Moving Environmental Health Forward: Insights and Opportunities

July 12–14, 2011

Strategic Planning Stakeholder Community Workshop Report

Facilitated by Dalar International Consultancy, Inc.
Raleigh, North Carolina, USA
www.dalarinternational.com

To the Participants at the NIEHS Stakeholder Community Workshop:

Please accept my deepest appreciation for your outstanding work at the Stakeholder Community Workshop that was just concluded. Thanks to your participation, we had an energetic and productive meeting. I will never forget the opening moments of the creation of our "agenda wall" in which dozens of exciting ideas were advanced for discussion! The discussions themselves were wide-ranging and informative. I heard many people comment on how much they were learning from interacting with the many different viewpoints represented in the meeting.

As we closed the meeting, we were just beginning the task of identifying strategic themes, by coalescing and aggregating all the various ideas that had been discussed and reported. During the next phase of the Strategic Planning process, our main task will be to continue the building of these themes, incorporating not only the ideas generated at the Workshop, but also the input we received from our Visionary Ideas website. The reports from the Stakeholder Community Workshop will go up on the NIEHS website for public review before the beginning of August. Later this fall, we will pull from all the collected material to create our draft mission, vision, and Strategic Goals at a smaller workshop planned for sometime in October.

It is our commitment to strive for maximum transparency during this process, so we hope you will continue to be engaged and to check for updates at our Strategic Planning website, found at http://www.niehs.nih.gov/about/od/strategicplan/index.cfm.

Again, thank you so very much for your demonstrated commitment to NIEHS and its work. I know that together, we can look forward to an exciting new era of scientific opportunity and advances in environmental health.

Linda

Linda S. Birnbaum
Ph.D., D.A.B.T., A.T.S Director,
National Institute of Environmental Health Sciences and National Toxicology Program

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Consultant's Notes

NIEHS is engaging in a strategic planning process to set the Institute's scientific and governance direction for the next five years (2012–2017). This report captures the work done during one phase of the broader year-long strategic planning process: the 2011 NIEHS Strategic Planning Stakeholder Community Workshop, that was held 1pm July 12th through 1pm July 14th at the Sheraton Imperial Hotel, Research Triangle Park, North Carolina. Information pertaining to the broader strategic planning process can be found at http://www.niehs.nih.gov/about/od/strategicplan/index.cfm. The Stakeholder Community Workshop process included identifying key stakeholders to be invited, with invitations going to a mixture of scientists, public health policy, regulatory experts, management of scientific research , communication experts , and non-scientific staff . To make the most of the time and the expertise of the people at the meeting, the strategic planning core group chose to use Open Space Technology as the meeting method, and to engage Dalar International Consultancy, Inc. to assist in planning and facilitating the meeting.

Following a formal welcome by NIEHS Director Linda Birnbaum during which she expressed her desire for truly engaged participation, the meeting began with a blank agenda wall as per the Open Space Technology method. Within one hour, the 171 participants generated 124 topics and created a very full agenda wall. The topics were assigned to specific meeting spaces and times. Breakout discussion sessions were 75 minutes long, with two sessions on Day One and four on Day Two. The person who posted the topic took the responsibility of convening the breakout discussion and of filling out a report to capture the discussion highlights and recommendations. Note that recommendations that emerged might be those of even a single person in the group, and did not require consensus to be captured. As the meeting progressed, certain topics became redundant or were grouped together by the conveners. At the end of 1 ½ days of the meeting, 97 discussion groups had taken place and submitted reports.

The meeting format for the morning of July 14th was designed to achieve the goal of clustering the 97 reports in such a way that strategic themes emerged. After reading the 97 reports, participants were given five sticky dots for voting for the reports for which they had the greatest personal energy. The reports that received the most votes became priority topics around which participants clustered the remaining reports. Thirteen clusters were formed. A participant volunteered to convene a breakout discussion for each of these emergent clusters and to create a report including discussion highlights and identification of a "recommended strategic goal." Thirteen reports were submitted from these breakouts.

The 97 reports from the July 12th/13th portion of the workshop and the 13 reports from July 14th comprise valuable information for the strategic planning process of NIEHS. These reports are included in their entirety in this document, as they were input by the convener (or their designate) of the discussion. No changes or alterations were made to any report except those made by the convener at the time of the workshop.

In a process to obtain additional data, 12 recommended strategic goals were posted for voting and participants were given another 5 sticky dots to vote on the them. (Two of the recommended strategic goals related to exposure. Only one of them was posted for voting although there is a report for both). The results of the vote are noted right on the reports. The combined output of this Stakeholder Community Workshop will be of great value to NIEHS as it moves toward the next stage of the strategic planning process in October.

The consulting team is deeply appreciative to have been in service to NIEHS and to all participants at the Community Stakeholder Strategic Planning workshop.

Birgitt Williams,
President,
Dalar International Consultancy, Inc.
www.dalarinternational.com

Reports of Discussions

Report 1: Research Intersection between Environmental Health Science and Social Determinants of Health

Convener: Jose F Cordero

Brief History:

1. It is time to expand environmental health justice to include the quantitative and qualitative measures of socials determinants of health.
2. The economic crisis is expanding the impact of social determinants of health
3. The gap between the wealthy and the poor is widening and it has a serious impact on health

Discussion Highlights:

Social determinants of health relate to medical literacy, knowledge, and access to health care.

We must go beyond the environmental justice concept and broaden it to include social determinants of health.

Examples: The built environment has a component of social determinants of health that should be consider in studies of environmental health risk factors.

Asthma: There are important difference in risk by socioeconomic and by race and ethnicity that should be clarified.

New perspectives on poverty include that is may be considered a cause of death for certain conditions.

Recommendations:

1. NIEHS should sponsor the development of a report on the impact of social determinants of health on environmental health.
2. NIEHS should sponsor research at the intersection of environmental health and social determinants of health
3. NIEHS should sponsor and develop transdisciplinary centers at the intersection of environmental health and social determinants of health
4. NIEHS should sponsor mentoring of scientists on the relationship of environmental health and social determinants of health

Discussion Participants: Androphy, Bruce; Claudio, Luz; Cordero, Jose; Goulding, Gina; Hricko, Andrea; Swenberg, James; Woychik, Rick; Nolan, Martha

Report 2: Identification of pre-, peri-, and post-natal environmental factors that contribute to variation in neurodevelopmental outcomes

Convener: Geraldine Dawson, Autism Speaks

Brief History: Our understanding of the role of early developmental exposures on the developing nervous system is still extremely limited. Studies of the etiology of conditions such as autism spectrum disorder (ASD), schizophrenia, and depression, suggest that both genetic susceptibility and environmental factors contribute to risk. For example, in the case of ASD, the prevalence of this condition has increased by over 600% over the past few decades. Three sources of evidence indicate that environmental risk factors are contributing to the increased prevalence of autism: First, epidemiological studies indicate that factors such as broadening of the ASD diagnosis, diagnostic substitution, increased awareness and access to services, only account for approximately 50% of the increase in ASD prevalence. Second, numerous studies have identified several environmental risk factors, such as reproductive assistive technology, infection during pregnancy, suboptimal birth conditions and prematurity, advanced parental age, and exposure to pesticides and air pollutants, can contribute to increased risk for ASD. Third, a recent study involving a relatively large sample of identical and fraternal twins showed that the concordance rate for ASD in fraternal twins was much larger than previously reported and much larger than that in non-twin sib pairs, implicated the role of a shared prenatal environment. By identifying the specific environmental risk factors, along with the mechanism of risk, prevention of neurodevelopmental disorders and promotion of optimal outcomes is possible.

Discussion Highlights: The following challenges and scientific areas of investigation were highlighted:

1. Phenotyping: Better characterization of sub-phenotypes and more rapid and quantitative phenotyping methods that can be used in large epidemiological studies targeted to neurodevelopmental disorders; development of etiologically relevant endophenotypes that can be incorporated into broader, general population-based studies
2. Role of de novo CNVs to increased risk of neurodevelopmental disorders
3. The need for animal models for neurodevelopmental disorders
4. Effects of reproductive assistive technologies on risk for neurodevelopmental disorders
5. Influence of air pollution and other environmental contaminants on risk for neurodevelopmental disorders.
6. Family studies as a method for better understanding of environmental risk factors for neurodevelopmental disorders.
7. Epigenetic influences
8. Cross-collaborative (cross-breeding) project as a way of screening for environmental contributors to environmental risk

9. Usefulness of induced pluripotent stem cells for screening potential toxicants that may have etiological significance.

10. Need for better exposure assessment methods.

Recommendations:

1. There is a need for better characterization of sub-phenotypes among neurodevelopmental conditions, such as ASD, that can inform etiologic heterogeneity. For example, are there specific phenotypes that can be linked to specific exposures?

2. There is a need to develop etiologically relevant endophenotypes for neurodevelopmental disorders

3. Recent studies show that there is an increased rate of de novo CNVs in regions of the genome where ASD risk genes are located. There is a need to identify environmental risk factors that are contributing to the increased rates of de novo CNVs, and the biological mechanisms involved. Among the candidate environmental factors that need to be explored are reproductive assistive technologies, such as ICSI and IVF, advanced parental age, hormones, and nutrition.

4. Studies that compare the phenotypes, exposures, and rates and types of de novo CNVs in fraternal twins, identical twins, and siblings, and their parents are recommended. Such studies would provide insight into the mechanisms by which de novo CNVs may be contributing to the etiology of neurodevelopmental disorders.

5. There is a critical need to better understand the biological mechanisms/pathways that underlying neurodevelopmental disorders, such as ASD. Approaches to increasing our understanding include gene knock-out and knock-in mice, mice bred for neurodevelopmental phenotypes (e.g. social withdrawal, repetitive behaviors), systems biology approaches and pathway analysis of genetic findings, induced pluripotent stem cells, among others. Once biological mechanisms are better understood, it will be possible to study candidate environmental influences on these pathways.

