



The National Institute of Environmental Health Sciences' research program on children's environmental health

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This article highlights the wide array of research programs supported by the National Institute of Environmental Health Sciences (NIEHS) that address issues related to children's environmental health. Special attention is given to the interagency, collaborative Centers for Children's Environmental Health and Disease Prevention Research program. A brief description of each of the eight centers highlights scientific foci and research efforts to date. In addition to discussing NIEHS-supported research programs, the article emphasizes the NIEHS' commitment to the promotion of translating basic research findings into public health knowledge so that culturally sensitive and applicable interventions may be developed. *Journal of Exposure Analysis and Environmental Epidemiology* (2000) 10, 630–637.

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Introduction

Research demonstrates that children are uniquely vulnerable to environmental pollutants and that a new pattern of childhood illness is emerging (Landrigan et al., 1999a,b). In the past 15 years, the prevalence of childhood asthma increased by nearly 87% and the awareness of the possible role environmental exposures play in other diseases has grown¹ (Mannino et al., 1998). In light of these trends, the National Institute of Environmental Health Sciences (NIEHS) continues to assert its strong commitment to advancing our understanding of the health effects of environmental pollutants on our children and to developing best practices for preventing adverse impacts. The Federal Executive Order of 21 April 1997, "Protection of Children from Environmental Health Risks and Safety Risks," spurred many Federal efforts to consider special environmental conditions that pose a health risk to children. For NIEHS, the Executive Order affirmed and strengthened its work in children's environmental health.

Human health and human disease result from three interactive elements: environmental factors, individual susceptibility and age. The mission of the NIEHS is to

reduce the burden of human illness and dysfunction from environmental causes by understanding each of these elements and how they interrelate.

The NIEHS achieves its mission through multi-disciplinary biomedical research programs, prevention and intervention efforts, and communication strategies that encompass training, education, technology transfer, and community outreach. For more than 20 years, the NIEHS has supported investigations that work toward enhancing our understanding of the relationship between exposure to environmental pollutants such as lead, polychlorinated biphenyls (PCBs) and DDT and the health of children. Through the years, NIEHS funding for research, both within and outside the Institute, has remained strong.² In addition, research programs have become more dynamic by incorporating community participation and placing a greater emphasis on translating investigation results into effective public health interventions.

During the last few years, NIEHS has developed innovative approaches to stimulating cutting-edge research on children's environmental health issues. These new efforts fit within three programmatic themes: (1) children's environmental health and disease prevention research, (2) health disparities and community outreach activities, and (3) training and education.

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¹American Lung Association. Asthma in Children. Fact Sheet (September 1999).

²NIEHS. Children's Health Research of the National Institute of Environmental Health Sciences. Pamphlet (1999).

Centers for Children's Environmental Health and Disease Prevention Research

The cornerstone for children's environmental health research was created in 1998 in response to recommendations that a comprehensive, national, child-centered agenda be developed (Landrigan et al., 1998). The NIEHS, the Environmental Protection Agency (EPA), and the Centers for Disease Control and Prevention (CDC) collaborated to establish a dynamic, multidisciplinary and community-based program entitled, Centers for Children's Environmental Health and Disease Prevention Research. The program promotes the translation of basic research findings into applied intervention and prevention methods, thereby enhancing awareness among children, their families, and health care practitioners regarding detection, treatment, and prevention of environmentally related diseases and health conditions (Deary et al., 1999). The four aims of the program are to:

- Provide for multidisciplinary interactions among basic, clinical, and behavioral scientists interested in establishing outstanding, state-of-the-art research programs that address environmental contributions to children's health and disease.
- Support a coordinated program of research/prevention centers that pursue high quality research in environmental aspects of children's disease, with the ultimate goal of facilitating and accelerating translation of basic scientific knowledge into clinical applications or intervention strategies that can be used to reduce the incidence of environmentally related childhood disease.
- Develop fully coordinated programs that incorporate exposure assessment and health-effects research with development and validation of risk management and health promotion strategies.
- Establish a national network that fosters communication, innovation, and research excellence with the ultimate goal of reducing the burden of morbidity among children as a result of exposure to harmful environmental agents.

Integrating laboratory science with applied intervention strategies makes the children's centers unique. Researchers investigate the health effects of environmental exposures and develop and evaluate risk management strategies for disease prevention and health promotion within diverse groups of children. Community participation ensures the appropriateness of the intervention strategies, in addition to strengthening the capacity of community members to participate in processes that shape such efforts. Participation in public-health research, a requisite of the program, facilitates outreach and education efforts of the centers.

