Challenges Facing the NCS: Integrating Social, Biomedical and Environmental Factors in One Comprehensive Study

National Children's Study Assembly Meeting
December 29-30, 2005
Washington, DC

Virginia A. Rauh, ScD.
Columbia Center for Children's Environmental Health
Mailman School of Public Health, Columbia University

Many individuals have proposed social-contextual approaches to understanding environmental health, resulting in, but not limited to, the following reports:

- *Racial and Ethnic Approaches to Community Health, 2010: Addressing Disparities in Health, 2005 (CDC)*
- *Framework for Cumulative Risk Assessment, 2003 (EPA)*
- *From Neurons to Neighborhoods, 2000 (Committee on Integrating the Science of Early Childhood Development)*
- *The Role of Environmental Hazards in Premature Birth: Workshop Summary, 2003 (IOM)*
- *Young Children Develop in an Environment of Relationships, 2004 (Nat. Sci.Council on the Dev. Child)*
- *Ensuring Risk Reduction in Communities with Multiple Stressors: Environmental Justice and Cumulative Risks/Impact, 2004 (Nat. Envir. Justice Advisory Council)*
- *Life Course Perspective (N. Halfon)*

The conceptual integration of many complex domains has been achieved:

- We have produced dynamic contextual models that combine gene-environment interactions, changes in social context, environmental and biological factors to trace the effect of the timing of events on developmental trajectories (Dawson et al., 2000; Meaney, 2001)

- We know that gene expression may be determined by the physical, psychological and social environment (Kandel, 1998); we recognize that social relationships can influence the expression of DNA throughout a person's lifetime

- Building on the expertise of the Work Groups and others, many of the NCS hypotheses are already fully integrated

The real challenge for the NCS:

To formulate and test research questions so as to arrive at the *right* answers to the *right* questions

Why is this so difficult when testing integrated causal models?

The right answer to the wrong question (Type III error)*

This may arise when methods designed to test hypotheses about inter-individual variation are used to address questions about increases in rates over time or disparities between groups.

Most epidemiologic methods were developed to study causes that distinguish individuals within a population and research questions are best addressed with data that include substantial variation in the variables of interest. Variation is usually maximal at the individual level.

**Kimball, 1957; Schwartz & Carpenter, 1999*

Why conduct the NCS?

1. Changing patterns of disease
2. Changing environments
3. Unique vulnerability of children
4. Environmental factors are now known to contribute to disease in childhood and adulthood
5. Diseases of environmental origin are costly

Why conduct the NCS?

1. Changing patterns of disease
2. Changing environment
3. Unique vulnerability of children
4. Environmental factors are now known to contribute to disease in childhood and adulthood
5. Diseases of environmental origin are costly

Changing patterns of disease

The problem

Sharp increases over the past 50 years in rates of asthma, autism, childhood cancer, obesity, type 2 diabetes, neurobehavioral disorders, certain birth defects, and chronic neurodegenerative diseases of adulthood

The research objective

To identify the causes of these increases in disease rates over time, and emerging (or persistent) population disparities in the rates of these diseases

Changing patterns of disease

The problem

Sharp increases over the past 50 years in **rates of asthma**, autism, childhood cancer, obesity, type 2 diabetes, neurobehavioral disorders, certain birth defects and chronic neurodegenerative diseases of adulthood

The research objective

To identify the causes of the increase in asthma rates, and the causes of population disparities in rates of asthma

Asthma as a public health problem: What is known about rates and trends?

- Prevalence and severity have increased in past 20 years (Eggleston et al., 1999), despite improvements in air quality (clark et al., 1999); the increase may be global (Jones, 1998)
- In the U.S., the largest increase is among inner-city children and young adults (Eggleston et al., 1999)
- Hospitalization and morbidity rates for nonwhites are more than twice those for whites (Clark et al., 1999)

What types of associations do we observe?

- Poor outdoor air quality exacerbates symptoms among asthmatic children (Clark et al., 1999); hospitalizations and ED visits are associated with ambient air pollution levels (Norris et al., 1999)
- Role of stress in the etiology of asthma may involve interactions between immune, neuroendocrine, and behavioral factors (Wright et al., 1998)
- Urban living may be associated with higher levels of stress (Marshall & Agarwal, 2000)
- Genetic predisposition to form IgE to allergic proteins on airborne particles may be involved in sensitization (Eggleston et al., 1999)
- Immunologic sensitivity may interact with exposure to allergens to affect asthma (Rosenstreich et al., 1997)
- Interventions that address multiple rather than single risks are more likely to reduce asthma morbidity

Formulating hypotheses consistent with the questions of interest (asking the right questions)

- Which children are most likely to develop asthma?
  (an individual-level question)

  Children with specific genetic susceptibilities (allele frequencies) are at increased risk for asthma
- Why is the overall prevalence of asthma rising?
  (a question of changing rates over time)

  Cleaner living environments lead to a shift in immune response from Th1 to the more allergic Th2, thereby reducing the protective effect against allergies
- Why do the rates of asthma differ between groups?
  (a disparity question)

  The threshold at which a genetic predisposition to asthma is expressed is likely to be lower in an environment where children are exposed to high as compared to low levels of chronic stress
- What are the underlying biological mechanisms?
  (a molecular-level question)

  Oxidative stress-related genetic variants interact with tobacco smoke to alter the risk for the developing asthma

How could we get the right answer to the wrong question?

