Population Health and the Environment

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The Challenge of Complexity

It has been noted that the single characteristic describing the frontiers of contemporary science is complexity (Dean 1993a). Riley (1987) has opined that members of the human species do not grow old in laboratories. Disease and aging processes must be gleaned not from studies of any single subject or cohort but from many cohorts under the most widely varying social and temporal conditions.

Many theories and methods account for the complexity of disease and the range of factors and influences shaping health. Wulff et al. (1986) have noted that the biomedical mechanical model of disease that for so long has dominated the scientific paradigm guiding research on human health is being increasingly questioned. They suggest that important findings in the fields of epidemiology, occupational health, social medicine, and sociology are building new bodies of knowledge about the role of environmental and social influences in health maintenance and promotion. In the investigations of many crucial health problems, studies designed to accept or reject hypotheses about single factors have serious limitations for recognizing multicausal mechanisms.

The recognition of complexity and multicausal phenomena and the need to look at the whole person, indeed, at entire populations, have been accompanied by an interest in the social sciences because of the rich range of study designs and methodologies they offer for research on human health and behavior (Abell 1991). Sociological and related methods have gained additional attention because of their ability to explore an event in the context of its occurrence. Riley (1993) has used aging as an example of the dynamic processes shaping and preserving health or leading to decline and...
disease. A population perspective on the topic must account for the long term influences arising from being born into and growing up in a particular historical context along with the contemporary influences of the social and physical environment. The same logic readily applies to chronic disease processes and to health maintenance. (Dean 1993b)

Ory et al. (1992) summarize the point:

It has been known for some time that causal influences are not simple, but the extent of the complexity was not anticipated. Not only is it common rather than exceptional that multiple influences are involved in causing an outcome, but also causal influences often have multiple outcomes. In order to gain knowledge of this reality, [research must examine] the complex interconnectedness of many types of influences.

Influences on a New Paradigm of Inquiry

Various factors have been noted (House 2002) as having modified the scientific perspective over the recent past. One has been the increase in life expectancy as infectious disease declined in the developed world and chronic diseases became epidemic. No longer was a disease-specific etiologic agent identifiable as the culprit in illness. A new way of thinking evolved in which risk factors for disease—multicausal influences—became the focus of studies. House (2002) notes that in the beginning the search for risk factors remained biologically focused, but later the focus expanded to include environmental, behavioral, and eventually psychosocial risk factors.

Soon investigators (Graham and Reeder 1972) showed that exposure to such agents was socially patterned.

Another factor influencing the expanding inquiry was the work demonstrating the limits of modern medicine. Several landmark studies (Fogel 1991; McKelvey 1988; McKinlay and McKinlay 1977), showed that the most dramatic advances in life expectancy occurred before the development of germ theory or its widespread application. More recently, it has been posited (Bunker et al. 1994) that only 1 year in the entire 35-year increase in life expectancy in the United States realized in the past century has been because of therapeutic or preventive medical practices. The rest was primarily because of improved nutrition and reduced exposure to air- and waterborne infection. Such data eventually gave rise to the well-known depiction of causes of premature mortality, as seen in Figure 1 (McGinnis and Foege 1993). A most salient feature not as evident pictorially from Figure 1 is the growing acceptance that the interaction of these potential causes actually produces the health consequence.

Yet another influence has been the dramatic evolution in the theories and methods of the social and behavioral sciences in the past half century and, in the words of House (2002), their “confluence with strands of biomedical thinking.” As noted, combining approaches from biology, physiology, epidemiology, sociology, and psychology, researchers began to confront problems more comprehensively and with more varied methodologies. For example, whether and how a given potential environmental factor is appraised as stressful and is responded to physiologically is moderated by other social, psychological, or physical–chemical–biological characteristics of individuals and their situational context and social environment (House 1981).
The Question of Disparities in Health

In a real sense, then, the camera lens has been widened to include the influence on health and disease of scientific endeavors beyond the biological. A guiding question in population health studies has been, why are some people healthier than others? Hayes and Glouberman (1999) distinguish this query from equally important but different questions. More generally, in public health the guiding question is, what must we do to keep people healthy? In medicine the question is, how do we diagnose and treat people? In health promotion the concern is how we improve the health of the population? The salient feature of population studies is that they compile evidence systematically across populations to understand how and why various factors influence health outcomes. Several areas of research have contributed greatly to the evidence base.