The improved communication between researchers and community members strengthens the knowledge base of communities, health care providers and decision makers regarding detection, treatment, and prevention of environmentally related diseases in children.

By utilizing the rich expertise and resources of universities, community-based organizations, and public health institutions across the Nation, the centers are better equipped to conduct studies on the causes and mechanisms of children's disorders having an environmental etiology; to identify relevant environmental exposure pathways; and to intervene to reduce hazardous exposures and their adverse health effects, with the ultimate goal of decreasing the prevalence, morbidity, and mortality of environmentally related childhood diseases. The eight centers (Figure 1) are developed around a central scientific theme, focused on the role environmental agents play in particular illnesses such as asthma, developmental disorders, and childhood learning. Now a year old, each center supports at least two basic research projects and one community-based intervention research project.

Columbia University School of Public Health: Columbia Center for Children's Environmental Health

Through interrelated studies, the Columbia Center for Children's Environmental Health seeks to improve our understanding of potential environmental risk factors for children's health, particularly asthma and early child development (Perera et al., 1999). Utilizing molecular epidemiology in concert with community-based intervention, the center addresses three hypotheses: (1) pre- and postnatal exposure to particulate matter (PM), polycyclic aromatic hydrocarbons (PAHs), environmental tobacco smoke (ETS) and household allergens increase the risk of asthma and/or developmental impairment; (2) inadequate nutritional status exacerbates the impact of these exposures; and (3) community-based interventions can reduce the risk of disease. Two projects examining these



Figure 1. The Children's Environmental Health and Disease Prevention Centers.

hypotheses are in progress. From this investigative research, the center is implementing an indoor air pollution and allergen control intervention project to evaluate the effectiveness of community education for reducing asthma rates.

Using a prospective molecular epidemiologic study, researchers are examining the influences of outdoor and indoor pollutants on fetal growth and early child development in a cohort of inner city, minority children from northern Manhattan and the South Bronx. Investigators are following 400 infants, whose mothers were enrolled before their last trimester, from the last trimester to their second birthday. Questionnaires are being used to collect data on environmental exposures, socioeconomic status, food consumption, activities, and health status. In addition, biomarkers are being examined from cord and maternal blood samples taken at the time of delivery.

Building upon the aforementioned project, investigators are utilizing the questionnaire and biomarker data collected to examine environmental risk factors and the cause of childhood asthma. This project is monitoring and modeling exposures to ETS, diesel exhaust, and PM because investigators are concerned about the interaction of home allergens to other air pollutants. In addition, measurements of infants' immunoglobulin E (IgE), lymphocyte proliferation and cytokines are being obtained.

The center works closely with community-based groups to develop and implement targeted interventions. For example, in collaboration with West Harlem Environmental Action, Inc (WEACT), the center has developed materials for environmental health education campaigns, conducted a health fair in Washington Heights, and conducted a conference about children's health and the urban environment. To enhance their responsiveness to the communities in which they work and the effectiveness of their intervention strategies, the center recently established a Community Advisory Board of partner agencies and individuals. The greatest fruit of the center's partnership with communities is an education project entitled "Healthy Environment, Healthy Child," which targets women of childbearing age and informs them of ways to minimize their child's exposure to environmental risks in the home.

University of Southern California: Children's Environmental Health Center

The center at the University of Southern California (USC) represents collaborative efforts between USC, the University of California Los Angeles (UCLA), and community members (Gilliand et al., 1999). The center's focus is the health impact of outdoor and indoor air pollutants on children's respiratory health. Three primary projects are in progress. A controlled, laboratory-based project, involving

human subjects as well as mice, examines the capability of environmental tobacco smoke to alter the amount and types of immunoglobulin and cytokines produced in the nose. Using adult and child volunteers, researchers are monitoring these effects after exposing them to controlled amounts of tobacco smoke and ragweed pollen. An anticipated outcome will be a better understanding if children are more susceptible to tobacco smoke than adults. Mice are being used to address genetic and age-related questions that may elucidate the possible role of second-hand smoke on developing asthma.

An epidemiologic study investigates the effect of long-term air pollution exposure on thousands of children and adolescents living in 12 communities in southern California. Children's dietary intake and genetic factors are major foci of this investigation. To test if there exists a relationship between the consumption of certain foods high in antioxidants, genetic factors, and a child's susceptibility to air pollution, researchers are sampling buccal cells and gathering food-frequency questionnaires.

