The National Children's Study and the Children of Wisconsin

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ABSTRACT
Prospective, multi-year epidemiologic studies such as the Framingham Heart Study and the Nurses’ Health Study have proven highly effective in identifying risk factors for chronic illness and in guiding disease prevention. Now, in order to identify environmental risk factors for chronic disease in children, the US Congress authorized a National Children’s Study as part of the Children’s Health Act of 2000. Enrollment of a nationally representative cohort of 100,000 children will begin in 2008, with follow-up to continue through age 21. Environmental assessment and examination of biomarkers collected at specified intervals during pregnancy and childhood will be a major component of the Study. Recruitment at 105 sites across the United States is planned, and will begin at 7 Vanguard Centers in 2008, including Waukesha County, Wis. The National Children’s Study will provide information on preventable risk factors for such chronic diseases as asthma, certain birth defects, neurobehavioral syndromes, and obesity. In addition, the National Children’s Study will provide training in pediatric environmental health for the next generation of researchers and practitioners.

THE NEED FOR THE NATIONAL CHILDREN’S STUDY
Patterns of illness among children in the United States and in other industrially developed nations have changed substantially in the past 100 years.1 Infant mortality has declined while life expectancy has increased. With notable exceptions, such as HIV/AIDS, infectious diseases have receded as leading causes of illness and death.2 Today the major illnesses confronting children in the United States are a group of chronic conditions including a number of psychosocial and behavioral conditions termed the “new pediatric morbidity.”3

Many of these diseases may be caused or exacerbated by environmental factors. These include asthma, for which incidence and mortality have more than doubled.4 Incidences of childhood and young adult cancers, such as acute lymphocytic leukemias, brain cancer, and testicular cancer have increased by 10%,5 40%,6 and 68%,7 respectively, over the past 15-30 years, despite declining mortality. The incidence rates of some birth defects, such as gastroschisis, have increased sharply.8 Neurodevelopmental disorders—including learning disabilities, dyslexia, mental retardation, attention deficit disorder, and autism—are highly prevalent and affect 5%-10% of the 4 million babies born in the United States each year.10 Childhood obesity has become an increasingly important epidemic among American children.11

Chronic childhood illness is very expensive both monetarily and in terms of parental days of work lost. A recent study of the direct medical and the indirect societal costs associated with 4 categories of illness that are linked to environmental exposures in American children—lead poisoning, asthma, cancer, and neurobehavioral disorders—found the total costs to amount to
$54.9 billion annually. In Wisconsin, we estimate that the environmentally attributable cost of these 4 diseases in 2000 ranged between $1.19 and $1.59 billion.

Although much remains to be learned about associations between the environment and disease in children, evidence is accumulating that environmental exposures make important contributions to etiology. Numerous pollutants in the indoor environment have been shown to be triggers for childhood asthma including mold and mites, cockroach droppings, animal dander, and certain pesticides. Similarly, ambient pollutants—airborne fine particulates, ozone, oxides of nitrogen, and diesel exhaust—also have been shown to increase incidence of asthma and to trigger asthmatic attacks. Reduction in children's exposures to these indoor and outdoor air pollutants has been shown to reduce frequency of asthma and number of hospitalizations. Neurobehavioral impairment has been observed following exposure of the developing brain to even low levels of lead, methylmercury, pesticides, polychlorinated biphenyls, and ethanol. A recent National Academy of Sciences (NAS) study suggests that almost a third of developmental disabilities in children are caused by environmental factors acting alone or in concert with genetic susceptibility.

A NAS Committee on Pesticides in the Diets of Infants and Children explored in detail the differences in patterns of exposure and biological vulnerabilities to pesticides and other chemicals that exist between children and adults and also considered the implications of those differences for risk assessment and regulation. This NAS Committee noted 4 fundamental differences between children and adults that contribute to children's heightened susceptibility to toxic chemicals:

1. Children have disproportionately heavy exposures to environmental toxins as a consequence of their greater intake kilogram-for-kilogram of food, water, and air, coupled with their unique behaviors—in particular, hand-to-mouth behavior.
2. Children's metabolic pathways, especially in the first months after birth, are immature. In many instances, children are less able than adults to deal with toxic compounds.
3. Children are undergoing rapid growth and development. These developmental processes create windows of great vulnerability in which the course of development can be permanently disrupted by environmental toxins.
4. Because children have more future years of life than most adults, they have more time to develop chronic diseases that may be initiated by early exposures. Progress thus far in elucidating the role of the environ-ment in chronic childhood disease has been slow and incremental. Nearly all studies have examined relatively small populations of children; have considered only 1 chemical toxicant at a time; have had little statistical power to examine interactions among chemical, social, and behavioral factors in the environment; have had limited ability to examine gene-environment interactions; and have suffered from brief duration of follow-up. Also, many previous studies have been retrospective in design and thus have been forced to estimate past exposures from limited and sometimes biased historical data.