6. As genomics research identifies potential biologic pathways underlying neurodevelopmental disorders, studies examining the influence of environmental influences on these pathways (eg., capitalizing on work done in the toxicogenomics, and other such initiatives) should be conducted.

7. Studies on the contribution of environmental contaminants, such as air pollution, pesticides, and others, to the etiology of neurodevelopmental disorders are needed.

8. There is a continuing need for large cohort (case-control, prospective, high risk siblings, and others) epidemiological studies that can identified the unique and combined effects of environmental risk factors and their interaction with underlying genetic susceptibility. The National Children's Study offers a unique and important opportunity to study gene-

environmental interactions and their contribution to the etiology of neurodevelopmental disorders, such as ASD, ADHD, depression, schizophrenia, intellectual disability, and so on.

9. Studies that explore the role of nutrition during the pre-conception, prenatal, and postnatal period as a contributor to variations in intellectual abilities and neurodevelopmental outcome are needed.

10. Studies are recommended that explore the role of epigenetic mechanisms in the etiological of neurodevelopmental disorders.

Discussion Participants:

Geri Dawson

Rob McConnell

Clarice Weinberg

Craig Newschaffer

William Schrader

David Armstrong

Jose Cordero

Palmer Taylor

Report 3: Moving beyond the conventional notion of "bad" substances causing disease while "safe" substances do not. Exploring how benign substances can turn specific genes on or off and looking at how these substances may have a different impact on males and females.

Convener: Virginia Ladd

Brief History: An expanding body of science is showing that the environment has many diverse effects on triggering the onset of disease in humans. Impacts on health go far beyond the conventional notion of 'bad" substances causing disease while "safe" substances do not cause disease. The field of epigenetics is demonstrating that even benign (unstudied) substances can turn on specific genes on or off. Therefore, DNA is no longer the sole determinate of disease. Other factors include epigenetics and the microbiome play a role. Nano technology is capable of delivering supposed "safe" substances directly into the cell structure.

Discussion Highlights:

Factors that may influence individual differences to an environmental trigger other than the traditional chemicals in both mice and humans are:

- Hormonal status
- Genes
- Diet – vitamin D
- Stress states
- Infection
- Aging
- Housing
- Lack of parasites- the too clean theory

Recommendations: Increased research into:

- Study of epigenetics,
- Study of untested "safe " products including substance deliver methods such as nano particles in cosmetics,
- Study of difference in male/female responses to environmental triggers,
- role of infection and stress as an environmental triggering factor in disease,

- study of the full range of potential interactions between diseases (cancer and autoimmune) and the wider range of environmental triggers we currently study, including the study of synergistic interactions among environmental factors and disease,
- study of the environmental factors in the significant increase in autoimmune diseases in the developed world.

Discussion Participants: Virginia Ladd, Gina Goulding, Richard Woychik

Report 4: What is the environment? What is the scope? Is there a box?

NIEHS as the ultimate integrative institute in the NIH and broader arena.

Fate and transport of contaminants and hazardous substances in the environment. Is it ours (NIEHS). If not, how do we coordinate on this issue with other agencies.

Convener: Victoria Seewaldt, M.D., Ed Levin, Ph.D., Heather Henry , Ph.D.

Brief History:

NIEHS has an opportunity to be an integrative force that helps people to stay healthy. The public is interested in the relationship between the environment, food, health, and wellness. There was a perception that NIEHS's scope has been too limited. The scope was on single point source pollution and disease. There was missed opportunity to broaden this perspective to integrate with cutting edge scientific discoveries and to go beyond a traditional definition of environment. Current scientific thinking finds connectiveness between how the environment impacts our health and how we as a species impact the environment. That instead of focusing on the one gene that causes cancer that many integrated "small factors" contribute to health and disease. To promote wellness requires integration between many disciplines and the community.

Discussion Highlights:

The environment is a moving target that changes as the field advances.

The goal is to be cross cutting and integrative

There was disagreement on whether the scope of how the term "environment" is defined:

> One view is that given limited resources, the focus needs to be "boxed"
>
> The second view is that the scope should be defined broadly as new scientific discoveries are made.

Information and discovery should be a synergistic two way street between NIEHS and the scientific community.

NIEHS can serve as an honest broker of information

There needs to be new methods and messaging to communicate to the public the key role of environment in health and disease.

Part of the message should be preventing disease and staying healthy.

Examples of the environment:

> Environment is multifactorial and modifiable

Exogenous factors such as air pollution, water pollution, chemicals, hormones, pesticides, endocrine disruptors.

The environment also includes psychosocial stress, nutrition, income, obesity, education.

Fetal environment, sex differences, age

Targets are health and injury as well as disease

Recommendations:

1. Promote a message of health and wellness.
2. NIEHS should be an honest broker of health and environmental information to the public, students, researchers, and the world community.
3. NIEHS should be a driver in finding solutions e.g. green chemistry, healthy lifestyle, nutrition, obesity prevention.
4. The solutions should be integrative, cross disciplinary, and forward thinking.
5. Integrating with other institutions and institutes and the community is important for finding solutions.

Discussion Participants:

Trevor Archer, Terry Collins, Barry Dellinger, Dana Dolinoy, Michael Gould, Joe Graedon, Phillip Hanawalt, Heather Henry, Paul Jung, Ed Levin, Daniel Madrigal, Cheryl Marks, Richard Mural, Karen O'Brian, Heather Patisaul, Richard Paules, James Putney, Ericka Reid, Victoria Seewaldt, Fred Tyson, Scott Williams

Report 5: Environmental/Geospatial informatics.

Convener: Marie Lynn Miranda

Brief History:

- New technologies are generating terabytes of data, as result of substantial investments by NIH and other research agencies, as well as private sector entities
- Underinvestment in methods for Data architecture and statistical and mathematical modeling – therefore unable to fully organize, architect, and analyze these data
- Abundant data from non-traditional sources such as industry, transport sector, marketing, insurance etc. is relevant to NIEHS

Discussion Highlights:

- Need perspectives from wide range of disciplines including expertise outside of health sciences (astronomers, engineers, economists, electrical engineers etc.)
    - Examples are professions that look for patterns in large datasets
- Abundant data, need improvement in computations, hardware, software and training program
- Spatial-temporal technologies can be used to construct objective estimates of exposure in prospective framework
    - These issues would be essential to Critical Developmental windows.
- Think about non-traditional sources of data- commercial sources (insurance companies, grocery stores, advertising agencies) i.e. public private partnerships- to predict behaviors, exposures, SES among other critical variables.
    - Think about sectors with overlapping interests- transport, utilities, public civil engineering, flood control etc.
    - How to sort through/take advantage of industries/sciences that may have already developed relevant methods
- Important to attend to confidentially issues
    - Start a discussion regarding different standards for commercial/industry use of data vs. public health research use.

Recommendations:

- Workshop to bring together people from different government agencies, industries/sectors as well as researchers from different disciplines.
    - Discuss what data exist, how can it be linked, how can be leveraged in support of EH research.
    - Who is looking at/exploiting large datasets?
- What are the most relevant exposures that can be characterized using environmental informatics,
    - Built environment, Air pollution, diet, physical activity
- Develop a meta-data registry with an associated wiki-like criticism system for entering, validating and sharing for QA/QC.
- Invest in the pipeline of technical staff and researchers trained in Environmental Informatics
- Invest in statistical and mathematical modeling/methods development

Discussion Participants:

Balshaw, Boyles, Bradfield, Cory-Slechta, Drew, Fargo, Fasman, London, McAllister, Miranda, Umbach, Wright.

Report 6: How Can NIEHS better Disseminate Information

Convener: John Morawetz

Brief History: There is a lack of tools available to distribute information appropriate to the community.

Discussion Highlights:

Electronic Information

-Information overload
-Access
-Credibility!
-Communication strategies
-Research focus
-Local authorities
-Plain language: 30 second sound bites
-Communication about hazards
-GIS
-"Communication-research"
    -how to package
    -evaluate effectiveness

Recommendations:

****Make It a Priority: Strategy Goal

-Training of communicator (funding)
-PR in the science communication
    -why it is relevant
    -how to use information
-Define "dissemination" of EHS information
-Add requirement for communication dissemination to grant funding/DIR
-EH Communication program
    -resources and staff
    -training to communicate with public
    -media training
    -tailor information to audience
    - link to community organizations
-Link with sister agencies, local government, union, etc.
-Role for NTP (interagency)
-Training programs (T32) to include communication science information
-"Mandate" outreach
-Capacity building to develop and communicate clear messages and how to use information
-"Go to" website on how to communicate information
-Develop resources to be ability to communicate science information in context; Internal/Extramural to NIEHS (lay summary)
-Develop surrogates (Worker training, community based = appropriate audience)

-Guidance on what is appropriate
    -guidance to researcher in developing message
    -guidance on audience to target and how that group can best receive the information
-New Tools to communicate (Tool Kits)
-Evaluate tools used
-Develop relationship with media community (local, national)
    -Questions/answers section
-EHP maximize "front" section
    -evaluate effectiveness
    -science education
    -market/pitch (news section)
        -MD offices
        -local papers

Why Topic is Important

-Fiscally-constrained times to promote continued funding: build support
-Results of research/understanding is often hard to convey
-Lack of emphasis on communication at NIEHS

Who to Involve

-Media
-Communities
-Healthcare providers (translation)
-Researchers
-Policy makers
-Health departments (WIC)
-Professional societies
-EHS educators
-Workers

Discussion Participants:

Androphy, Bruce
Austin, Joellen Harper
Edwards, Lisa
Germolec, Dori
Graedon, Joe
Haynes, Erin
Hricko, Andrea
Jung, Paul
Kostant, Amy
Lucier, George
Madrigal, Daniel
Miller, Aubrey
Miller, David
Mirer, Frank
Moore, Nuala
Morawetz, John
Nolan, Martha
O'Fallon, Liam
Reid, Ericka
Thigpen Tart, Kimberly
Wolfe, Mary

Report 7: Create a global focal point for online environmental health databases, and seek means of linking and integrating their contents.