The last project is a community-based asthma prevention/intervention study of inner city, primarily minority, children with diagnosed asthma. The overarching goal of this intervention is to evaluate the effectiveness of comprehensive environmental health education programs in the reduction of household exposures, such as dust mites and roaches, and clinical improvement of asthma.

The center is utilizing the Community Outreach and Education Program (COEP) component of the separate NIEHS Core Center at USC to enhance community outreach. The COEP links the center and the community by creating awareness of health issues and research opportunities in children's environmental health and promoting collaborative education and projects in the community.

Johns Hopkins University School of Medicine: Center for the Asthmatic Child in the Urban Environment

The Center for the Asthmatic Child in the Urban Environment focuses its efforts on understanding how exposures to environmental pollutants and allergens may relate to airway inflammation and respiratory morbidity in children with asthma living in the inner city of Baltimore and developing effective strategies to reduce morbidity by changing these exposures (Eggleston et al., 1999). To fulfill its goal, the center has created a multidisciplinary program that includes both basic and applied research programs in combination with a community-based prevention research project. Two basic science research projects examine mechanisms that produce inflammatory responses in the airway. Utilizing mice, one considers the genetic basis for airway susceptibility to an inflammatory response to ozone,

while the other investigates the means by which particulate matter may exacerbate an allergen-driven inflammatory response.

The first project is generating high-resolution linkage maps of the regions of mouse chromosomes 17 and 11 carrying O₃ susceptibility loci with the goal of searching for homologous human susceptibility loci by way of comparative mapping approaches. By developing congenic mice that possess different genetic risk factors to inflammatory response and epithelial injury and exposing them to O₃, researchers plan to evaluate the mechanisms through which the susceptibility locus adapts susceptibility. Investigators anticipate this research will provide a means to characterize humans who are at risk to oxidant exposures.

The second laboratory project is using genetically altered mice (susceptible A/J and resistant C3H/HeJ) to understand the exacerbation of allergen-driven inflammatory responses. The three goals of the project are to: (1) establish an exposure response relationship between PM and allergic airway responses in A/J mice; (2) determine the biological effects of PM exposure on resistant mice; and (3) determine the role of interleukin 6 (IL-6) in mediating PM-induced allergic asthmatic symptoms by neutralizing its activity *in vivo* and examining PM-induced effects on allergic airway responses.

Investigators are developing an epidemiologic study that will compare ambient exposures to household pollutants and allergens and their impact on children's morbidity from asthma. Researchers will collect biological and psychosocial data on the children recruited to participate. In addition, the center is implementing a community-based prevention project to test the effectiveness of current intervention methods for reducing exposures to potentially harmful pollutants. The principal aim of the project is influencing change in home environmental exposures with currently recommended procedures, such as allergen-proof bedding, air filters, pest control services, and smoking cessation programs.

Demonstrating its commitment to community outreach, the center established a Community Advisory Committee. At regularly scheduled meetings, center directors and members of the community-based studies work together to refine protocols and to develop feasible methods of executing them.

Mt. Sinai School of Medicine: The Mount Sinai Center for Children's Environmental Health and Disease Prevention Research

The Mount Sinai Center for Children's Environmental Health and Disease Prevention Research seeks to identify, elucidate and prevent developmental deficits in children that result from exposures to environmental toxicants in the

inner city such as pesticides and PCBs. To address this issue, the center supports five different projects. A community-based project in east Harlem, NY is being carried out in collaboration with the Boriken Health Center. Receiving guidance from a Community Advisory Board, its goal is to reduce exposures to pesticides and other developmental toxicants among expectant mothers through integrated pest management and dietary change.

Two epidemiologic projects are examining the impact of environmental exposures on neurodevelopment. The first, a retrospective study of African-American men, is studying the relation of prenatal PCB exposure to neurodevelopmental outcomes in adolescence. Researchers are reevaluating the cognitive ability and other measures of neuropsychological status of 162 young African-American men who have been followed through childhood and adolescence. In addition, analysis for PCB exposure is being carried out on samples of prenatal maternal serum. The second, a prospective epidemiologic study of an ethnically diverse cohort of mothers and their children, explores this topic in light of current exposures to environmental toxicants in the inner city. In addition to PCBs, investigators are examining the importance of diet for neurodevelopment and health outcomes.