Possible sources of the error:

- The causes of inter-individual variation in risk for asthma do not appreciably contribute to the current incidence of asthma
- The causes of rate differences between populations (ie, ethnic/racial groups) and the causes of inter-individual differences interact in creating the current incidence in the population of interest
- The causes of inter-individual differences are also causes of the current incidence, but they are not the causes of the rate difference between the groups.

What are some possible consequences of these Type III errors?

1. We correctly identify the sources of variability with respect to inter-individual risk of asthma, but incorrectly conclude that these factors explain the overall increase in asthma rates or group differences in asthma rates.

2. We educate patients and providers with respect to best practices, but rates of hospitalization for asthma do not change because rodent and cockroach problems associated with poor housing in the community are invariant.

Changing patterns of disease

The problem

Sharp increases over the past 50 years in rates of asthma, autism, childhood cancer, obesity, type 2 diabetes, neurobehavioral disorders, certain birth defects and chronic neurodegenerative diseases of adulthood

The research objective

To identify the causes of the increase in rates of obesity, and the causes of population disparities in rates of obesity

Obesity as a public health problem: What do we know?

- Prevalence of obesity has increased in the U.S. in recent years (Wolfe et al.,1994; Dalton, 1997)
- Genetic factors account for a significant proportion of the variance in body mass index (Hewitt, 1997)
- The number of fast food restaurants per square mile has increased in many regions.
- There is a significant association between individual activity level and risk of overweight (Ching et al., 1996).
- Being overweight as a child increases the risk of developing diabetes at age twenty-one years (Sinha et al 2002)

How could we get the right answer to the wrong question?

Possible sources of error:

- The causes of inter-individual variation in risk for obesity (e.g., genetics) do not appreciably contribute to the current incidence of obesity. Genes produce proteins related to a greater or lesser propensity for appetitie dysregulation.

- The causes of rate differences between populations and the causes of inter-individual differences interact in creating the current incidence in the population of interest. The threshold at which a genetic predisposition to obesity is expressed is likely to be lower in an environment where fast food is plentiful and advertising is effective, as compared to an environment of limited or healthier food resources.

What are some possible consequences of these Type III errors?

1. We correctly identify the sources of variability with respect to inter-individual risk of obesity, but incorrectly conclude that these factors explain the overall increase in obesity rates.
2. We educate children about healthy dietary practices and this has some public health usefulness, but fail to address the contextual factors such as advertisements to eat unhealthy foods in unhealthy amounts, and the increase in sedentary activities (tv and computer games). There are no changes in rates of obesity because the causes of the rate differences between populations and the causes of interindividual differences interact in creating the current incidence rate of obesity.

Why conduct the NCS?

1. Changing patterns of disease
2. **Changing environment**
3. Unique vulnerability of children
4. Environmental factors are now known to contribute to disease in childhood and adulthood
5. Diseases of environmental origin are costly

The changing environment

The problem

Rapid proliferation of synthetic chemicals (high-production–volume) since the 1950s; fewer than half have been tested for toxicity or other adverse effects; children are disproportionately exposed because of dietary patterns and age-related behaviors

Characteristics of the built environment may influence diet, activity patterns, neighborhood safety, and exposure to potentially toxic substances

The objective

To determine whether specific environmental exposures are associated with disease (e.g.,what is the lowest level at which a substance is toxic to humans? How do specific social conditions affect the course of development?)

Examples of the changing environment

The problem

Use of organophosphate pesticides in homes (now banned) and for agricultural purposes (not banned)

Socially and physically unhealthy forms of housing

The objective

To determine whether specific environmental exposures are associated with disease (e.g.,what is the lowest level at which a substance is toxic to humans? How do specific social conditions affect the course of development?)

Many more examples that are in your own fields of expertise

So how do we come up with the right questions?

- Setting priorities
- Selecting the general classes of research questions that are relevant to the health of America's children
- Embracing an interdisciplinary focus
- Soliciting input from community advisors
- Allocating scant resources appropriately
- Designing an overall sampling strategy that permits the formulation of research questions concerning rates of disease, as well as individual risk of disease
- Designing a second stage sampling strategy that ensures sufficient variability in risk factors so as to permit the testing of interactions

How do we come up with the right answers?

That's what the Vanguard Centers, the Steering Committee, and all of the future study sites (many of you) will be working on for a long time.