Previous large prospective epidemiologic studies have yielded invaluable gains in knowledge of disease causation for adults and have provided critical tools for prevention and treatment. For example, the Framingham Heart Study (Framingham, MA) was established in 1948, at a time when heart disease and stroke were epidemic in the United States. The goal was to identify preventable risk factors. Within a few years, data from Framingham identified cigarette smoking and elevated cholesterol and hypertension as preventable causes of cardiovascular disease (CVD); later analyses elucidated the influence of elevated triglycerides, sedentary lifestyle, and diabetes on CVD. This information provided the blueprint for the major reduction in CVD incidence that we have achieved in the United States over the past 4 decades.

PLANNING AND DEVELOPMENT OF THE STUDY

In response to the need for a similar study for children, the President's Task Force on Environmental Health and Safety Risks to Children recommended in 1998 that a large prospective epidemiologic study of American children be undertaken. In response, the US Congress, through the Children's Health Act of 2000, authorized the National Institute of Child Health and Human Development (NICHD) “to conduct a national longitudinal study of environmental influences (including physical, chemical, biological and psychosocial) on children’s health and development.” The Centers for Disease Control and Prevention, the US Environmental Protection Agency and later the National Institute of Environmental Health Sciences and a number of other federal agencies joined the NICHD in planning and conducting this study.

For the past 4 years since the legislation authorizing the National Children’s Study (NCS) was enacted, working groups have met to develop hypotheses to comply with the dictum of the Children’s Act of 2000. These hypotheses will guide researchers in their study
of the environmental links to diseases that affect not only children, but adults as well, including asthma, cardiovascular diseases, neurodegenerative diseases such as Parkinson’s, diabetes, obesity, and osteoporosis. A more detailed description of study hypotheses is available at www.nationalchildrensstudy.gov/.

The National Children’s Study has awarded 7 academic institutions contracts to establish Vanguard Centers, including a joint effort of the University of Wisconsin and the Medical College of Wisconsin, where enrollment of participants (25% pre-conception and the remaining women prior to the second trimester) and data collection of environmental samples including air, water, soil, dust, and water in and around the household as well as collection of biological specimens such as cord blood, urine, personal expelled air, maternal blood, and buccal cells will be field tested by the Vanguard Centers in advance of the other 97 sites. These enrollment and sampling protocols and timelines, which include frequent home and clinical visits over the first 3 years and semiannual visits during childhood and adolescence, will be adjusted to ensure quality data and high retention rates for the full study launch that will enroll 100,000 children from birth to age 21.

The recipients of the Vanguard Center awards demonstrated expertise and experience with large prospective cohort epidemiologic studies, and in many cases, expertise in the growing field of environmental pediatrics. They are:

- University of California in Irvine with Children’s Hospital of Orange County (for the Orange County, Calif study site)
- University of North Carolina in Chapel Hill at Chapel Hill with Battelle Memorial Institute, and Duke University (for the Duplin County, NC study site)
- Mount Sinai School of Medicine in New York with Columbia University Mailman School of Public Health, New York City Department of Health and Mental Hygiene, University of Medicine and Dentistry of New Jersey, and Columbia University Department of Obstetrics and Gynecology (for the Queens County, NY study site)
- Children’s Hospital of Philadelphia and Drexel University School of Public Health with University of Pennsylvania (for the Montgomery County, Pa study site)
- University of Utah in Salt Lake City (for the Salt Lake County, Utah study site)