Convener: Philip Wexler

Brief History:

Health studies that contain environmental data are scattered worldwide. The databases use disparate methods for describing exposures and doses. The research therein tends not to be well characterized and there is no overarching ontology.

Discussion Highlights:

It would be good to look at successful models, e.g. 1. NCI Cohort Consortium – a model of pooling data from disparate epidemiology studies, 2. Comparative Toxicogenomics Database -uses a controlled ontology, although there is still a need to build the exposure portion. There is a need for environmentally relevant ontologies

Recommendation:

Convene a recurring workshop to create an inventory of databases, technologies, and environmental health relevant ontologies with the goal of integrating environmental health data and making it publicly available across studies.

Seek ways to facilitate integration. This would provide an increased ability to pool data and to analyze diverse data.

Recommend the National Library of Medicine (NLM) as a focal point from which environmental health resources can be accessed. NLM already has certain structural components in place and the ultimate structures developed could become standard.

Discussion Participants: John Bucher, Allen Dearry, Stephanie Holmgren, Carolyn Mattingly, Jennifer Sass, Kristina Thayer, Philip Wexler, Deborah Winn

Report 8: Environmental Justice, Climate Justice and vulnerable and susceptible communities: How NIEHS can help build capacity towards understanding the role of the environment.

Convener: Peggy Shepard

Brief History:

Healthy People 2020's push includes understanding health disparities; understanding this is important. Recent incidents (Katrina, BP) illustrate the impacts to disadvantaged communities. Attention needs to be given to exposures due to climate change and the health impacts.

The Executive Order on EJ is being reinvigorated. The Interagency EJ Task Force that includes NIEHS represents a new opportunity to recommit and raise the visibility of vulnerable, susceptible populations and communities.

Vulnerable populations like children are more vulnerable; least studied, least protected, not included in emergency planning. Need to retain emphasis on children and early life exposures.

Recent IOM report on climate, indoor environments and human health. Indoor environments are already compromising human health

Environmental justice has fallen off NIEHS' radar significantly; was once more prominent and created the opportunity for partnerships and capacity building that has created a cadre of organizations a decade later as leaders in the environmental health advocacy and CBPR field.

Climate justice is an area of needed research that can address some EJ concerns.

Discussion Highlights:

We haven't done enough probabilistic modeling, so when disasters happen, we aren't able to make good decisions.

EJ outcomes generally lead you down a path that is policy- and politics resistant

What's the policy product, data that shows if you build houses a certain way, a certain distance from a highway, you get a tangible clinical results.

Try to identify research centers, study sections, reviewers, who value that. . . need specific RFAs;

How does the environment current impact these diseases, and then look at how climate change will affect them?

Asthma has been that disease; how has that worked so far?

Asthma is a small amount of the total impact; bigger impact is cardio-vascular.

Diseases related to climate change: asthma,

Inflammation and obesity: how does the environment modify the likelihood of becoming obese and how does being obese affect your ability to adapt to your environment?

Is no planning for research for when a Katrina happens again. What happens during recovery, to make sure children and other vulnerable populations.

EJ communities need to be more involved in research being done in their communities.

NIEHS has gotten away from community partnerships, and capacity building; and have gotten away from that, to "education and outreach." Need to get back to the original.

EJ issues at NIEHS have basically been pushed into the PEHP program (and isn't really any EJ work in there)

If you write the RFA correctly and people on study panel review it correctly, you will get more emphasis on EJ

How does a changing physical environment affect health, especially of vulnerable populations, children and disadvantaged communities.

In past, EJ research has been just documenting the problem;

Emphasis on multi-level interventions, wholistic (more CDC-sh)

Recommendations:

NIEHS should pick up IOM report thru one of its FACAs, and adopt some of the recommendations into its strategic plan.

Fund broad networks for interventions) for climate change as was done for inner-city asthma project; healthy homes model

Move away from biomedical approach to a more wholistic approach

Refocus the agency on environmental justice

- Mitigation/adaptation piece requires work on the built environment
- Use other funding sources, such as contracts

COEC cannot be optional

Do research on green retrofit, green buildings

Go beyond mechanisms of toxicology

EJ research has to move to interventions

NIEHS needs to collaborate more with other Institutes and other Federal agencies

NIEHS should have dedicated research to study what happens to vulnerable populations, children and disadvantaged communities, in climate disasters and recovery.

Modify RFA evaluation criteria. Need to get away from grants focused on "novel" approaches, but have to show impact. Not impact on the field, but impact on public health and disease. Has to be translational (not bedside type of translational).

Need to return to community-partnerships and get equity in funding between community partners and academic partners.

Create permanent mechanisms to provide funding for capacity building and engagement in disadvantaged communities.

Create a standing study section that reviews EJ/community health oriented projects, to generate sustainable community capacity to ask the right questions and translate into action.

Discussion Participants:

Barnett, Claire

Brody, Julia

Brugge, Douglas

Germolec, Dori

Gray, Kathleen

Hood, Darryl

Peden, David

Stroebel, Carol

Wilson, Sacoby

Wright, Beverly

Report 9: Human Toxicology Project

Convener: Andrew Rowan

Brief History:

Following the NRC 2007 Toxicology in the 21st Century report, a consortium of NGOs and companies was put together to promote the establishment of an international big biology project (a la the Humane Genome Project) entitled the Human Toxicology Project. Toxicology has been an observational science for many years. Adverse effects in animals following chemical exposure are extrapolated to human experience using overly simplistic methods. The use of these animal-intensive approaches prohibits the evaluation of the tens of thousands of chemicals in commerce today. Over the past several decades, new technologies have been developed that have provided new insights into the normal biology of human diseases. Our challenge is adopting these new technologies and insights and applying them to the development of new predictive toxicology and risk assessment tools. These efforts will require multidisciplinary approaches involving toxicologists, bioinformaticists, geneticists, epidemiologists and many others. The challenge is how to develop and refine the new technologies coming on-stream to move forward in the most efficient and cost-effective manner to produce a quicker, cheaper and more predictive human risk assessment.

Discussion Highlights:

Robert Rickard – the HTP Consortium (6 multinationals, two NGOs, one research institute and one university) seeks to accelerate the transformation of human risk assessment away from the low and cumbersome animal methods to a new approach based on an understanding of key pathways elucidated by a range of high-throughput assays and improved bioinformatics tools and moving away from animals. Need international coordination and then international regulatory acceptance.

Develop a set of tiered approaches with HTS as first tier followed by different biological models to add depth to available data.

Discussion of mixtures led to a suggestion that one could begin to elucidate key pathways using SiRNA approaches to knock out genes in a cell one-by-one and identify key pathways that either protect from or sensitize to a particular toxicant.

Bioinformatic needs are a particular problem. New trainees are hired away as fast as they complete their training.

It is fairly obvious how the NP would be engaged and important in this idea but how would the intramural program be engaged? The intramural “reward” system does not necessarily encourage laboratories to support this type of activity. Possibility of developing better rewards and a “translational” health function to ensure that various NIEHS sectors all contribute to vision.

Recommendations:

1. Bio-informatics will be a key need as data volume increases. Address the need for producing more bioinformatics specialists and retaining them in NIEHS.
2. Look to change organizational culture to focus attention on translating new technologies (wherever developed within NIEHS) into the growing international attention to a new approach to toxicology.
3. Establish an extra-mural funding program to help coordinate and support the elucidation of critical pathways, new assays to follow those pathways, the use of functional genetics to support pathway elucidation and assay development.
4. Encourage and ease the dissemination of data to key publics such as epidemiologists and NGOs.

Discussion Participants:

Andrew Rowan, Janice Allen, John Cidlowski, Michael DeVito, Craig Newschaffer, Jerry Phelps, Robert Rickard, James Swenberg, Jack Taylor, Ray Tice,

Report 10: Define translational research and its role in EHS

Convener: John Groopman

Brief History:

Translational research is a multidimensional set of strategies used to address the application of a spectrum of basic and applied science findings to impact human health. This work is bidirectional that informs and uses basic science findings to disease and health and the findings from disease and health studies to focus and prioritize basic science studies. NIEHS has a central role to play as a facilitator and convener of the translational research paradigm.

Discussion Highlights:

- The impact of translational research should be manifest in outcomes affecting public health policy and regulation, clinical investigations both in patient and in communities, should inform environmental medicine and have an evaluation component to assess the efficacy of these investigations. Metrics for success are also needed as a tool.

- The field of translational research in EHS is propelled by the convergence paradigm that brings the physical, engineering and life sciences together to focus on the multidisciplinary problems of EHS and help to propose alternative solutions to these problems.

- Translational research is a multidirectional continuum that spans the universe of health and integrates different types of research from basic mechanistic and applied studies to intermediate investigations to impact on health.

- This work runs across the life span. Translational research needs to capture information needs for translational efforts aimed at all stages of life, health and disease.

- There is a preeminent role for NIEHS in this work. These studies inform regulatory policy and decision making and the application of results from NTP. This work informs policy setting priorities. There is a critical need for NIEHS to engage in the broad education of state/local, government, academic, industry and other stakeholders. To achieve a research workforce with the broad perspective required for translational research, training of students in the environmental underpinnings of health and disease (both medical students and public health professionals) are critically needed.

- The economics of translational research and its impact on EH was raised as a need and the need to have these studies funded was also discussed. There are issues raised by the current state of health care economics and the structure of the health care delivery system that have profound impacts on our ability to design, test and fund translational and prevention research.

- Overall a need to expand and develop a toolkit of biomarkers for translational research needs to be developed both for national and international investigations. This work has major global

health opportunities for NIEHS since many environmental exposures are trans-border affecting the health of people at great distance from their sources.