Mothers and infants in the cohort study will also be included in an investigation of genetic factors that control metabolism and excretion of pesticides. Using biological samples collected from the mothers and infants, researchers will examine mutations in the enzymes that activate and detoxify organophosphates and other pesticides. In a laboratory investigation, researchers are performing experiments in cell lines and female rat pups to examine the mechanisms by which environmental toxicants may affect neuroendocrine and early reproductive development.

University of Michigan School of Public Health: Michigan Center for the Environment and Children's Health

The prevalence of asthma in the city of Detroit is particularly high, reflecting trends found elsewhere among urban populations and communities of color. The center at the University at Michigan School of Public Health investigates aspects of pediatric asthma that can translate into risk assessment and comprehensive neighborhood and household interventions (Clark et al., 1999). Community participation led to the formation of the Community Action Against Asthma (CAAA) program that consists of community partners and university researchers and is intended to integrate intervention and exposure assessment studies.

The CAAA considers two hypotheses: (1) that individually tailored interventions help to reduce exposure to environmental contaminants and to improve respiratory

health, and (2) that exposure to common indoor air contaminants will aggravate the health of asthmatic children.

The intervention project couples a community-based intervention strategy with an evaluation mechanism. The intervention phase takes place at the household and neighborhood level. After identifying asthmatic children through screenings at school, their parents are being asked to enroll in the project. Community outreach workers visit each household 12 times in a 2-year period to work with the families in identifying and minimizing exposures to household allergen that are known to provoke asthmatic reactions. Participating households receive educational documents in addition to other materials to reduce indoor asthma triggers. In an effort to reach a wider audience, community outreach workers collaborate with neighborhood groups on raising awareness about asthma and how families and communities may reduce childhood exposure to environmental threats.

Researchers with the CAAA are using a well-validated asthma screening questionnaire to determine the prevalence of asthma in elementary-aged children in African-American and Latino populations of Detroit. From the data collected, investigators anticipate identifying the principal factors associated with increased risk for asthma and determining if seasonal and daily changes in outdoor and indoor air contaminants explain fluctuations in the severity of asthma. To better understand the relationships between exposures and activity patterns of asthmatic children, researchers are collecting data at the neighborhood, school, and personal level. In addition to collecting data on outdoor and indoor air contaminants, investigators are placing special emphasis on psychosocial factors.

In the laboratory, researchers are studying the role of chemokines during an asthmatic attack. They seek to identify the important mediators responsible for asthmatic attacks in the hope that their research may lead to the development of specific therapies to block the mediators. To accomplish this task, investigators are performing microscopic analyses of lungs and nerves of the airway that have been injected with chemokines, developing a mouse model of asthma-like pulmonary inflammation to cockroach allergens, investigating the signals responsible for inducing the cell to make chemokines by sensitizing cells and challenging them with cockroach allergens, and testing the core hypothesis that chemokines are important in causing asthma.

University of Iowa School of Medicine: The Etiology and Pathogenesis of Airway Disease in Children from Rural Communities

Rural communities introduce unique environmental exposures that are known to play a role in airway disease. Grain

dust and endotoxin, commonly found in farming communities may adversely affect children. Such exposure may lead to asthma and other respiratory diseases. The center at the University of Iowa School of Medicine is taking a multidisciplinary approach to studying environmental models of asthma and to investigating the biological origin and persistence of airway disease in children (Schwartz, 1999).

Using mouse models, the role of grain dust-induced inflammation and endotoxin-induced airway disease is being studied. Researchers are examining the combined role of respiratory syncytial virus (RSV) and endotoxins in inflammation of airways. In addition, they are developing a mouse model to better understand development of persistent environmental airway disease. Investigators are also establishing new approaches that will facilitate investigation of airway cell interaction that is the basis for the inflammatory response to grain dust. A multicomponent intervention research project has been developed that coordinates environmental interventions with other health care improvements to address asthma in children who live in rural communities.

University of Washington School of Public Health and Community Medicine: Center for Child Environmental Health Risks Research

The Center for Child Environmental Health Risks Research at the University of Washington is comprised of two laboratory-based studies and two field-based studies. The overall aim of the laboratory studies is to identify and characterize cellular and molecular mechanisms underlying susceptibility of children to pesticide-induced developmental toxicity. Researchers are evaluating *in utero* midbrain development and postnatal development of the cerebellum and hippocampus. They are assessing effects of pesticides *in vitro* for specific cell systems and *in vivo* for molecular, cellular and neurodevelopmental impacts. In addition, investigators are evaluating age and genetic polymorphisms in the context of potential factors impacting the susceptibility of children to organophosphate neurodevelopmental toxicity.

