**Introduction and Background**

South Dakota physicians who care for mothers, children and families need to be aware of and involved with the National Children's Study (NCS), the largest long-term study of children's health ever conducted in the United States.

The NCS was authorized by Congress with the Children's Health Act of 2000 and will examine the effects of the environment on the health and development of American children. This longitudinal study will include more than 100,000 children from a nationally representative sample who will be followed from before birth until age 21 (www.nationalchildrensstudy.gov). The term “environment” is broadly defined within the study to include a number of natural and man-made environmental issues. Environmental exposures to be considered include biological agents, chemical and social factors, physical surroundings, behavioral influences, genetics, cultural and family influences and geographic locations.

The National Children’s Study is led by a consortium of federal partners including: the U.S. Department of Health and Human Services (including the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Environmental Health Sciences of the National Institutes of Health and the Centers for Disease Control and Prevention) and the U.S. Environmental Protection Agency. Members of the NCS Federal Advisory Committee oversaw the planning and groundwork for the design and development of the study. More than 2,400 obstetric, pediatric and environmental health researchers from federal agencies, the private sector and non-governmental organizations were included in working groups that helped the NCS Federal Advisory Committee and the lead federal agencies. These scientists, along with representatives from community groups and professional organizations, contributed to the identification of key children's environmental health questions.

A set of core hypotheses (Table 1) was developed that encompass exposures and child health outcomes of public health significance. These hypotheses were important in guiding the study design and determining the necessary sample size. This list continues to evolve, and over the course of the study it is expected that hypotheses will be refined and new questions will emerge, while other hypotheses may become outdated and will be discarded.

By studying children through different phases of growth and development, researchers will be better able to understand the role of environmental factors on health and disease. Unprecedented increases in autism, asthma, diabetes mellitus and obesity are being seen in South Dakota, Minnesota and across the nation. These diseases, combined with injury and schizophrenia, result in $642 billion nationally in health care costs each year. Evidence indicates that environmental exposures may be, in part, responsible for such sharp increases in incidences, yet definitive linkages have yet to be established in most cases. Determining the causes of these diseases is imperative for developing preventative measures, and the NCS aims to address this. The study also will allow scientists to find the differences in health care access and disease occurrence that exist among groups of people in order for these disparities to be addressed.

**Study Design**

Study participants will come from 105 study locations across the nation (Fig. 1), ensuring that diverse ethnic, racial, economic, religious, geographic and social groups are represented. Universities, hospitals and other nearby facilities will make up the Study Centers that will carry out research in the study locations. In September 2005, South Dakota State University (SDSU), along with collaborators from Cincinnati Children’s Hospital Medical Center and the University of Cincinnati Department of Environmental Health, was awarded a contract by the National Institute of Child Health and Human Development (NICHD) to serve as one of seven Vanguard Study Centers. Teams from the Vanguard Center will be the first to work with communities to recruit participants, collect and process data, and pilot new research methods for the full study.

Locations followed by the SDSU Vanguard Center include segments of Brookings County in South Dakota, and Yellow Medicine, Pipestone, and Lincoln counties in Minnesota (BYPL). The BYPL Study Location is important to ensure that the NCS includes children who live in rural areas.
### Special Features

#### Table 1.
Main Hypotheses of the National Children’s Study. (Used with permission of the NCS, www.nationalchildrensstudy.gov)