One such area is the studies of early childhood experiences and what Hayes and Glouberman refer to as the “biological embedding of life experience” (Hayes and Glouberman 1999). Ample evidence (Hertzman and Weins 1996; Wadsworth 1997) points to the lifelong impact on health of experiences of the child during important developmental phases. Material conditions for child and family, generally measured as socioeconomic status (SES), have been shown to affect life outcomes independent of disease. “Gradients in health status are mirrored in gradients of socioeconomic status, and relative material equity [has] a substantial influence on both the slope of health gradients and overall health status rankings” (Hayes and Glouberman 1999).

Research into work and working conditions is another area contributing to the evidence base. Physical exposures at the worksite that lead to disease have been shown to be mediated by social environments, for example, lack of control over the worksite (Marmot et al. 1991). Finally, research on social networks and support systems has been an important area of contribution. Connections to family, friends, and community are strongly related to health status (Heaney and Israel 2002), and social cohesion appears to be an important aspect of sociobiological translation of experience into health outcomes.

Over time, studies in these and related areas have suggested that the social and physical environments may have a far stronger impact on important aspects of health than do individual behaviors, and, at minimum, shape the individual behaviors associated with disease (Haan et al. 1989). Figure 2 illustrates the upstream and downstream determinants of health (Kaplan 2004). Although recent population health research underscores the importance of socioeconomic factors in producing health or disease, the equivalent contribution is the recognition of the interaction of these factors with physical environments and biological phenomena. Schwartz et al. (2001) describe the complexity:

[A]lthough population level factors ultimately cause disease by affecting individuals, they do not necessarily enter the body in a simple causal chain that can be reduced to some particular individual level factor. Rather, the pathways through which characteristics of populations enter the body are likely to be numerous and interactive. Social and environmental factors, for example, determine proximity to infectious agents, influence immune status, and help shape health behaviors. Social factors interact with the specific biological and social history of the individual to shape the particular health manifestation.

They go on to note that characteristics of populations also influence definitions of health and disease. Social factors affect expectations and acceptance of conditions in a community or society as normal or not normal. These factors also influence what researchers choose to examine and how they conduct their investigations.

In summary, several concepts are integral to the population health perspective and approach to scientific inquiry. One is acknowledgment of the complexity of disease and the need to focus on the multiple determinants of health. Another is recognition that determinants interact to have a profound impact on the health of individuals and communities. Yet another is
the determining role of socioeconomic factors in the health of a population; that is, health is linked to the distribution of wealth across a population. Indeed, some have ventured that advances in the biological and molecular determinants of disease are unlikely to reduce the population disease burden of socioeconomic position (Kaplan 1998). This perspective proposes that study of the biological and molecular mechanisms of disease should be viewed as complementary to and not as a substitute for a rigorous effort to understand the social, community, and policy determinants of population health (Kaplan and Lynch 1997).

National Interest in the Population Perspective
Population studies and the perspective they reflect have shaped not only research but also health policy and programs internationally, especially in North America. Health Canada (the Canadian national health authority), beginning with the Lalonde Report in 1974 (Lalonde 2002), has proposed that changes in lifestyles and social and physical environments could lead to greater improvements in health compared with further investments in existing health care delivery systems (Health Canada Online 2002). The 1986 World Health Organization’s Ottawa Charter for Health Promotion focused on the broader socioeconomic and environmental factors that affect health. The determinants specifically discussed included income level, education, and the physical environment where one lives and works as important influences on health. The U.S. Department of Health and Human Services through its Healthy People 2010 Objectives (2000) has set as the second of two overall national goals the elimination of disparities in health status among subgroups of the population, namely, racial and ethnic minority groups, women, people with low incomes, people with disabilities, and specific age groups (i.e., children, adolescents, the elderly). Figure 3 illustrates the strong interest of the U.S. Department of Health and Human Services in the population approach.