The objective of the field studies is to reduce pesticide exposure in children of farm workers by identifying and breaking the pathways by which children come in contact with pesticides. A risk assessment approach is utilized to allow research findings to be translated into information that is directly useful in developing public health intervention and prevention strategies to reduce the incidence of adverse environmental impacts on children's health.

Researchers from the center have developed a Community Advisory Board to assure the relevance of the study to the affected communities. The Board works with research-

ers to develop survey instruments and provide recommendations for pesticide sampling. Educational materials that focus on interventions are being developed to initiate discussions with workers and their families about the take-home pathway. Novel intervention strategies will be evaluated for success.

University of California at Berkeley, School of Public Health: Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS)

Small children, or *chamacos*, as they are referred to in Spanish, are the heart of the center's research at the University of California at Berkeley. The CHAMACOS project focuses on low-income, primarily Latino pregnant women and children in the Salinas Valley region who are likely to be exposed to a variety of hazards in the environment, including pesticides and potential respiratory irritants such as pollens, molds, dust mites, animal dander and endotoxins (Eskenazi et al., 1999). Researchers are assessing the neurodevelopmental and respiratory health effects in children of low-level chronic contact to these exposures. The goal is to determine the level and pathways of exposure to pesticides, to assess their potential health effects, and to translate the findings into sustainable strategies to reduce the exposures to children.

The center, in concert with its community and health partners, is enrolling a cohort of 500 pregnant women and their newborns. The women and children will be followed for 2 years during which time investigators will assess the neurobehavior, growth and respiratory function of the children at set times. In addition, researchers will collect and analyze biological and ambient samples to estimate levels of *in utero* and postnatal exposures of the child. The center and its community partners are defining the scope of work to evaluate the impact of interventions in the home on the reduction of pesticide exposures in children.

Additional NIEHS children's health efforts³

Although the Children's Centers comprise a keystone of NIEHS support for research on children's environmental health research, the Institute champions other cutting-edge efforts that address the health of children, especially children from disadvantaged communities. Among these are programs in Environmental Justice, Community-Based Prevention/Intervention Research, NIEHS Core

Centers, and K-12 Environmental Health Sciences Education.

The primary objective of the NIEHS Environmental Justice: Partnerships for Communication program is to establish methods for linking members of a community, who are directly affected by adverse environmental conditions, with researchers and health care providers. Development of community-based strategies to address environmental health problems requires approaches that are not typically familiar to the research and medical communities. The distinctive needs of individual communities and their inhabitants are seldom considered in identifying environmental health problems and devising appropriate medical intervention procedures. This program is designed to develop new modes of communication and to ensure that the community actively participates with researchers and health care providers in developing responses and setting priorities for intervention strategies. A number of these projects focus on issues with particular relevance to children, such as asthma, pesticide exposures, and effects of urban smog.

The Community-Based Prevention/Intervention Research (CBPIR) Program aims to implement culturally relevant prevention/intervention activities in economically disadvantaged and/or underserved populations adversely impacted by environmental contaminants. It is intended to foster refinement of scientifically valid intervention methods and to strengthen the participation of affected communities in this effort. Community-based prevention/intervention research thus seeks to expand our knowledge and understanding of the potential causes and remedies of environmentally related disorders, while at the same time enhancing the capacity of communities to participate in the processes that shape research approaches and intervention strategies. Given the complexity and magnitude of environmental health problems, research endeavors aimed at improving our knowledge of and ability to resolve these issues can benefit from establishing collaborative relationships with the communities experiencing these problems. Community-research partnerships benefit the researcher and the community. These partnerships can, for example, facilitate the definition of important environmental health issues and concerns, ensure the development of culturally appropriate measurement instruments, and establish trust that will enrich the value of data collected.

Research projects address agricultural pesticide exposure, asthma and lead poisoning, and are conducted in a manner that reinforces collaboration between community members and research institutions. Relevant results are disseminated to the community in clear, useful terms. Moreover, these studies are designed to give due consideration to social, economic, and cultural conditions that influence health status. Identifying and incorporating

³More information for the following programs may be obtained from the following web site — <http://www.niehs.nih.gov/dert/programs/translat/home.htm>.

unique cultural factors into intervention strategies may result in increased acceptability, use and adherence. This approach seeks to maximize the potential for change in knowledge, attitudes, and behavior. Only through communication and partnership formation, can we ensure that research findings reach and are made relevant to affected individuals and communities.

