The current generation of children in many countries have a shorter life expectancy than their parents’ generation, mainly due to changes in public health policies. Specifically, we suggest there is a link between the continuing emphasis in biomedical research on individualized, therapeutic solutions to human disease and the increased reliance on individual choice in response to environmental and/or public health threats. We suggest that continued research emphasis on these traditional approaches to the exclusion of other approaches will impede the discovery of important breakthroughs in human health research necessary to understand the emerging diseases of today. We recommend redirecting research programs to interdisciplinary and population-focused research that would support a systems approach to fully identifying the environmental factors that contribute to disease burden. Such an approach would be able to address the interactions between the social, ecological, and physical aspects of our environment and explicitly include these in the evaluation and management of health risks from environmental exposures. 

Key words: public health, risk assessment, systems biology. Environ Health Perspect 115:1261–1263 (2007). doi:10.1289/ehp.10373 available via http://dx.doi.org/ [Online 28 June 2007]

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The Forest for the Trees: A Systems Approach to Human Health Research

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We explore the relationship between current research directions in human health and environmental and public health policy. Specifically, we suggest there is a link between the continuing emphasis in biomedical research on individualized, therapeutic solutions to human disease and the increased reliance on individual choice in response to environmental and/or public health threats. We suggest that continued research emphasis on these traditional approaches to the exclusion of other approaches will impede the discovery of important breakthroughs in human health research necessary to understand the emerging diseases of today. We recommend redirecting research programs to interdisciplinary and population-focused research that would support a systems approach to fully identifying the environmental factors that contribute to disease burden. Such an approach would be able to address the interactions between the social, ecological, and physical aspects of our environment and explicitly include these in the evaluation and management of health risks from environmental exposures. Key words: public health, risk assessment, systems biology. Environ Health Perspect 115:1261–1263 (2007). doi:10.1289/ehp.10373 available via http://dx.doi.org/ [Online 28 June 2007]

The current generation of children in many countries have a shorter life expectancy than their parents’ generation, mainly due to changes in public health policies. Specifically, we suggest there is a link between the continuing emphasis in biomedical research on individualized, therapeutic solutions to human disease and the increased reliance on individual choice in response to environmental and/or public health threats. We suggest that continued research emphasis on these traditional approaches to the exclusion of other approaches will impede the discovery of important breakthroughs in human health research necessary to understand the emerging diseases of today. We recommend redirecting research programs to interdisciplinary and population-focused research that would support a systems approach to fully identifying the environmental factors that contribute to disease burden. Such an approach would be able to address the interactions between the social, ecological, and physical aspects of our environment and explicitly include these in the evaluation and management of health risks from environmental exposures.
starvation, outweighing the risk posed by MeHg (McMichael and Butler 2005; Passos et al. 2003; Tuomisto et al. 2004). Furthermore, the suggestion that simply altering patterns of fish consumption is a viable solution neglects systemwide effects on resource depletion, pollution, and environmental destruction from overfishing (Sala and Knowlton 2006). This example suggests that, by not taking into account social and economic forces, our focus on personal choice and therapeutic fixes is failing to provide long-term solutions and is inadequate for protecting a large fraction of the global population. Alternatively, could we improve our health through a more integrated examination of the primary causes behind environmentally mediated diseases?

Our reliance on carbon-based energy, particularly coal-fired power plants, accounts for two-thirds of mercury emissions globally (Pacyna et al. 2006), making this the major determinant of MeHg in the global ecosystem, and hence the major determinant of MeHg in the fish we eat. In addition to mercury contamination, carbon-based energy increases our exposure to several air pollutants linked to increases in both immune-based diseases and cardiovascular diseases (Luke et al. 2006). Furthermore, carbon-based energy is the key determinant of global climate change with far-reaching impacts on infectious diseases, malnutrition, freshwater supplies, and heat-related mortality (McMichael et al. 2006; Patz et al. 2005). Finally, carbon-based energy is a key driver in the planning and development of our built environment, which is linked to a host of emergent diseases related to decreased physical activity and the obesity epidemic (Corburn 2004; Saelens et al. 2003). This suggests that a health policy that addresses risks associated with carbon-based energy may be much more effective for reducing disease worldwide than current recommendations of altering fish consumption. In addition, this example clearly highlights the inadequacy of the single chemical exposure/single endpoint risk assessment to develop robust health policies. To effectively evaluate the relative importance of proximal and distal upstream factors affecting environmentally mediated diseases and to compare the downstream effects of possible solutions, we propose a systems approach to health assessment that specifically evaluates the linkages between our societal choices, our environment, and our health.