<table>
<thead>
<tr>
<th>Pregnancy Outcomes</th>
<th>Neurodevelopment and Behavior</th>
<th>Child and Health Development</th>
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<td>• Among women without diabetes before pregnancy, impaired glucose metabolism during pregnancy is associated with risk of major congenital malformations of the heart, central nervous system, musculoskeletal system and all birth defects combined.</td>
<td>• Repeated, low-level exposure to nonpersistent pesticides, including carbamates, organophosphates and pyrethroids in utero or postnatally increases risk of poor performance on neurobehavioral and cognitive examinations during infancy and later in childhood.</td>
<td>• Family resources and processes shape the structure and quality of children’s home, childcare, and school experiences and economic opportunities. These resources and processes affect children’s developmental and health trajectories and mediate and/or moderate other environmental influences on children’s outcomes.</td>
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<td>• Intratuterine exposure to mediators of inflammation due to infection of vaginal, cervical or uterine sites or of more distal sites (e.g., periodontal disease) is associated with an increased risk of preterm birth.</td>
<td>• Prenatal infection and mediators of inflammation are risk factors for neurodevelopmental disabilities such as cerebral palsy and autism.</td>
<td>• Geographic area of residence is associated with exposure to social, physical, psychological and environmental factors that increase the risk of developing health problems and decrease access to protective resources.</td>
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<td>• Children whose conceptions were aided by assisted reproductive technology (ART) are at increased risk of fetal growth restriction, birth defects and developmental disabilities in comparison to children who were conceived without ART.</td>
<td>• Exposures to adverse psychosocial, chemical and physical environments and other stressors during vulnerable periods of pregnancy and early childhood can interact with genotype to cause or modulate behavioral problems in childhood.</td>
<td>• Exposure to media from stationary and mobile sources can have both positive and negative short- and long-term effects on children. Exposure to specific media content will lead to developmental trajectories along a continuum of prosocial to antisocial behavior.</td>
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<td>• Maternal subclinical hypothyroidism is associated with adverse pregnancy outcomes and neurodevelopmental disabilities.</td>
<td>• Prenatal infection and mediators of inflammation during pregnancy and the perinatal period are associated with increased risk of schizophrenia.</td>
<td>• Interactions between children and families and the formal child care, school and religious institutions in their communities influence children’s cognitive, social and emotional development.</td>
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<td>• Positive influences and protective factors in children’s development, including family processes and parenting, biologically based child characteristics, and access to and use of high-quality community services, have direct and indirect positive effects on development.</td>
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Although most study locations are a single county, the BYPL site includes four counties to ensure that 250 births per year for five years will be enrolled in the study.

Families from randomly selected segments within the four counties will be asked to join the study. The first study activity conducted in the field was identifying and recording the addresses and locations of dwelling units within each study segment. Over the course of eight weeks, BYPL research staff spent approximately 350 hours and covered 12,500 miles to list more than 15,000 households. In the spring of 2009, research staff will visit all listed dwelling units in the BYPL Study segments to identify prospective households and enroll women of reproductive age who are not sterile. Once a woman is enrolled, she will be contacted on a regular basis to determine whether she is planning to become pregnant or is pregnant. BYPL’s first births are expected in Fall 2009.

NCS Centers will use computer-based questionnaires and interviews to collect medical history and information regarding dietary intake and personal product use; environmental samples to measure air, dust, soil and water quality; physical examinations to record height, weight and blood pressure; ultrasound measurements of fetal growth; observations of behavior, focusing on mother-child interactions;
and biological samples of blood, urine and breast milk, as well as samples of umbilical cord blood and placenta at the time of birth. Follow-up visits will occur on a regular basis until the participants reach age 21.

Unique Rural Issues

Many of the health concerns nationwide are also local concerns in South Dakota and Minnesota. In addition, environmental exposures in rural areas require investigation. Studies have found that rural children are more likely to die young and more likely to be hospitalized than their urban peers. Although rural environments are often perceived as pristine, rural families may have distinctive environmental exposures that predispose them to adverse health outcomes. This is an important concern for our state because South Dakota’s population is 48 percent rural. Close proximity to agricultural operations, eating wild game harvested with lead ammunition and consumption of contaminated well water, are possible hazardous exposures of South Dakota’s children. Not only will the NCS investigate what exposures are harmful to a child’s growth and development, but it also will determine which exposures are harmless or even helpful (i.e., social and family support, appropriate nutrition, etc.).

Conclusion

In conclusion, the Brookings, Yellow Medicine, Pipestone and Lincoln (BYPL) county families’ participation in the National Children’s Study will help us learn how to improve the health of children. The success of the National Children’s Study relies on the support of obstetricians, family physicians, pediatricians and nurses to help in recruiting and retaining 1,250 families in the BYPL Vanguard Center. Physicians, who are one of the most trusted sources of information, are uniquely positioned to help the research team build relationships with families and to encourage their participation in the study. The BYPL Vanguard Center team is currently conducting outreach activities with area physicians and nurses, providing an overview of the study and learning how to best integrate the NCS protocols in the clinics and hospitals. The team is working on ways to minimize provider and patient burden while maintaining strict scientific integrity. The study has put the BYPL counties on the map, and participants and community members can help improve the understanding of children’s health and development. Results from the NCS will form the basis of child health guidance, interventions, and policy for generations to come. Residents and community members should feel proud they are part of such an important project.

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