### Table 1. Demographic and Health Indicator Data of Vanguard Sites

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Midwest</th>
<th>South</th>
<th>East</th>
<th>West</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wis</td>
<td>Minn*</td>
<td>Minn†</td>
<td>Minn‡</td>
</tr>
<tr>
<td>Population 1990</td>
<td>304,715</td>
<td>6890</td>
<td>10,491</td>
<td>11,884</td>
</tr>
<tr>
<td>Population 2000</td>
<td>360,767</td>
<td>6429</td>
<td>9895</td>
<td>11,080</td>
</tr>
<tr>
<td>1990-2000 % change</td>
<td>18.4</td>
<td>-6.7</td>
<td>-5.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>Persons per square mile 2000</td>
<td>649.4</td>
<td>12</td>
<td>21.2</td>
<td>14.6</td>
</tr>
<tr>
<td>Median Income</td>
<td>$62,800</td>
<td>$31,607</td>
<td>$31,909</td>
<td>$34,393</td>
</tr>
<tr>
<td>% White, Non-Hispanic</td>
<td>93.2</td>
<td>98.4</td>
<td>96.4</td>
<td>95.4</td>
</tr>
</tbody>
</table>

#### Birth Related Health Indicators

| Live births | 4421 | 56 | 121 | 113 | 309 | 728 | 30,819 | 9376 | 45,366 | 21,197 |
| Births per 1000 population | 12.1 | 8.7 | 10.2 | 12.3 | 10.9 | 14.8 | 14.5 | 12.2 | 15.1 | 19.4 |
| Infant Deaths (#) | 15 | 1 | 1 | 0 | 0 | 9 | 151 | 114 | 685 | 111 |
| <2500 g (%) | 5.7 | 7.4 | 5.8 | 4.5 | 5.2 | 10.3 | 7.8 | 6.5 | 6.1 | 6.89 |
| 1st Trimester Prenatal Care (%) | 95.6% | 75% | 61.7% | 87.3% | 86.6% | 79.8% | 65.6% | 89.3% | 91.3% | 75.7% |

* Lincoln, Minn
† Pipestone, Minn
‡ Yellow Medicine, Minn
§ All figures from Census 2000 (http://factfinder.census.gov/home/saff/main.html?_lang=en)
† Figures for 2001, 2002, or 2003, depending on the county.
Table 1 presents the diverse demographic and birth-related health characteristics of the Vanguard study sites. A map of 105 study locations is provided in Figure 1.

**BENEFITS OF THE STUDY**
It is hoped that the National Children’s Study will provide information on preventable risk factors for such pediatric chronic diseases as asthma; certain birth defects; neurobehavioral syndromes such as dyslexia, attention deficit hyperactivity disorder, autism, and schizophrenia; and obesity. As results emerge from the National Children’s Study, pediatricians will be able to translate these findings into clinical practice to guide the provision of care. The National Collaborative Inner City Asthma Study identified immediate health benefits of environmental interventions that decrease exposure to indoor allergens, including cockroach and dust-mite allergens.34 Similar guidance will be critical in the effort to stem the tide of childhood obesity. Just as the Bogalusa Heart Study has described the predictive power of childhood body mass index with adult adiposity with its concomitant comorbidity risks of CVD, diabetes, cancer, etc,35 the National Children’s Study promises to describe the factors that predict childhood obesity and provide pediatricians with evidence-based guidance to pass on to their patients and family members. An additional benefit will be the rich database the National Children’s Study will provide for the next generation of pediatric researchers.

Since the selection of the Vanguard Centers in September 2005, few outside of those closely involved in the preliminary work of the National Children’s Study seem to be aware of this federally initiated study. In a recent survey mailed to members of the Wisconsin American Academy of Pediatrics, 8.3% of the practicing pediatricians (n=277; 35.4% response) knew about the National Children's Study. In contrast, after learning about the study, 71.7% reported their full support for full federal funding for the National Children’s Study, projected to be $2.7 billion over 25 years.36 These pediatricians recognize the real and significant promise that a study of this magnitude and breadth holds to help stem the tide of this rising epidemic among our nation’s children.

For the National Children’s Study—and Wisconsin and Waukesha County in particular—to contribute positively to improving the health of our nation’s children, the support of the entire medical community is critical. Further, the support of the communities in Waukesha County will play a pivotal role in assuring money allocated toward this goal will be well spent in successfully recruiting and retaining the families enrolled in the National Children’s Study. Finally, we will need the support of our politicians to secure funding in the coming years for the continuation of the study. With all these people and resources working together, we have the greatest chance of success in improving the lives of the future generation.

**REFERENCES**


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