Currently, growth of systems-based approaches in health research is most evident at the molecular level, with an increased collaboration between molecular biologists and computer modelers (Ideker 2004; Kritikou et al. 2006). Though the overall concept originates in physiology and is far from novel, the present goal of these methods is progression to a cellular-level systems understanding, then to the organ level, and eventually to the organism level (Kitano 2002), building networks of interactions between molecules, cells, tissues, and organs to form a predictive view of an individual organism (Figure 1). Predicting molecular-level processes, taking advantage of high-throughput technologies developed at the molecular level (chIP on chip, microarrays, proteomics), is clearly a rich area in current human health research. Although it is evident that this research is having critical impacts on defining therapeutic solutions to disease by identifying specific genetic components and/or molecular targets, these bottom-up approaches minimize complex environmental influences as determinants of health. Progression of systems biology will depend on the parallel development of top-down approaches, to identify essential environmental systems, link components within these systems, and quantitate impacts on human health (Figure 2).

The framework proposed in Figure 2 incorporates levels of organization beyond the individual, including effects of the social environment, the ecosystem environment, the

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**Figure 1.** Systems biology framework for the individual. Current systems biology methodologies take advantage of high-throughput data generated at the molecular level in the hope of one day translating these maps of molecular interactions into cellular-level responses, then intercellular responses, and finally to an organ-level response. The interconnections between organ systems will need to be elucidated to understand an organism-level system.

**Figure 2.** Interaction network between our environment and our health. Human health is determined not only by various molecular, cellular, and organ system–level systems, but by our environment, including social (all interaction within our species), ecosystem (all interactions with other life on earth), physical (all interactions with nonliving components of the earth), and extraterrestrial (planetary position, energy from sun, gravity). Arrows indicate major highways of interaction determining potential routes of global or local changes within these systems. All systems have the potential to affect the individual’s health status.

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physical environment, and the extraterrestrial environment, all of which play a central role in the health of the individual human being. Within this proposed framework, the social environment includes all aspects of interaction within our species (e.g., government and politics, economy, industry, built environment, community, family), whereas the ecosystem environment includes interactions with all other forms of life on earth. Most important, our ecosystem is our food supply, but it also serves as a reservoir for vectors of infectious diseases, and is the source of numerous therapeutic interventions. Our physical environment includes all nonliving aspects of the earth, such as water, air, mineral, climate, natural disasters, and previously living organisms (e.g., coal).

Finally, extraterrestrial environmental factors include all planetary effects, such as sunlight and gravity, which alters health directly (e.g., skin cancer), or indirectly through interaction with physical-, ecosystem-, and social-system-level effects. This figure is intended to highlight the importance of interactions between these three environmental systems in determining the health status of an individual.

The fundamental challenge for implementation of this approach will be the integration of computational biology, evolutionary, and ecosystem-based approaches, found at the intersection of more traditional mathematics and biology departments, into biomedical and public health research, as others have noted (Koopman and Lynch 1999; Levins and Lopez 1999; McMichael 1999). The use of health impact assessments in community design and public policy evaluation is an example of an initial step toward implementing a systems approach to human health (Cole et al. 2005), yet more widespread use and subsequent further development of this approach is needed. For example, the application of network theory in biology and economics will need to move beyond genomic systems and profit/loss, respectively, to incorporate environmental networks. In addition, temporal aspects of network relationships, on the geological, evolutionary, and generational scale, are an important component that must be addressed to create sustainable health.

Our genome is the product of environmental pressures that have molded the genetic makeup of species throughout evolution. Our remarkable adaptability is attributed partly to our capacity to modify our environment; yet how much can we transform the environment before it is detrimental to the survival of our species? At what point will our capacity to adapt be overwhelmed by the rate at which we are changing our environment? Is it only through a fully integrated systems approach, explicitly linking research on the human system with research on the environmental system and coupled with an effective strategy of applying this research, that we can hope to make the scientifically sound and sustainable environmental decisions that are critically needed now.

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