Another major NIEHS initiative is the NIEHS Core Centers program. Established in 1963, this program promotes cross-cutting, innovative research by supporting core facilities that act as a focus to stimulate multidisciplinary interactions. A recent development is the creation of a Community Outreach and Education Program (COEP). Each center develops a COEP to foster strengthened community participation and education, and most importantly, to ensure that research findings are translated into effective public health applications. As demonstrated by the USC Children's Center, these COEPs often have a focus on children's environmental health issues.

Educational materials are an important part of exposure reduction at the community level. As such, the K-12 Environmental Health Sciences Education program strives to improve the understanding of environmental health issues by all students and to expand career awareness for those interested in pursuing research and service occupations in environmental health sciences. Initiatives within this grant program support development of instructional materials for use in grades K-12 and teacher enhancement and development activities to provide teachers with the skills needed to teach environmental health science. An important element of these programs is their design to ensure the success of all students, regardless of background or ability, especially those from underrepresented populations. In addition, these projects promote parental and community involvement so that both students and parents become more aware of environmental health concepts and issues.

Based upon the above and other related programs, the NIEHS is in an excellent position to elucidate the underlying causes and mechanisms responsible for disparities in health. Throughout 1999, the NIEHS sponsored three regional workshops, a National Institutes of Health (NIH) concept forum, and a New York Academy of Science conference, each of which was devoted to developing a research agenda to address health disparities. As a result of this input from scientists, health care providers, policy makers, and community representatives, the NIEHS has developed a program entitled, *Health Disparities: Linking Biological and Behavioral Mechanisms with Social and Physical Environments*.

The purpose of this research program is to foster multidisciplinary research that will elucidate underlying mechanisms by which the interaction of physical exposures and the social environment leads to health disparities. Physical exposures include physical agents (e.g., radia-

tion), chemical agents (e.g., pesticides) and biological agents (e.g., pathogens, harmful algal blooms). The social environment includes socioeconomic status (SES), residential factors, education, cultural variables, institutional and political forces, familial factors, and media influences. The ultimate goal of this research is to understand the sources of disparities in health among the U.S. population, especially between lower SES groups and higher SES groups. Via this initiative, the NIH seeks to clarify biological, social, and behavioral processes that lead to health disparities stemming from the interaction of social and physical environments as a basis for ultimately developing intervention strategies. Projects will possess collaborative efforts between social/behavioral scientists and biomedical scientists and not be limited by disease end points.

Summary

As evidenced by the continued development and support of new and innovative programs, the NIEHS is committed to improving the health and well being of children. As these programs bring together researchers, clinicians, community members and public health workers, great strides will be taken to further our understanding of the mechanisms through which environmental agents affect our children's health. Figure 2 illustrates the interaction between the wide array of novel NIEHS programs outlined and discussed in this article. This knowledge will lead us to develop and implement appropriate health promotion and disease prevention strategies to reduce the levels of environmental exposures and to decrease the

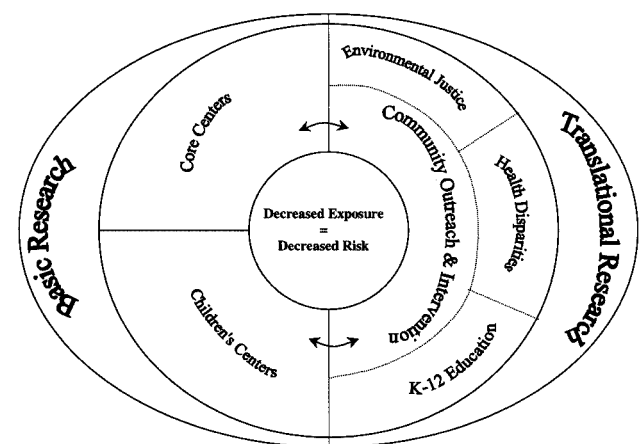


Figure 2. Interaction between NIEHS research foci. This graphic illustrates the strategy the NIEHS embraces. To demonstrate that decreased exposure is equivalent to decreased risk, basic research, including both mechanistic and population-based research, must be translated into public health knowledge so that culturally sensitive and applicable interventions may be developed.

burden of environmentally induced diseases in children across the United States.

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