Several research and programmatic strategies have been natural outgrowths of the population health perspective. The most obvious is the shift to examination of health in populations rather than individuals and determination of risk for the collective rather than a single subject. As Rose (1992) has framed the problem, the task is the study of characteristics of populations not individuals. This idea is not easy to apply and has triggered significant debate among epidemiologists (Hochstim 1970). An oversimplification of the proposition is that cause of disease may not be a matter of averaging individual cases across a population but rather may rest in the relationship between determinants, in other words, seeking the relationship between wholes and parts (Schwartz et al. 2001). Further, remedies targeted at subpopulations (e.g., a high-risk group) may be inadequate...
(Rose 1992). At least one study has shown, for example, that only one-third of myocardial infarctions over a 5-year period actually occurred in those with high levels of risk factors. Two-thirds occurred in those at low risk. Such data have led some population health experts to conclude that "broad, community based approaches that address the entire population may be most effective in reducing the population burden of many diseases” (Rose 1992). Achieving this shift requires great care in developing research strategies that can reveal causes at levels of organization other than the individual level (Schwartz et al. 2001) and discovering means of intervention that do not simply widen the gap between the healthy and the ill, the rich and the poor.

Another strategy emerging from the population perspective is engagement of the public in the investigation of health problems and their resolution. This strategy accepts that disparities in health status—largely emanating from socioeconomic differences—are best understood by the people who experience the greatest illness burden. They therefore constitute a major resource for guiding examination of the circumstances and events that influence health outcomes. Fostering public participation in setting the research agenda operates on the premise that energy, skills, and intimate understanding of what produces health or disease can be mobilized into national efforts to improve health. The term “participatory action research” is most often used for this construct, and it has been identified by the Institute of Medicine as a guiding principle of public health in the 21st century (Institute of Medicine 2002, 2003).

A third strategy is conscious investigation and amelioration of injustices in distribution of wealth that give rise to the many disparities observed in the health of subpopulations. The arena of work often labeled environmental justice is an application of this principle. Such research includes examination of the particular health risks and health outcomes for populations that are economically vulnerable and therefore are more likely to live in physical environments that increase their exposure to potential health hazards or experience other daily assaults that affect their well-being.

The evolution of the population health perspective and resulting research and programmatic approaches have led to exciting and often controversial undertakings over the past decade. The National Institute of Environmental Health Sciences (NIEHS) during Ken Olden’s administration emerged as a leader in population health explorations that often entailed considerable risk and, when successful, the promise of significant payoff for the public’s health.

Population Health at NIEHS in the Olden Years

Before the advent of leaders such as Ken Olden, the National Institutes of Health focused almost exclusively on the cellular, molecular, and (subsequently) genetic aspects of scientific inquiry. During the Olden years, NIEHS entered the forefront of organizations exploring the possibilities and challenges offered by the population health approach to research. In addition to the ongoing commitment of NIEHS to excellence, Ken Olden led the institute toward new ways of understanding the research mission. He acknowledged and spoke eloquently of the need to translate basic findings into usable technology and policy. He recognized the importance of and encouraged the communication of findings so that informed decisions could be made for the public good. He established initiatives and programs that reached out to all stakeholders in resolving environmental health problems, including local communities, and encouraged links between communities and resources of research institutions and the NIEHS. He traveled the country to hold town meetings designed to engage communities in understanding and resolving their own health problems.

NIEHS Initiatives

In various ways, principles and perspectives of population health have been reflected in work sponsored by the NIEHS in the past decade. Studies have addressed the biological and chemical determinants of health within the wider context of other contributing variables. Some investigations have focused directly on environmental equity, and others have focused on engaging the public in environmentally directed investigations. Some have been completed and have already added to the evidence base for program and policy. Others are under way and hold promise. Together, they represent the continuum of basic research through application of research findings in medicine, regulatory decision making, and public health practice. They are primarily projects of the Division of Extramural Research and Training. A brief summary of a few exemplary projects in priority areas in which the NIEHS has been the sole funder or a major collaborator in funding emphasizes that population health and its
focus on multilevel deterrence of disease received serious consideration in the Olden years.

Cancer Prevention

Until work by NIEHS grantee Gerald Wogan (Croy et al. 1980), the study of the role of aflatoxin B₁ in the development of liver cancer was hindered by inadequate data on intake, excretion, and metabolism of aflatoxin in humans. The role of potential underlying factors, including diet and exposure to hepatitis viruses, was also unknown, and data were lacking on cancer morbidity and mortality. Wogan’s animal studies gave rise to work by Groopman and Kensler (1999) and the development of biomarker technology to assess exposure. Applying these biomarkers to human populations showed the strong interaction between hepatitis B virus exposure and aflatoxin in the development of liver cancer. People both positive for the virus and exposed to the agent are 60 times more likely to develop liver cancer than those unexposed. This work led in turn to an examination of intervention strategies. A good example is the prophylactic use of chlorophyllin dietary supplements (Wang et al. 2001). Trials in China where chlorophyllin is available inexpensively over the counter suggested that the strategy is promising and comprises an approach that is public health efficacious, across the population, and cost effective for reducing liver cancers in exposed populations.