- Translational research includes intervention research, and these interventions and prevention trials can be for individuals, high-risk groups and communities.

Recommendations:

NIEHS needs to develop and build a convening or connector group to facilitate the communication and translation of the basic, applied and population sciences to the broad needs of the EHS community (scientists, policymakers, and the public). We very much need to move beyond the ad hoc strategies that have been historically used and we should think about using the "cooperative group" model that has facilitated the translation of basic findings to drug efficacy trails. In environmental health this would be conceived to facilitate the translation of basic and applied work to human validation studies. At the same time this cooperative group would raise research opportunities for the basic and population community for further investigations. In summary, there is an evident opportunity to put an 'E' (environment) into the new National Institute for Clinical Translational Research that broadens this new endeavor beyond the bench to bedside paradigm to a bench to community structure.

Discussion Participants:

Bird, Brody, Conti, Fessler, Froines, Garantziotis, Groopman, Hall, Hanawalt, Holsapple, Howard, Leikauf, Miller R, Newton, Sandler, Sinks, Suk, Taylor, Vogt, Walker N, Woodruff, Zeldin, Thompson, Sinks

Report 11: 3D Atlas of Cell Types in the Nervous System Defined By Molecular Phenotypes and Connectivity

Convener: Jonathan D. Pollock

Brief History: Over the past ten years a large number of tools have been developed to analyzed gene expression in the nervous system. However, the functional unit of an organism is the cell and not a gene. Analysis of gene expression with these tools is not dynamic. There is a clear need to define cell types by their position, connectivity, and the genes expressed. Technology such as TRAP technology is now making possible the identification of cell types based on molecular phenotypes. Identification of cell types on the basis of molecular phenotypes provides the basis for creating tissues to screen toxicants and to examine dynamic changes that occur in cell types based on changes in expression.

Discussion Highlights:

- What resolution is needed to define a cell type in the nervous system?
- What is the best organism to use to visualize dynamic changes produces by environmental toxicants and stressor?
- Identification of conserved dynamic changes in gene expression in cell types exposed to toxicant will be useful for identifying mechanisms of action.
- Definitions of cell types provide the basis for tissue engineering that enable screening of toxicants and overcome limitations of screening tissue culture cells.
- Zebrafish is an ideal organism to combine morphological changes with changes in gene expression in defined cell types. The zebrafish is transparent where morphological changes can be imaged with syncotron computer tomography and at the same time visualized epigenetics and gene expression in defined cell types in real time.
- Developed advanced imaging methods that can probe changes in gene expression in single cells in at any level within the human brain.

Recommendations:

Create 3D atlas of cell types in the nervous system of mouse and zebrafish as baseline for measuring dynamic changes in cell types.

Develop statistical algorithms for defining cell types are needed.

Use Molecular phenotypes as standard for creating tissues from embryonic stem cells. These tissues can be used for high-through screening of toxicants.

Combining syncotron computer tomography to identify morphological changes with dynamic changes in gene expression in cell types, defined by molecular phenotype, in response to environmental insults in zebrafish.

Identify conserved dynamic changes in cell types in response to environments stressor in vivo across species.

Develop new technologies that can image changes in gene expression in defined cell types in the human brain.

NIEHS should encourage grantees to take advantage of existing molecular neuroanatomy resources.

Discussion Participants:

Bruce Androphy

David Balshaw

Marie-Francoise Chesselet

Shuk-Mei Ho

Michael Pino

Antonio Planchart

Jonathan Pollock

Report 12: Early Life Exposures (periconceptual through adolescence) leading to Later Life Impacts (child to old age) – Prevention and Interventions

Convener: Cynthia Bearer

Brief History: Why now? Several factors lead to timeliness of this topic such as: Emerging human data indicating its validity; basic science mechanisms such as epigenetics and stem cell biology, implying biological plausibility; broaden definition of environment (nutrition, stressors); recognition of critical windows of hypersensitivity during development; the recognition of susceptible responders (prior exposures leading to susceptible individual, 2 hit theory); rising incidence of diseases that have been related to childhood exposures; concept that early interventions are more effective at repair, normalization of development and/or compensation; the start of the NCS as a vehicle for such needed longitudinal studies; data on changing male reproductive function and increase in prostate cancer; data suggesting adolescent exposure leading to increase in breast cancer; cutting edge technology enabling asking these questions; technology to deal with complex systems; increasing public awareness and hence pressure to address these questions; indicators that show that US children's health falling behind that of other nations.

Discussion Highlights:

- Need computational models for complex systems.
- Various stressors/exposures – must first understand basic biology to understand impact/reaction of system to stressor
- Need to develop model systems – molecular, cellular, animal, etc. Dependent on the question being addressed.
- Must consider child-mother-father as a unit
- Biomarkers are needed of both recent and distant exposures/impacts
- Getting away from toxics: How do exposures change pathway of development (low level exposures/subtle changes in outcome)
- Need to understand what this system (early response to environment leading to change in adult) is for evolutionarily, why has it evolved?
- What biological samples do we need to store for future/collaborative/ongoing studies? What cell types? Organ tissues? Epigenetics has focused on lymphocytes, are there other potential tissues/cells? Target tissue may be impossible to access, need to identify surrogate tissues.
- Need to include genetic information into data analysis/research design.

- For biomarkers of effect, need to know mechanism to validate biomarker. Other biomarkers may be independent of mechanism and are validated in other ways, such as biomarker of exposures or biomarker of cell growth.
- Concerns were raised about disease specific research. Should we have a disease focus?
- Multi-hit hypotheses require longitudinal studies.
- Need to study the populations of progenitors and stem cells in tissues – reduction of these populations by early exposure may lead to life long impact.
- Windows of susceptibility maybe windows of opportunity (windows where intervention more effective at repair, undoing, compensation)
- Combinations of nutrients and stressors
- Is there transgenerational passage? No compelling evidence yet as requires 3rd generation (great grand kids of exposed parent). However, folate supplementation in animals results in changes in 7th generation (increased of in utero abortions)
- Balance measures of outcomes or changes with exposure assessment and exposure endpoints – what is the exposome?
- Need to define critical period of susceptibility to what type of exposure. Model of 3D space with life span, exposure/environment, gene. (See diagram). Identify critical windows for big outcomes associated with common exposures.
- Research problem is overwhelming. Need for groups of researchers informing each other and the model. How can multiple inputs be put into a common understanding?

Recommendations:

- Need exposure platforms and better methods to measure and define a complex "exposome"
- Need platforms for epigenetics
    - Measure these changes broadly
- Need better informatics for both epigenetics and exposome
- Need critical stage specific biomarkers
- More strategy around integrating studies at molecular, animal, individual and epidemiology levels. Level of complexity of issue and longitudinal nature requires structure beyond programs & centers.

- NIEHS needs to create a research strategy like the NIH Roadmap concept – integrated R01's around a common question, integrated intramural research programs
- This problem requires interdisciplinary/multidisciplinary research
- Could NIEHS convene a "like" researchers network? Working models include:
    - CGH Atlas for mutations associated with cancer
    - Children's Environmental Health Centers with yearly exchange of information meetings
    - Children's Oncology Group
    - NICHD Neonatal Research Network
    - NICHD Maternal-Fetal Medicine Research Network
- Establish cores within centers to facilitate interaction and efficiency
- Increase communication of resources (cores & services) and research results to "outsiders" of individual institutions.
- Facilitate integration of research via cores, network meetings, interinstitutional program projects, etc.

Discussion Participants:

Bearer – convener
Bernstein
Collman
Denison
Finnell
Foster
Hennig
Ho
Hollingsworth
Hubal
Johnson
Kleeberger
LaMerrill
Lawrence
Lee
LeMasters
Nicholas
Rizzo
Russ
Sills
Slikker
Worth
Zeisel
Waalkes

Report 13: Global Environmental Change and Human Health

Convener: Howard Frumkin

Brief History: This group considered macro-scale global environmental changes, including climate change, ecosystem changes, biodiversity loss, depletion of resources such as water, land, and fossil fuels, all with respect to human health. Most of the focus was on climate change.

Recommendations:

Paradigm shift

- NIEHS should orient its portfolio toward the biggest environmental contributors to the burden of disease both domestically and globally. By this measure global environmental change, including global climate change, needs to be a top priority for the Institute. The soon-to-be-released Global Burden of Disease study should help inform this targeting.
- NIEHS should balance the traditional focus on reductionist, mechanistic biomedical research with a complementary focus on synthetic, systems-based science, incorporating ecosystem ecology, earth sciences, veterinary medicine, and other fields. The One Health paradigm should be useful here.

Institutional actions

- NIEHS should take leadership within the Federal government in research on human health aspects of global environmental change. There is a pressing need for this research, and no other agency is positioned to lead it.
- NIEHS should partner with other agencies to plan, fund, and support needed research. This will help leverage both funds and scientific expertise.
- NIEHS should build a dedicated program within the Institute that would drive research on global environmental change and human health, rather than simply assign bits of this work to various existing activities.
- NIEHS should identify and utilize the expertise of existing scientific staff, but should also make a substantial investment in adding expertise in fields now under-represented, such as ecology, hydrology, modeling, and others.
- NIEHS should create a network of academic Centers of Excellence on Global Environmental Change and Human Health, akin to the Children's Environmental Health Research Centers. These Centers should be highly interdisciplinary, and funding should be long-term to assure sustainability. The Centers should focus on both research and training. NIEHS should collaborate with other agencies to co-fund these Centers.

- Similarly, NIEHS should collaborate with other agencies, such as EPA, NOAA, and the Department of the Interior, to support health components of research supported by those agencies. Efforts such as the regional networks carrying out the national climate assessment should include a health component, which NIEHS should support.

