infants who did or did not received anti-hypertensive therapy.
- *Necrotizing Enterocolitis Surgery Trial (NEST)*: Necrotizing enterocolitis (NEC) is a condition in which the intestines become inflamed. NEC occurs in 5 to 15% of extremely low birth weight infants. Outcome for infants with NEC is poor. This randomized trial is testing the hypothesis that treatment of the intestines via an initial laparotomy, rather than with initial drainage, will increase survival without neurodevelopmental impairment at 18-22 months adjusted age. Currently, the trial has enrolled 99 infants.
- *Single-Dose Vitamin E for Prevention of Intracranial Hemorrhage*: This pilot trial examined the feasibility, safety, and efficacy of administering one dose of Vitamin E within four hours of birth to extremely low birth weight infants at risk for hemorrhage within the brain. Results showed that a single dose of vitamin E did reduce, but not eliminate, deficient levels in the blood of infants at 24 hours of age.
- *Inhaled PGE1 in Neonates with Sub-Optimal Response to Inhaled Nitric Oxide*: Hypoxemic respiratory failure (HRF) is a rare, but life-threatening, condition in which infants have low partial pressure of oxygen in their blood. The condition affects approximately 2 to 9% of infants and results in significant morbidity and mortality. This pilot study is evaluating the feasibility and safety of prolonged administration of



intravenous prostaglandin in infants with HRF who do not respond to traditional treatment with inhaled nitric oxide.

- *Hydrocortisone for Extubation*: This study is testing the safety and efficacy of a 10-day course of hydrocortisone for infants who are less than 30-weeks gestational age and are intubated at 14- to 28 days of life. The study will examine whether hydrocortisone decreases moderate or severe bronchopulmonary dysplasia and moderate or severe neurodevelopmental impairment at 18 to 22 months corrected age.
- *Neurodevelopmental Effects of Donor Human Milk vs. Preterm Formula in ELBW infants (MILK)*: Strong preliminary evidence suggests that maternal breast milk feedings confer multiple health benefits to extremely low birth weight (ELBW) infants, including up to an additional eight points in IQ over non-breastfed counterparts. In addition, rates of sepsis and necrotizing enterocolitis are lower in these infants, and they experience shorter hospital stays and fewer re-hospitalizations in the first year of life. The NRN has begun a randomized trial of fortified donor human milk versus preterm formula for ELBW infants receiving no or minimal maternal milk, to compare neurodevelopmental and health outcomes at 22 to 26 months corrected age.
- *Transfusion of Prematures (TOP) trial*: Virtually all ELBW infants become anemic in early life, and approximately 90% receive one or more blood transfusions. Transfusions, however, are initiated at inconsistent hemoglobin thresholds. This NRN trial, currently under development, will randomize infants <1,000g birth weight and <29 weeks gestational age to receive red blood cell transfusions at either a higher (liberal transfusion) or lower (restrictive transfusion) hemoglobin threshold.
- *Early Onset Sepsis study*: This study, co-funded by the Centers for Disease Control and Prevention, determined: (1) current hospital-based rates of early onset sepsis (EOS) in term and preterm infants in the era of intrapartum antibiotic prophylaxis; (2) the organisms associated with EOS and meningitis in neonates; (3) asymptomatic and symptomatic infants by gestational age and pathogen; and (4) associated mortality rates by pathogen group. The most frequent pathogens were group B streptococci (GBS) in term infants and *Escherichia coli*.
- *Survival and Morbidity Outcomes of Very Low Birth Weight Infants with Trisomy 18 and Trisomy 13*: The NRN is currently collecting data on infants born with Trisomy 13 and Trisomy 18. These rare genetic conditions, in which infants have additional copies of chromosomes 13 or 18, result in life-threatening conditions – Patau Syndrome for Trisomy 13 and Edwards Syndrome for Trisomy 18. The NRN is using its Generic Database to examine delivery room interventions and mortality and morbidity rates for early preterm infants born with these anomalies.
- *Inositol for Reducing Retinopathy of Prematurity*: Retinopathy of prematurity (ROP) is an abnormal growth of the blood vessels in the eye that occurs primarily in very premature infants when the eye's blood vessels, sensitive to extremes oxygen levels, must finish developing outside the protective environment of the uterus. ROP is a leading cause of blindness and other vision impairments. Co-funded by the National Eye Institute, the Inositol trials are testing whether 6-myoinositol can reduce severe ROP.