A new NIEHS study pursuing cancer prevention demonstrates the magnitude of work often necessitated by population approaches. The Sister Study is examining prospectively the environmental and familial risk factors for breast cancer and other diseases in a cohort of 50,000 sisters of women who have had breast cancer. These healthy sisters have approximately twice the risk of developing breast cancer as other women. The study design allows assessment of exposures before the onset of disease and creates the basis for testing new hypotheses as they emerge. The cohort will be followed for 10 years and provide annual information on each woman, including medical history and changes in exposures. Just over 300 new cases of breast cancer are expected to occur in the cohort each year, producing 1,500 cases by the end of the follow-up period. Analyses will assess the independent and combined effects of environmental exposure, genetic polymorphisms, and other factors such as response to exposure. Additional risk factors—smoking, occupational exposure, alcohol, and diet—will be monitored through a range of biological, chemical, and psychological measurements. The results are expected to significantly increase understanding of the multiple factors interacting to put women at risk of breast cancer.

Heart Disease

Most studies of air pollution focus on the lung. However, in the 1970s NIEHS-supported researchers began a 15-year prospective study of > 8,000 people in six U.S. cities (Dockery et al. 1993). The shorter life expectancy found among subjects living in more polluted areas was attributable primarily to cardiopulmonary causes. In subsequent work, associations were noted between small particulate matter in the air and hospital admissions, cardiovascular mortality, and increased frequency of defibrillator discharge (Peters et al. 2000; Samet et al. 2000). Further, certain subgroups of the population were shown to be at particular risk, for example, the elderly and those with pre-existing medical conditions. The discovery of the relationship between cardiovascular disease and the toxic effects of small particulate matter in the air has had significant import for standard setting and for air quality research.

Asthma

Asthma has been on the rise worldwide for more than a quarter century, and the role of air pollution in asthma exacerbations has been a focus of NIEHS research. Increases in the number of symptoms, hospitalizations, and deaths from asthma related to air quality have been noted, particularly for the elderly and children. The problem of asthma in children is especially troublesome. Among the chronic diseases, it is the leading cause of school absenteeism and also causes millions of lost work hours each year for parents who must care for sick children. The direct and indirect monetary costs associated with the disease are staggering. Recent work by NIEHS-funded investigators has illustrated the importance of clean air for controlling asthma. For example, > 3,500 children with no previous history of asthma were studied (McConnell et al. 2002). Over a 5-year period, those who were very active in sports in areas with high ozone concentrations were > 3 times as likely to develop asthma as children who did not play sports. Findings support the idea that ensuring clear air for all could derive special benefits for vulnerable groups.
LEAD POISONING
Lead was once a ubiquitous agent of illness, and efforts to reduce its presence in gasoline, paint, and other consumer products have been accelerated by NIEHS-sponsored researchers. A growing body of work over time has shown that levels once considered nontoxic (e.g., < 20 µg/dL blood level) could, in fact, produce significant health problems for children (Needleman et al. 1972). Children with levels < 10 µg/dL have been shown to have reduced IQ scores. In other words, lead exposure even at low levels can produce behavioral and cognitive deficits. Some populations are particularly vulnerable. For example, lead has been found more frequently in homes in low-income communities. Findings from this body of research led U.S. agencies to set more stringent national regulations for reductions in lead content in paint, gasoline, water pipes, and canned foods. The contextual implications of a drop in blood lead levels in American children are many. The Centers for Disease Control and Prevention (CDC) estimates that reductions in blood lead levels not only increase the wage-earning potential of a child as an adult by increasing cognitive functioning but also reduce the risk of high blood pressure and kidney disease in adults.