- There is a pressing need for capacity-building both within NIEHS and extramurally, both domestically and internationally. The Centers of Excellence mentioned above should place strong emphasis on training multidisciplinary scientists, and should engage in international collaboration to that end. NIEHS should utilize other existing and innovative training mechanisms to support capacity-building in global environmental change and human health.

Research priorities

- NIEHS should prioritize its research investments in global environmental change and health, since not every important topic can be covered. Focus will help assure impact. There have been several recent efforts to identify research agendas, some supported by NIEHS; these can be a starting point for priority setting.

- Key research priorities include identifying and quantifying the impacts of global environmental change on health, developing methods such as modeling and forecasting, and identifying healthy approaches to both mitigation and adaptation. Translational science in this context means a focus on practical applications of science to adaptation and mitigation measures; these deserve substantial support.

- An important part of the scientific agenda in global environmental change and human health is the development of indicators, to provide useful information about environmental factors, associated human health impacts, and trends over time. NIEHS should support the development, testing, and use of such indicators.

- As sustainability assumes a larger place on the national agenda, NIEHS should support research that will yield decision support for the healthiest approaches to sustainability.

Discussion Participants:

Balbus
Breysse
Castranio
Claudio
Conti
Gasiewicz
Gilliland
Kwok
Long
McConnell
Miller, Aubrey
Rosenthal
Schrader
Schroeder
Sen
Serabjit-Singh
Stokes
Thomas
Thompson
Zenick

Report 14: Wireless technologies to assess environmental exposures

Convener: Jonathan Pollock

Brief History: NIH initiatives such as the Exposure Biology Program have demonstrated that portable devices and widespread technologies such as cell phones worn or carried by a person can capture chemicals in the environment, portion sizes of meals, stress, and cravings for cigarettes among other data. There are limitations to the existing devices. One problem is that many devices are not sufficiently miniaturized. Another is that they be able to capture substances in the environment, but they do not collect biological specimens so biologically relevant dose levels of exposures cannot be assessed. It should be possible to collect biospecimens using miniature personal portable devices, analyze them inside the device for particular chemical substances in those biospecimens using a miniature mass spectroscopy type of technology, and transmit the results wirelessly.

Discussion Highlights: The group thought that it should be possible to collect perspiration, saliva, exhaled air from persons and other specimens or dust, ambient air, etc. into a device which would analyze it using mass spectroscopy, geocode the location, and then send the geospatial data and exposure and biological dose data to a central location. Currently the types of devices available for measuring exposure typically have to be mailed or given to the study participant who is instructed on how to use it, the participant wears or uses it for a period of time, and then the device has to be sent back and the environmental analytes measured in a central laboratory, which is expensive, requires extra effort on the part of the study participant and study staff, and, if the sample was not correctly collected or analyzed, there may be no way to re-capture the data. The obvious challenge to this idea is in miniaturizing the device to collect the air, saliva, etc. and analyze the specimens. It would work best if this new device could be built into an existing cell phone or whatever other device is currently popular (i.e., the device has to be “cool” and in vogue), which would likely enhance the likelihood that people carry the devices and would comply with providing the specimens. Efforts would have to be made to assess and minimize selection bias due to certain types of demographic groups being more or less likely to have the device, be able to, and actually use the device. Other challenges are privacy concerns people have about being tracked and making the device simple enough to help ensure high acceptability to users. It is interesting to speculate on whether one could do genotyping this way.

Recommendations: Set a goal of creating and deploying a device that would be inside a cell phone or ipod type of device which could capture saliva, perspiration, ambient, air, etc.; analyze it using mass spectroscopy; geocode the location; and then send the geospatial data and exposure data to a central location. Develop some strategies such SBIR or industry partnerships, etc. to make it happen.

Discussion Participants: Jonathan Pollack, Deborah Winn, Heather Nicholas

Report 15: Should NIEHS be a global diplomat?

Convener: Trisha Castranio

Brief History: Environmental health is a concern of global magnitude and as a leader in EHS, I believe NIEHS should direct capacity-building and research efforts to better inform our global partners.

Discussion Highlights: The consensus was to lead as diplomats (training in response, outreach and education) rather than police (policy makers) global EH issues.

Pros:

Building global EH capacity generates goodwill through collaborations with international agencies and governments. Best efforts include capacity building in education and training in record keeping, data collecting, preparation and risk management for global change.

Building intramural capacity to participate in global EH activities through partnerships with CDC, NIH, local and state agencies and establish in-house expertise on global EH issues.

Increase visibility of NIEHS

Demonstrate our commitment to global EH issues

Cons:

Global diplomacy is component of HHS mission and not directly part of NIEHS mission

Obvious resource limitation

Recommendations: For the reasons listed above, we recommend NIEHS establish itself as a leader in global EH.

Discussion Participants: Trisha Castranio, Bono Sen

Report 16: Seek means to track and provide public access to environmental health history

Convener: Philip Wexler

Brief History: Environmental health has a rich history which is often neglected, forgotten, and not adequately chronicled. It would be helpful to have a repository of such history, publicly available online.

Discussion Highlights: NIEHS' 50th anniversary will be coming up in several years. This would be an opportune moment, and opportunity for promotion, for the Institute to chronicle both its own institutional history and seek ways to more broadly connect with other attempts to capture environmental health history. Rachel Carson's *Silent Spring* can be said to have ushered in the modern day environmental movement in the US, although there are many older events and statutes throughout the world. The history of lead poisoning is a public health success stories. The tragedy of Bhopal lead to the Toxics Release Inventory. Numerous other important historical incidents such as DES, Minimata Bay and methylmercury poisoning, and Love Canal need to be kept vivid in our memories. The present and future build upon the past

Recommendations: Establish an initiative, if not formal office, within NIEHS to consider its own history, those of the environmental health movement, research accomplishments, regulatory achievements, environmental disasters, and influential scientists. Such a project could link to the Toxicology History Association and its activities.

Discussion Participants: Joellen Harper Austin, Heather Nicholas, Jerry Phelps, Philip Wexler

Report 17: Regenerative Approaches to Correcting Complex Structural Birth Defects

Convener: Richard H. Finnell

Brief History: Despite advances in environmental health sciences that include the recognition that maternal folate supplementation reduces the risks for some structural birth defects (neural tube, craniofacial and conotruncal heart defects and others), the prevalence of complex congenital abnormalities as a whole has not been substantially reduced over the last 100 years. As prevention remains imperfect, it is of potential interest to expand our focus and consider newly initiated efforts to correct-either *in utero* or post-parturition-infants born with structural abnormalities.

Discussion Highlights:

- Concept of environmentally-induced birth defects (structural) has been largely replaced with an emphasis on the developmental origin of adult diseases. For the sake of 'teratologists'/'reproductive toxicologists', it is important to expand the definition of 'birth defects' to encompass environmentally induced changes during development that potentially impact the life of the conceptus.

- As our knowledge base of the genomes of humans as well as model organisms has increased dramatically, the identification of developmental pathways have enlightened our understanding of many structural birth defects, most notably those of the neurocristopathies. It should be possible to use this emerging information to develop pre-conceptional, *in utero*, post-parturition approaches to correct developmental defects.

- Understanding developmental pathways that are critical to embryogenesis (e.g., notch, Shh, Wnt, etc.) can inform us about adult diseases.

- Are there environmental factors/stimulants that could promote *in utero* healing?

- Does *in utero* surgery to correct structural malformations such as spina bifida actually alter epigenetic markings that might have serious, adverse consequences in later life?

Recommendations:

- Need something like the Northern European model of large mother-child cohorts to study the effects of environmental exposures on birth outcomes, as well as the diseases of childhood and beyond. The newly initiated Children's Health Study goes towards meeting this need, but it needs to be larger.

- Regeneration recapitulates development. Need to learn the underlying basis/mechanisms that promote regeneration to 'heal' developmental defects, both structural and neurobehavioral. Thus it is critical to learn more about the environmental factors that impact developmental processes.

- Promote the use of model organisms with which to identify stemness factors or appropriate developmental pathways to target in efforts to promote regeneration and correcting of both structural and neurodevelopmental abnormalities.

Discussion Participants:

- Antonio Planchart
- Karin Russ
- Clarice Weinberg
- William Slikker

Report 18: Acquired DNA modification (both DNA sequence and epigenetic modifications) may provide an integrated dosimeter of environmental exposure and be a useful predictor of disease

Convener: Jack Taylor

Brief History: A central problem of environmental health science is that exposures often take place years prior to disease and do not persist in the body. DNA is one of the few molecules capable of capturing this information and this record can persist across many years and cell divisions. In addition these DNA modifications may be directly important in the etiology of disease. Rapid advances in DNA sequencing and related technologies make it possible to characterize such changes in single cells or small populations of cells. Although other Institutes are characterizing inherited variation in the genome and epigenome and modifications with disease state, they are not characterizing the induced changes that come from exposure. NIEHS can lead this effort

Discussion Highlights:

- Technologies for characterizing vast amount of genetic and epigenetic modifications are just now available opening a tremendous opportunity.

- Although it is assumed that mutations/modifications accumulate with age and exposure, this has not been directly documented.

- A number of important low hanging fruit exist that NIEHS can quickly harvest and become a leader in the field:

    What is the rate of accumulated modification in somatic stem cells?

    Do modifications increase with age (e.g. by comparing rate in young vs. old)?

    Are rates of modification tissue specific?

    Do environmental exposures affect rate of modification (e.g. comparing sun exposed vs. sun unexposed skin; dioxin exposed people vs. unexposed)?

    Are modification rates affected by inherited genotype (e.g. SNPs in DNA repair, metabolism).

    Does diet affect rate of accumulated modification?

-By investigating both sequence and epigenetic modifications (methylation, histone modification, miRNAs) we can investigate exposures that are both genotoxic and those that are not genotoxic.

