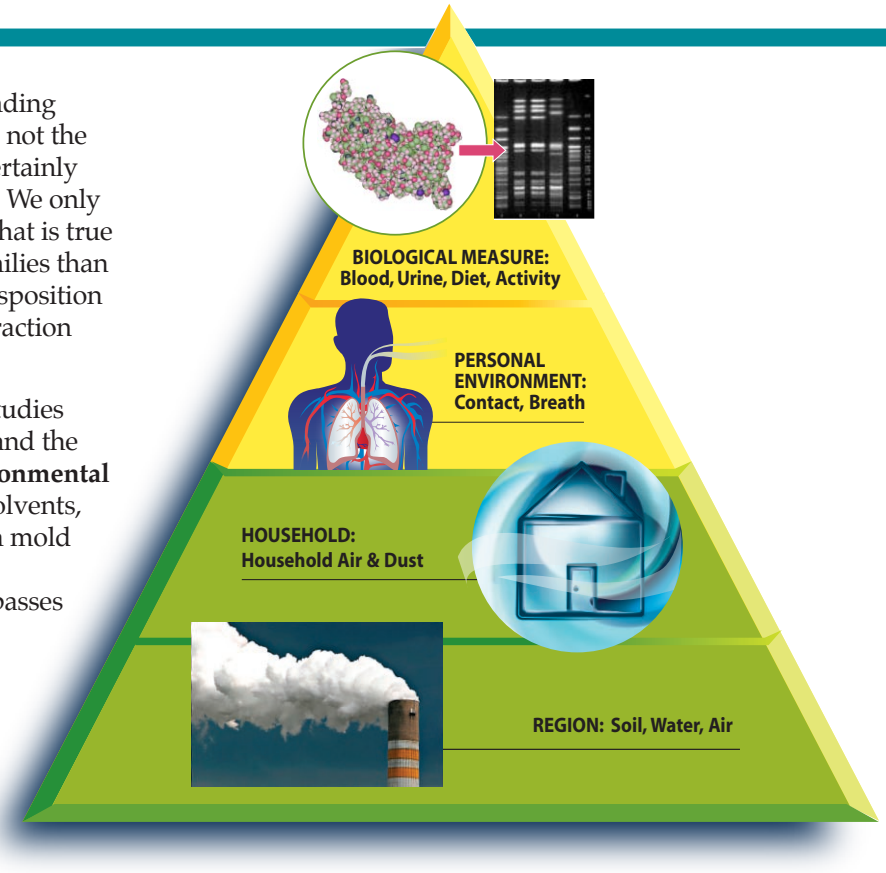
New Technology For Detecting Biological Responses to Environmental Factors

While genetics plays a major role in understanding the cause of human disease, genes alone are not the whole story. Differences in our genetic makeup certainly influence our risk of developing various illnesses. We only have to look at family medical histories to know that is true — some diseases are clearly more common in families than in unrelated persons. But whether a genetic predisposition actually makes a person sick depends on the interaction between genes and the environment.

Environmental health is the field of science that studies how the environment influences human biology and the risk of developing disease. In this context, **"environmental exposure"** means chemicals such as metals and solvents, and biological agents such as toxins released from mold and bacteria, that are contaminants of the natural environment of air, water, and soil. It also encompasses lifestyle factors such as diet and physical activity.



For most common diseases, such as obesity, asthma, and neurodegenerative disease, environmental exposures represent an important factor contributing to the development and progression of disease. Other factors include the presence of other medical conditions or diseases, diet, activity level, and medications taken. In addition, whether an individual develops disease as a function of environmental exposure also depends on the type of exposure, the amount of the exposure, and the timing of the exposure with regard to a person's age and stage of development.

Thanks to research like the Human Genome Project, we can precisely measure genetic variability between individuals. However, right now we cannot measure exposure to environmental agents with the same precision.

Our goal is to achieve this same **precision** in measuring environmental influences and the body's response to these factors. That will allow us to link specific environmental factors to specific diseases. It will also allow us to determine how genetic susceptibility is influenced by environmental exposures.

How Do We Measure Human Exposure?

There are many ways to measure environmental exposures to humans. Most commonly, levels of specific chemical and biological agents are measured in samples of air, water, soil, and food taken from the environment where a person lives or works. Because these measurements are obtained from the regional and household environments, they do not provide accurate measures of exposure to individuals.

Sometimes exposures to humans are measured by the amount of a specific chemical, biological or dietary factor in a sample of blood or urine from the person. While these types of measures tell us how much a person was exposed to, they provide no information about how an individual is responding to a particular agent. Nor do they tell us the relative contribution of multiple dietary and lifestyle factors, and the impact of genetic variability, on the likelihood of developing disease.

Evidence suggests that the biological response to the exposure, rather than simply the exposure, is more tightly related to the ultimate impact on human health. Thus, to understand how both genes and environmental exposures affect human health, we need to develop new methods to precisely measure the **biological response** of individuals to environmental exposures.