NIEHS-sponsored research has also examined the effectiveness of potential interventions for reducing effects of lead poisoning. Rogan and colleagues (Dietrich et al. 2004), for example, evaluated chelation therapy with succimer in children 1–3 years of age to determine the neurodevelopmental benefits when the children reached 7 years of age. They found that the therapy lowered average blood lead levels for approximately 6 months but produced no cognitive, behavioral, or neuromotor outcomes. These findings underscored growing acceptance of the need to take environmental precautions to preclude lead exposure.

HEALTH DISPARITIES
In the past decade in concert with the National Cancer Institute, the National Institute on Aging, and the Office of Behavioral and Social Science Research, the NIEHS engaged in funding a new generation of research centers designed to conduct cutting-edge research into the differences in health outcomes, access, and care across populations. The Centers for Population Health and Health Disparities are employing community-based research approaches involving community stakeholders in the planning and implementation of research. The centers are addressing some of the nation’s priority health problems for which data show significant differences in health outcome for subgroups of the population.

For example, Wright and her colleagues at the Channing Laboratory center in Boston, Massachusetts (Wright et al. 2004b), examined exposure to violence and the levels of asthma in children living in low-income urban neighborhoods. They found that greater exposure to violence was independently associated with asthma morbidity after simultaneous adjustment for SES, housing problems, and other adverse life events. Keeping children indoors, thereby presumably increasing their exposure to airborne allergens and increasing their sensitization, was one of the mediators of the exposure to violence and asthma relationship. These researchers also found that higher stress levels for caregivers of younger children were associated with higher total immunoglobulin E levels in the children (Wright et al. 2004a).

The Johns Hopkins center in Baltimore, Maryland, has examined multilevel determinants of cognitive decline in residents 50–70 years old in selected neighborhoods in the city (Schwartz et al. 2004). These studies have shown large and statistically significant differences in neurobehavioral test scores on the basis of race and ethnicity, with African American scores lower than those for whites. Significant differences remained after controlling for individual SES, health-related behaviors and health conditions, and blood lead levels. The collective findings from the centers are expected to shed light on important predictors and characteristics of disparities among those in vulnerable populations compared with the general public.

CHILDREN’S HEALTH
The NIEHS is now collaborating with the U.S. Environmental Protection Agency (U.S. EPA) and the CDC to establish centers that combine basic and applied research to focus on the health of children. Centers engage in both laboratory research projects and community intervention studies. The approaches used by the centers draw heavily on principles of population health. For example, the University of Michigan center (Schulz et al. 2002) has posited the focus of population health on intermediate factors such as limiting the number or size of industrial waste facilities and ensuring enforcement of regulations limiting noxious emissions in or near neighborhoods with high concentrations of poverty can affect health outcomes for vulnerable groups.
including ethnic minorities. Investigators at the Johns Hopkins University center have examined effective means to eliminate triggers to asthma in low-income neighborhoods, particularly cockroach allergen abatement (Eggleston 2003). They have shown that traces of the allergen can be found throughout homes, including in bedding and clothing. Initial studies on methods to reduce the presence of such an allergen suggest that more universal abatement strategies (e.g., general housing maintenance rather than long-term drug treatment of sensitized individuals) may be a more effective community-wide, public health strategy.

**Community-Based Participatory Research**

The Institute of Medicine’s 2002 report titled *Who Will Keep the Public Healthy?* outlined the major areas of preparation for the public health workforce in the 21st century (Institute of Medicine 2002). The report earned acceptance for the concept of community-based participatory research by agreeing with population health experts that the study and resolution of deeply embedded complex health problems, especially in communities with marginal resources, require full involvement of the individuals and groups that experience the problem first hand. The report recommended that all public health researchers and professionals receive training in appropriate research methods and public engagement strategies that could lead to innovative, resilient, and long-term solutions. Long before the Institute of Medicine report, the NIEHS began an initiative designed to engender full public participation in environmentally focused research. This effort has shown that innovations can indeed result when the bearers of the health burden join the researchers in generating new ways to alleviate it. For example, researchers at Wake Forest University in Winston-Salem, North Carolina, have studied exposure of migrant farmworkers to pesticides (Arcury and Quandt 2003). Wipe samples in homes of farmworkers revealed the presence of agricultural pesticides (oxyfluorfen and chlorpyrifos). Urine samples of residents indicated that traces of agricultural pesticides (oxyfluorfen and chlorpyrifos) may be a more effective intervention with specific education for parents and children. Researchers evaluated morbidity in low-income urban children who did or did not receive home environmental assessments followed by visits from a community health worker. They found that children who received the full complement of services had fewer asthma symptoms and higher scores on a quality of life index. In addition, on the basis of the results of environmental assessment, their homes were significantly less likely to exhibit potential triggers to asthma symptoms than those of children who received a low-intensity form of intervention. Work by this group is extending to the examination of combinations of home environment intervention with specific education for families on self-management of asthma.