Recommendations:

NIEHS should be leader in the field of acquired genetic/epigenetic somatic (stem cell) modification from exposure, diet, and aging

Patterns of modifications can be linked to environmental disease which can in turn be used to identify exposures that cause disease

RFA to gather best ideas for technologies and approach for using DNA as dosimeter

Opportunity to use both selected model systems/cell lines, animal, human populations

Environmental ENCODE project to select systems/exposures for detailed annotation

Discussion Participants: Begley, Bernstein, Hanawalt, Kemp, Shaughnessy, Williams, Zeldin, Pollock, Seewaldt, Adelman, Fargo, Others?

Report 19: Dose/Response application to Environmental Health

Convener: Cosette Serabjit-Singh

Brief History: While levels of asbestos have been measured in the environment and disease measured, there has been no dose response relationship established. Quantitation of hazards/human exposure is fundamental in risk assessment. This is recognized as a gap that NIEHS can and should address.

Discussion Highlights: Very little exposure data, either from populations or individual subjects are available. There is some occupational exposure information but is generally inadequate as there is no connection to biomarkers or physiological response. There is little or no information on exposure to or dose response for mixtures. Samples via the CDC are anticipated that will allow analysis of levels of mixture chemicals in subjects' blood.

Recommendations:

Dose

Develop/apply sensitive analytical methods to quantitate exposures in human populations to understand background levels and understand when abnormal exposures have occurred.

Response

ROC should incorporate dose/response

Translate outcomes from Tox 21/effects in model systems to quantitative exposures of human populations

Discussion Participants:

David Miller, Aubrey Miller, Mike DeVito, James Swenberg

Report 20: Systems Framework Approach to Integrate Environment, Genetics, and Temporal Susceptibility

Convener: Michael Gould; Dana Dolinoy

Brief History: Etiology of common disease is complex involving multiple low level environmental factors in combination with low penetrant genetic elements and influenced by life-stage of exposure. The NIEHS uniquely among NIH Institutes is poised to spearhead the discovery of environmental factors causing common diseases.

Discussion Highlights: It would be useful to develop a systems framework to quantitatively aggregate and model environmental factors in the context of genetics, and temporal susceptibility. The illumination of nodes and their connectivity (edges) is crucial to identifying priority environmental inputs of focus.

The enormous advancement in genetic and genomic tools has enabled and driven the successful infusion of a genetics/genomics perspective and investment across the efforts of other NIH institutes. Through a systems framework model such as proposed here, NIEHS would be poised to propagate environmental health perspectives and datasets to other institutes and agencies. In return, this will create opportunities for other groups to populate this systems framework model. This will add value to currently existing efforts.

It was discussed that a recent eWAS study utilizing NHANES data with recognized limitations in data collection and biological analyses experienced success in identifying greater than 40 environmental factors associated with disease. Information such as this can be used to populate the model and can be validated using animal models. The proposed systems framework model builds upon this early success and will extend and enhance the value towards understanding of the environment's complex contribution to health. It was also recognized that all data added to the model should undergo quality control based on accepted guidelines generated by NIEHS.

Recommendations: We recommend that a phased staging begin the development of a system framework model. This framework model will then be populated with existing environmental and genetic data, generated from animal models as well as human populations. Subsequent to initial data population, the framework will highlight important gaps can then be prioritized. This framework will continue to increase in value as more data is added can serve as a innovate guide for the environmental health research community and to translate science to public health.

This systems framework approach provides an integrated problem that would benefit from the synergistic collaboration of the three arms of NIEHS (Intramural, Extramural and NTP).

Discussion Participants: David Balshaw, Jose Cordero, Michael Fessler, Lynn Goldman, Michael Gould, James Kiley, Cheryl Marks, Patrick Mastin, Carolyn Mattingly, Craig Newschaffer, Richard Paules, Robert Sills, Raymond Tice, Fred Tyson, Thomas Vogt, Leroy Worth

Report 21: Human variability: Sources and contribution to differential susceptibility to exposures to environmental agents

Convener: Richard Denison

Brief History: Risk assessments typically rely on toxicology data derived from single exposures of single highly inbred strains of rodents to predict human risk. Yet we know the variability in both exposure and response among people is enormous, differing based on genetics, ethnicity, socioeconomic factors, health status, lifestage, nutrition, etc. A recent NAS report proposes reversing the presumption that for most exposures and endpoints there is a "safe" level below which no effect will occur, based on the concept that variability across the human population will in many or most cases swamp any safe threshold that may be seen in any individual. Our ability to directly measure genetic variability and our growing understanding of mechanisms that may account for and propagate that variability (e.g., epigenetics) makes it timely to undertake a greater effort to understand sources of variability in addition to genetics in the human population and the influence of such variability in disease incidence and susceptibility, including in specific subpopulations. Such information will aid in improving the ability of risk assessments to accurately characterize human risk.

Discussion Highlights:

- Layers of variability:
    - multiple and varied exposures (differ spatially, temporally, socially)
    - differential susceptibility
    - microbiome as newly recognized source of variability
- Need for more and better biomarker sets to reflect the full range of exposures we experience, then work back to identify specific causative agent; need biomarkers that differentiate genetic from epigenetic effects
- Fundamental lack of understanding of the 70% of variability not accounted for by genetics
- Recognition of concept of "exposome" – collective environment and exposures we experience over our lifetimes – and "responsome" – biological changes that ensue from those exposures
- What are major drivers of observed levels of variation
- Research project ideas:
    - Measuring and characterizing variability:
        - Test 20 strains of mice to characterize variation in gene expression
        - Start with agent and close variants (e.g., chemical analogs or class of chemicals such as NTP's study of perfluorinated chemicals); look at variation in response to

members of the class – might that identify a source of variability that can then be looked for across a population with differential susceptibility to that agent?

- Compare transcriptomes derived from 1000 human samples simply to characterize extent of variation beyond genetic
- Do the same with parents of triplets and the children – may have equally high statistical power to tease genetic influence away from other factors

Recommendations:

- Need to place greater priority on direct characterization of actual human variability, both generally and as seen in response to specific exposures or environments
    - Use animal studies in conjunction with human studies to provide insights into underlying mechanisms that may explain observed human variability
    - Then seek to identify such mechanisms in humans to better map sources of variability
- Look to mine data being compiled into large integrated databases for insights allowing better characterization of variability
- Seek to develop better sets of biomarkers of exposures and correlate them to types/classes of exposures, and ultimately to specific causative agents. Identify biomarkers that differentiate genetic from epigenetic effects.
- Keep an eye on ethical implications of studying human variability:
    - Avoid “blame the victim” outcomes that identify particularly sensitive individuals as outliers
    - How can studies that seek to correlate differential health status or outcomes in people to underlying differences in exposures or inherent susceptibility be conducted in a manner that doesn’t raise potential for discriminatory actions?

Discussion Participants:

Janice Allen, Claire Barnett, Christopher Bradfield, Richard Denison, Stavros Garantziotis, Dori Germolec, Erin Haynes, Elaine Hubal, Virginia Ladd, George Leikauf, Grace LeMasters, Richard Mural, Richard Paules, William Schrader, Richard Woychik

Report 22: Research translation/communication

Convener: Tracey Woodruff/Amy Kostant

Brief History: There is a need to communicate the value and goals of NIEHS, and NIEHS should be a leader in conveying simple messages about environmental chemicals and public health.

Discussion Highlights:

- NIEHS should be the leader in raising visibility of environmental chemicals as a preventable risk factor.
- Tricky to communicate uncertainty in science, risk assessment, and anything that might provoke pushback. Scientists need training and support to do this well.
- Can NIEHS do a better job providing succinct messages about environmental chemicals to become a resource for the public? Can NIEHS choose key topics for messaging and communications/public education outreach?
- Explore partnerships: interagency, stakeholders, NGOs
- Studies released one at a time – in a vacuum. It would be important to integrate results into a body of evidence.

Recommendations:

- NIEHS should have a communications strategy focused on public health outcomes, prevention and alternatives.
- NIEHS should apply or fund communications research – focus groups, polls, etc., to understand how different groups learn and perceive environmental health messages.
- NIEHS should adapt the NTP model for integrating and synthesizing research, and designate funds to apply it to extramural research. The goal is to simplify and unify messages about the knowledge and areas of action, i.e. what people should do.
- Proposal should include plans and funding for communication of outcomes and public health application, which may also include external partnerships to assist with communications.
- NIEHS should continue and increase support for community based participatory research and communication.
- Provide resources for communication across disciplines. For example, green chemistry and toxicology.
- Fund partnerships between environmental health and behavioral and social sciences to broaden usefulness of results, and to better understand how the public uses public health research
- Study the effectiveness of different communications interventions.

Discussion Participants:

Brody, Claudio, Collman, Dawson, Drew, Gray, Johnson, Kostant, Kwok, Lucier, Madrigal, Morawetz, Newschaffer, O'Brien, Rosenthal, Russ, Schroeder, Stroebel, Thigpen Tart, Wolfe, Woodruff

Report 23: Interactions of Chemical and Non-Chemical Stressors

Convener: Deborah Cory-Slechta

Brief History: Human diseases and disorders typically reflect the interactions of multiple risk factors, yet our toxicology models continue to study single chemicals in isolation from other risk factors and epidemiological studies focus on main effects. To truly understand the relationship of environmental exposures to human disease and dysfunction, we need to understand the role of the interactions of chemical exposures with other risk factors. This may result in understanding communities/individuals at greater vulnerabilities as well as interactions (factors) which may lead to mitigation of chemical effects (e.g., omega 3 fatty acids and methylmercury neurotoxicity).

Discussion Highlights: NIEHS has already begun to focus on interaction effects of multiple chemicals, but it is critical to include non-chemical stressors (e.g., stress, nutritional status, co-morbidity). This is the nexus of environmental health, as it includes vulnerability/susceptibility, mechanisms and ultimately defines a key area to apply translation strategies. Difficulties include quantification and benchmarking for some types of non-chemical stressors, but other institutes and scientific groups work on many of these problems already suggesting the need for partnership.