The Time is Right for New Technology

Without more precise measures of exposure, it will be very difficult to figure out why certain people develop disease and

PO BOX 12233
Research Triangle Park, NC 27709
Phone: 919.541.3345
http://www.niehs.nih.gov/
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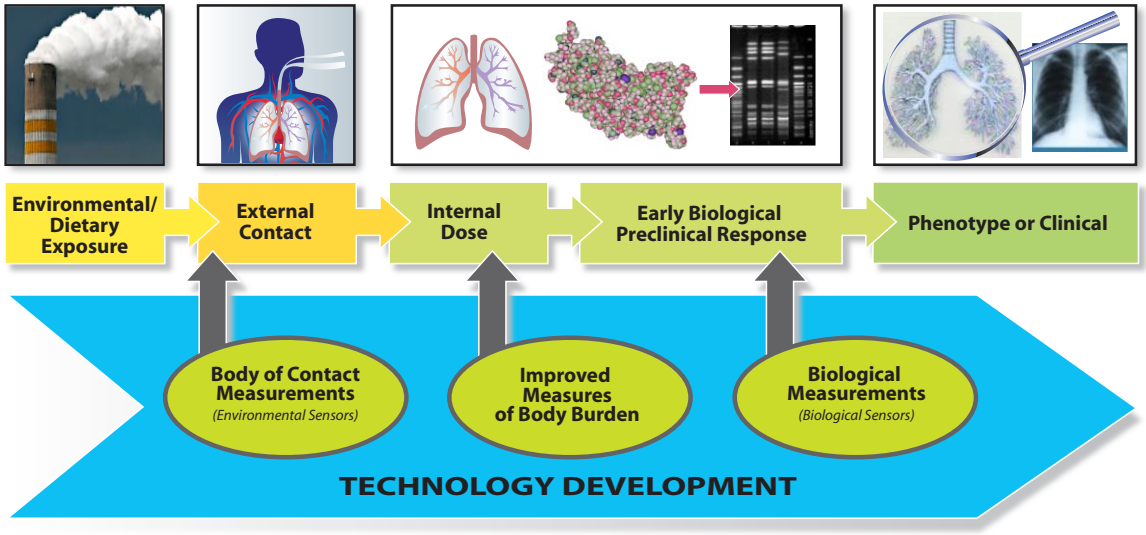
U.S. Department of Health and Human Services
National Institute of Health
National Institute of Environmental Health Services



others do not. To determine how our environment, diet, and physical activity contribute to illness, **new technologies** are needed, such as small, wearable sensors that can measure environmental agents that come in contact with the body. New devices also are needed to measure changes in human biology as a result of exposure, even when exposure occurred a long time ago.

Given the recent advances in biomedical research, this is the right time to take on this challenge. Capabilities currently exist for the global analysis of genes (genomics), gene transcripts (transciptomics), proteins (proteomics), and metabolites (metabolomics) in biological samples of blood and urine. Emerging fields, such as nanotechnology, molecular imaging, and sensor technology are beginning to yield products that can be adapted for **biomedical research**.

These emerging technologies represent important opportunities for providing new tools to measure the biological response to multiple environmental exposures while they are occurring and long after they have occurred. Ideally, these new technologies will generate measurements of **personal exposure** at multiple points in the continuum from exposure to disease. Specifically, they will provide measurements of exposures that come into contact with the body by the skin, nose or lung, and measurements of **early response** represented by disruption of biological functions that ultimately lead to disease.

Impact of Exposure Science on Human Health and Disease

Our vision is to use environmental health sciences to understand human disease and improve human health. Fundamental to this vision is the ability to quantify an individual's exposure, as well as the unique characteristics that account for individualized responses to common exposures. To achieve this, we must develop new tools for exposure science that will provide the same degree of precision that is achieved through genomic sequencing.

An important aspect of the National Institutes of Health (NIH) **Genes and Environment Initiative** will be to foster the development of improved methods for measurement of environmental exposures, diet, and levels of physical activity. This aspect will support an innovative program of technology development, with newly developed methods conducted initially in small-scale population studies, but then applied on a broader scale in large-scale population studies.

Between FY07 and FY10, the NIH will make a considerable investment in novel technologies and their application to public health and clinical practice. We expect this investment to result in the development of biological measures of environmental exposures such as pesticides, metals, and solvents, and lifestyle factors such as physical activity and dietary intake. The measures will provide early indicators of biological functions like inflammation, oxidative stress, and cell death that have been disrupted, and may result in disease.

While this will not be easy, the impact of this research on advancing **personalized exposure** assessment will be profound. In the absence of such information, it will remain difficult to evaluate the relationship between environmental exposures and human health. Deciphering the environmental and genetic risk factors for disease development and progression, specifically the interaction between environmental exposures and gene sequence differences, will enable researchers and clinicians to develop better strategies for **preventing, diagnosing, and treating disease**. Hence, the ability to develop, validate, and correlate exposure-response indicators with genetic variation will be critical to our success in reducing the burden of common diseases such as obesity, asthma, neurodegenerative diseases, and cancer.