**Environmental Justice**

As noted previously, a tenet emerging from population health research is that more equitable distribution of income and greater equity in the environmental and social advantages that SES confers will lead to community-wide improvements in health. The environmental justice program established by the NIEHS has had a long-term goal of enhancing environmental conditions by enabling community-based organizations to form viable partnerships with the research community. Such partnerships are to derive information that is current and salient for influencing policy. The goals of the grantees in the environmental justice program are to create public awareness, educate the community about environmental hazards, provide the means to detect health problems in the home, provide internships and courses in environmental justice, and create a network of resources for accomplishing these tasks. For example, researchers at San Francisco State University (Morello-Frosch et al. 2002) created a community-academic research collaborative in southern California to utilize recent advances in air emissions inventories and air exposure modeling data. They showed that communities...
of color bear a disproportionate burden in the location of treatment, storage, and disposal facilities and Toxic Release Inventory facilities. Longitudinal analyses of their data also suggested that facility siting in these communities, and not the market-based “minority move-in” explanation, accounted for the disparities observed. This research collaborative also investigated the health risks associated with outdoor toxin exposure from both mobile and stationary sources and found that race plays an explanatory role in predicting cancer risk distributions among populations even after controlling for other socioeconomic and demographic indicators. Such work has implications for both policy formation and future research into the origins of environmental inequality.

A Decade of Accomplishment

On Ken Olden’s watch, the NIEHS made significant and salient contributions to population health research, and his leadership was characterized by an openness and willingness to explore ideas that could include the unconventional to the unusual to the unpopular. His admonition, always, was to conduct the best scientific investigations possible and not to forget the potential for the findings to have an impact on the health of the public. Translation, communication, and involvement were characteristics of his discussions with the research community. Several topics received his special attention, and important studies likely would have fallen by the wayside had he not championed them. The Sisters Study is a fine example of how his commitment and persistence brought a complicated and highly promising endeavor to fruition. His interest in the possibility that lead chelation using succimer in children with moderate blood lead levels could reduce cognitive impairment led to completion of a long-term, risky undertaking. His influence in ensuring NIEHS supported work on uterine fibroids was instrumental in extramural population studies as well as in intramural investigations of relative risk for African Americans and whites.

The future research needs in population health are considerable. As noted by Kaplan and Lynch (1999), it is important to elaborate the causal pathways linking upstream social and economic policies to the emergence of environmental and other risk factors. It is important as well to move beyond the mindset that proximal and individual solutions are preferred for the resolution of public health problems. More upstream measures that affect policy and environmental controls may have much greater and wider impact on collective health.

Additionally, mobilization and involvement of communities in the scientific endeavor could be central to the understanding of critical health problems, participation in studies, and advocacy for needed change. Ken Olden’s leadership at the NIEHS helped create a foundation for research that moves us closer to understanding how to achieve optimum health for all Americans and resolve disparities that hinder our national advancement.

Summary

Environmental health science is an increasingly complex arena for research. To adequately examine problems extant in human populations and uncover potential solutions, researchers are integrating their findings from epidemiology and the social and behavioral sciences with biologically and chemically focused studies. Evidence increasingly shows that single-factor approaches have serious limitations for recognizing multicausal mechanisms. It is possible that social and physical environments more strongly impact important aspects of the health of a population than do individual behavior and factors and, at a minimum, can shape individual behaviors associated with disease. Further, socioeconomic factors are recognized as the major contributor to health disparities between populations. Health authorities worldwide have adopted a population perspective on developing programs and policies as well as exploring the resolution of these disparities. In a variety of ways, principles of and perspectives on population health reflect the work sponsored by the National Institutes of Environmental Health Sciences and encouraged by Ken Olden during his years as director. Population approaches to the prevention of cancer, heart disease, asthma, and lead poisoning are evident. Focus on environmental justice and community-based participatory research have evolved as important concepts. doi:10.1289/ehp.7644 available via http://dx.doi.org/

Notes

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