Recommendations: At the end of the day, this overarching need requires the resources for commitment. Begin by at least requiring assessment of sex differences not only in clinical studies but in toxicological studies as well. Consider additional NIH partnerships that include social/psychological sciences to bring these efforts into toxicological studies. Consider the transcriptome model as a mechanism to think about the intersections of chemicals and non-chemical stressors that may interact relative to any given disease/disorder.

Discussion Participants: Deborah Cory-Slechta, John Graedon, Marie-Francoise Chesselet, Mike Waalkes, Hal Zenick, Bob Wright, Nigel Walker, Dale Sandler.

Report 24: Nutritional modulation of environmental insults (or: Interplay of nutrients with toxicants to modulate health and disease)

Convener: Bernhard Hennig

Brief History:

Nutrition is currently of significant public awareness and a topic of interest to the general public (as well as to politicians). The general public and health professionals are interested in improving diet and nutrition to counteract the obesity and diabetes epidemics, etc. Some nutrients or bioactive nutrient metabolites can improve health and down-regulate the pathology of diseases.

Nutrition is a modifying parameter to modulate toxicological insults. Certain nutrients, such as high-fat diets, can amplify an environmental insult, whereas antioxidants or anti-inflammatory nutrients can buffer metabolic events associated with pathologies linked to exposure to environmental toxicants.

Discussion Highlights:

Metabolically, nutrition and toxicology share many mechanistic pathways involved in the pathology of various diseases.

There is a need to develop a metabolic platform that allows to interpret how nutrition can either increase or buffer environmental insults.

Certain diseases, such as atherosclerosis, are inflammatory diseases with pathologies progressing throughout life: thus, diet and nutrition as well as exposure to persistent environmental pollutants can interact to influence the kinetics of such inflammatory pathologies.

There is a great need to understand how nutrients interact with toxicants to modulate molecular pathways, metabolism and health/disease parameters. Animal models are needed to understand these complicated metabolic interactions; for example, the microbiome is influenced both by nutrients and environmental pollutants.

The importance of nutrition (nutritional modulation) spans across all age groups. Infants and the elderly have changing nutrient requirements. This has implications in cumulative risk assessment and risk management paradigms because nutrients can either act as stressors or buffers. Thus, diet can modify risks associated with pollutant exposure.

Data bases are needed to combine the complexity of information related to diet or nutrition, genetics, environmental exposure, etc., to risk of environmental pollutions and compromised health and disease pathologies (need to understand the significance of metabolic variations).

Nutrition fits well into aspects of research translation and community engagement activities.

Recommendations:

NIEHS is the appropriate institute to include nutritional parameters for studying disease potential of exposure to environmental pollutants. The mission of NIEHS is not limited to a particular disease or group of diseases. Also, NIEHS is interested in metabolism and whole-body effects. This is important because nutrition (nutrients), as well as environmental pollutants, can impact overall health and pathologies of numerous disease states.

Diet and nutritional interventions can be used to buffer hazardous exposure and associated risks. The question is "how can nutrition fit into the risk assessment paradigm"? This has implications for impacts on public health statements at the national and global level; nutrition includes global health.

Discussion Participants:

A. Boyles, T. Gasiewicz, D. Germolec, J. Graedon, B. Hennig, Shuk-Mei Ho, S. Holmgren, M. LaMerrill, L. Paige, M. Lee, K. McAllister, D. Shaughnessy, W. Suk, S. Zeisel

Report 25: New strategies for identifying toxicants

Convener: David Armstrong, Ed Levin, Jeanne Rizzo

Brief History: Identifying toxicants is central to the NIEHS mission. Historically this has been pursued primarily by exposing rodents to chemicals and looking for toxic effects in their tissues. This is a relatively slow and expensive process and doesn't work equally well for some tissues. For example, rodent hearts are not good models of human physiology. However the whole animal approach does have advantages in studying integrative approaches across organisms. There is a backlog of chemicals about which we know very little if any information. High Through Put Systems can advance our understanding of the biological activity of this chemicals.

Discussion Highlights:

The proposal was advanced that molecular understanding of physiology has advanced to the point where it might be feasible to start screening the molecular processes that are fundamental to life one by one with rapid, inexpensive fluorescent cellular assays.

Concern was raised that the chemicals available for high throughput screens might be only a subset of the complicated mixtures and compounds to which we are exposed.

Concern was raised that such screens should be physiologically relevant including cell-cell interactions and interactions across organ systems and validated subsequently in whole organisms. It was pointed out that genetically encoded indicators have the additional advantage that they can be transferred directly to many sentinel organisms.

The point was made that there are different rationales for screening. High Through Put Screening is suited to identifying potential toxicants. But by itself is inadequate to demonstrate the safety of any one chemical. HTS can be the first level of toxicity testing helping to direct further studies in whole animals.

Several additional new strategies for screening were mentioned briefly;

Accumulation of DNA damage assessed by whole genome sequencing;

Changes in individual microbiomes assessed by whole genome sequencing;

Use of differentiated human pluripotent stem cells in high throughput assays;

Use of fluorescently labeled brain circuits in developing zebrafish.

Recommendations:

Develop a list of the fundamental molecular processes that might be accessible to such screens.

Make cost comparison analyses of different approaches.

Integrate new molecular approaches with more traditional physiological approaches.

Whole animal research should continue to be pursued to discover additional physiological processes that are vulnerable to toxic insult that can be then modeled in further iterations of HTS.

Continue to expand the development and capacity of HTS. s

Discussion Participants: Archer, Trevor; Bucher, John; Cidlowski, John; Dellinger, Barry; Fasman, Ken; Foster, Paul; Froines, John; Goulding, Gina; Henry, Heather; Holsapple, Michael; Hughes, Claude; Kavlock, Robert; Levin, Edward; Miller, Richard; Pino, Michael; Jr. Putney, James; Rickard, Robert; Rizzo, Jeanne; Rowan, Andrew; Stokes, William; Taylor, Palmer; Umbach, David

Report 26: Developing Interventions for Environmental Disease

Convener: Peden

Brief History: While risk factors for environmental diseases and impact of environmental factors on a number of diseases are recognized, there is a significant lack of validated interventions to prevent or mitigate these risks and diseases. What approaches can be taken in this area.

Discussion Highlights:

1. What diseases/situations should be the focus for interventions?
    - **a.** Possibly focus on high prevalent diseases (CV disease, respiratory disease, reproductive diseases)
    - **b.** Focus on states of health which impact a number of diseases (e.g. obesity)
    - **c.** Focus on regions with high level pollutant exposures or fraction of exposed people
    - **d.** Identify/define susceptibility factors (pre-existing disease, age, genetics, social settings, occupation, GIS identified community risk factors)
2. What type of interventions should be considered?
    - **a.** Exposure reduction interventions (in home-air conditioning, HEPA filters, insect reduction, smoking reduction),
    - **b.** Nutritional interventions (studies improving access to and use of fresh fruits and vegetables, specific vitamin interventions, consumption of fish)
    - **c.** Pharmacologic interventions (chronic or episodic use of known and inexpensive drugs that are already available to test for prevention of environmentally induced disease events-e.g. inhaled corticosteroids, aspirin, anti-cholinergics)
    - **d.** Policy interventions (zoning, public space and school exposure restrictions, distance from roads/industry)
    - **e.** Treat exacerbations of existing disease or disease prevention?
    - **f.** Meta-analysis of existing data to improve power and reliability of outcomes
3. What are current impediments?
    - **a.** Agreement on the susceptible groups and diseases for initial focus (what is the low hanging fruit?)

b. Development of interventions to test (e.g. which dehumification device to use? Which dose of vitamins to test? Which food access maneuvers will be accepted? What specific changes in housing stock need to change?)

c. Testing specific interventions in large enough trials to make significant statements about the efficacy of the intervention?

4. Which approaches are needed?

a. Epidemiology-to identify groups at risk and review current data

b. GIS-couple with epidemiology to identify regions/populations at risk for environmental disease

c. Engineering-crucial if doing reduction interventions such as HEPA filtration, housing changes, etc.

d. Mechanistic studies-to identify susceptibility factors and pre-clinical testing of nutritional and pharmacologic interventions

e. Translational and clinical expertise and biostatsistics

f. Policy translation of research findings

Recommendations:

1. Develop a series of workshops to identify the specific environmental diseases (or health states) that should be the focus of intervention studies
2. Undertake review of current data (meta analysis) to inform study design and logistics
3. **Mechanistic studies for identification and confirmation of biological risk factors, targets of biolological interventions.**
4. **Epidemiological/GIS based studies to identify most impacted risk groups**
5. Need funding for development of specific test interventions (dosing and tox studies for drug/nutritional studies, development of devices and building interventions for exposure reduction strategies, phase I/IIa feasibility studies, field testing of behavioral/community interventions)
6. **Large scale multi-center network studies to provide high level evidence of efficacy of the tested intervention**

Discussion Participants:

Cynthia Bearer, Steve Kleeberger, Bruce Lanphear, Stephanie London, Rob McConnell, David Peden, Darryl Zeldin (apologies if anything was missed)

Report 27: Environmental Justice and Health Disparities Strategy & Grant Program

Convener: Sacoby Wilson

Brief History: NIEHS has had a significant role in addressing EJ and HD issues; however, it has lost its focus. Its commitment to investing in EJ & HD of vulnerable populations is not evident to its stakeholders.

Discussion Highlights:

1. NIEHS has the opportunity to re-focus on vulnerable communities with an emphasis on being proactive.
2. There are currently no existing Health Disparities (HD) Centers with a focus on environmental health.
    - While the National Institute of Minority Health and Health Disparities had a competitive supplement program on EH, it is ending.
    - Nothing looking at diseases with environmental etiology exists
3. Opportunity for great public health impact
4. An NIEHS EJ/HD Centers Program could have great impact for minority & vulnerable communities
5. An EJ & HD strategy should contain a focus on the following key elements:
    - Research
    - Community Education and Training
    - STEM Curriculum (Integrative Context) K-16 & Graduate
    - Transdisciplinary (engage sociologists, anthropologists, economists, etc.)
    - Capacity Building
        - Fellows
        - Community Scholars (Job Opportunities/skills development & AmeriCorp-like)
    - Pipeline
    - Cooperative agreements
6. Different grant mechanisms to support this work
    - Regional Centers

        - MSI-focused
        - Mentoring
        - Address local and regional community issues (use existing research tools, such as GIS/mapping tools)
        - Meet gaps within extant EHS Core Centers
            - Encourage researchers to do work in partnership with communities to address real EH issues of concern
            - Address data gaps with a priority on vulnerable populations
    - ViCTER/Glue grants to bring appropriate skills to bear on EJ & HD
    - Other mechanisms to build the capacity of community-centered institutions that serve environmental health disparity populations, community-based organizations, as well as promote/advance transdisciplinary research/partnerships.

7. An EJ & HD Strategy at NIEHS could:
    - Meet needs of HP 2010 & 2020
    - Facilitate/promote action on data for
        - public health impact
        - policy
        - prevention
    - Build, sustain, and nurture community-based organization capacity
    - Advance communication to vulnerable communities
8. Focus on prevention and public health at NIEHS is essential
9. Partnership building is a key issue and was a successful outcome from the past NIEHS EJ RFA.
10. There is a need to learn from and build off of the elements that worked from past & current programs. What is NIEHS currently doing in terms of HD and EJ? What is the balance in the NIEHS Portfolio??
11. Measuring and understanding impact is critical.
    - Qualitative and quantitative measures (scales & objectives)
    - Context of Social Determinants of Health

- Differential burden, exposures, risks, health outcomes (cumulative impacts)
- Identify prevention strategies.

12. Three legs of the EJ Stool
    - Environmental Hazards
    - Social Determinants of Health/psychosocial stressors
    - Access to PH resources/Interventions

Recommendations:

This group recommends that NIEHS

1. Develop a comprehensive EJ & HD strategy across the institute
2. Implement the EJ & HD strategy – develop funding opportunities that meet the critical needs:
    a. Research
    b. Community Education and Training
    c. STEM Curriculum (Integrative Context) K-16 & Graduate
    d. Transdisciplinary (engage sociologists, anthropologists, economists, etc.)
    e. Capacity Building
        i. Fellows
        ii. Community Scholars (Job Opportunities/skills development & AmeriCorp-like)
    f. Pipeline – investing in the future researchers
    g. Cooperative agreements
    h.
3. Find its niche within its mission – Act on prevention and promoting public health!
    a. Especially for vulnerable populations
    b. Consider in broad context of community development, urban planning, transportation, sustainability, etc.
4. Examine the NIEHS EJ/HD portfolio – how does it compare to other research supported by the institute. Id opportunities.

5. Focus on impacts – promote research that focuses on social determinants of health -- Differential burden, exposures, risks, health outcomes (cumulative impacts) that leads to identifying prevention strategies

6. Reflect on what has worked from past investments and build on it

Discussion Participants:

1. Sacoby Wilson (leader)
2. Beverly Wright
3. Darryl Hood
4. Peggy Shepard
5. Ericka Reid
6. Andrea Hricko
7. Rick Woychick
8. Jose Cordero
9. Lisa Edwards
10. Suk Mei Ho
11. Joellen Harper Austin
12. Liam O'Fallon (scribe)

Report 28: Clearest and Most Present Dangers from Occupational and Chemical Agents

Convener: Frank Mirer

Brief History:

It would be important to align NIEHS research portfolios and intervention activities with areas where these is likely greater public health impact of new knowledge, particularly knowledge which would inform evaluation of lower dose potency of the agent. Another driver of priority would be controversy over regulation or other public health intervention. Exposure circumstances may have become ripe for impact in recent years.

Discussion Highlights:

The convener's interest was the priority of research in particle effects, which have emerged since the mid ninety's from community studies, but which are common to air pollution, diesel particulate matter, nano technology, etc. This is an area where community studies may transfer to occupational.

The topic was poorly attended, there was limited enthusiasm for naming exposure circumstances, other. Some exposure circumstances mentioned were perfluorinated compounds, nanoparticles, naturally occurring asbestos-like fibers. The association of auto immune disorders with indoor use of pesticides and cosmetics. Increased prevalence of auto immune disorders among women may be accounted for by these exposures.

One participant suggest that prioritizing this way may not be a good method of strategic planning, because issues change over time.

Recommendations:

A better accounting for disposition of petitions to NTP for testing would be helpful. A method for petitioning to NIEHS for research consideration beyond testing could be established. Public health or regulatory impact should be better incorporated into RO1 and other research project evaluations.

Discussion Participants:

Edwards, Ladd, Long, Mirer, Nicholas, Sink (not all for entire time)

Report 29: Moving environmental Research findings to policy

Convener: Brugge

Brief History:

Why does it take so long to change policy and practice?

Discussion Highlights:

We discussed specific case examples that were both successful and not to illustrate how NIEHS, FDA, stakeholders and others can impact policy and practice.

We discussed importance of state and local initiatives and the limitations NIEHS has with respect to this level.

We discussed role NIEHS plays testifying and educating congress.

We discussed issues of territorial nature of agencies.

We discussed MOUs between agencies.

Much discussion on communication needs and challenges facing NIEHS at all facets and levels.

Recommendations:

Encourage more policy relevant research sponsored by NIEHS.

Educate investigators about what study design elements would make their research have more impact in policy circles.

Encourage more cross agency and intra-agency initiatives to impact public policy (more efficiency and less duplication of effort).

Discussion Participants: Trevor, Breysse, Brugge, Dawson, Howard, Jung, Patisaul, Nolan, Moore

Report 30: Traffic-related air pollution and human disease

Convener: Rob McConnell

Brief History: Important because:

Increasingly strong evidence that causal role in childhood respiratory disease, important unaddressed uncertainties in relationship to other health outcomes with major population impact. Near-source pollution associated with traffic proximity almost certainly different than currently regulated regional pollutants.

Common and increasing exposure, especially in developing countries, largely unregulated source pollutants, therefore potentially large public health impact might result from better understanding and development of interventions.

Discussion Highlights: Understudied outcomes, relevant pollutants, susceptibility, interactions with other exposures, mechanism, EJ implications:

There are plausible associations with multiple outcomes for which research could reduce uncertainties. Examples include neurodevelopmental outcomes such as autism, other neuroperformance outcomes; neurodegenerative outcomes such as accelerated cognitive decline, Alzheimer's disease; cardiovascular disease such as stroke, ASHD; respiratory outcomes such as lung function growth (in childhood) and decline in adult life leading to COPD, asthma in childhood and adult life; cancer, including lung, childhood leukemia, breast; perhaps metabolic disease including diabetes and obesity.

Multipollutant mixture a major challenge, both in identifying relevant chemicals and in assessing exposure. Exposure characterization of ultrafine particles, re-entrained road dust, largely understudied vapor components of the mixture are important research topics that need to be linked to toxicological study.

Potentially susceptible groups include large segments of the population, such as children, the elderly, pregnant women, the poor (for unknown reasons), some identified and likely many unidentified genetic variants.

Co-exposures may play important role in toxicity, including social factors and psychosocial stress, bioaerosols such as allergens and endotoxin, ozone.

Opportunities for mechanistic research to better understand likely causal mediators in inflammatory pathways and likely in other less well studied pathways, especially for less studied neuro outcomes.

Need to understand the distributions of these exposures to resource deprived populations that may also be more susceptible.

Implications for “healthy cities” and “smart growth” policies that promote development friendly to walking; caution is needed to mitigate increased exposure to near-traffic pollutants that may result from these policies.

Recommendations:

RFA (or series) on near-source traffic pollution?

Refinement of substantial uncertainty of association with less-studied outcomes;

Toxicity studies to identify relevant species, well integrated with better characterization of exposure markers for epidemiological studies;

Better understanding of mechanisms of effects, e.g. gene expression, epigenetic effects, linked with clinical and epidemiologic outcomes;

Better characterization of what makes people susceptible;

Interventions to reduce and mitigate exposures could be quite broad, including clinical dietary interventions (e.g. antioxidants); development and evaluation of commercial filters; urban design such as trees, barriers, partnering with traffic engineers and land use planners.

Opportunities for studies of inequities in exposure of susceptible populations could be linked to intervention studies.

Opportunities for better understanding of effects by examining exposures in other countries that are higher or have different source mixtures (ethanol, diesel, for example)

Discussion Participants:

Rob McConnell, Pat Breysse, Frank Gilliland, John Froines

Report 31: Healthy Buildings and Communities

Convener: Lisa Conti

Brief History: The impacts of anthropogenic changes to our natural world have considerable societal health effects. These effects are both at the micro and macro level leading to morbidity and mortality related to intoxications, injuries, mental health stressors and chronic diseases such as obesity and diabetes. As our population expands, we are building new developments and also need to retrofit existing infrastructure (another building boom), having opportunities to refine our designs for health promotion and resiliency rather than untoward impact.

Discussion Highlights:

General

- This topic requires systems thinking and is a One Health issue (impacts human/animal/environmental health).
- It is cost effective to be preventative and have a greener environment.
- There is a gap between human health and sustainability practices.
- There is insufficient attention paid to health effects of products; industrial pressure is overwhelming to our regulatory agencies and suppresses information dissemination.
- NIEHS has a history of Healthy Building Initiative.
- Lower income communities are likely disproportionately impacted leading to environmental justice issues.
- There is a growth in imports for building materials which may lead to increased exposure/injury due to lack of source regulations.

Micro

- Increase use of PVC is due to technical and cost preference. However, we are building an enormous store of future dioxin burden as the material is burned. There is increasing evidence of dioxin in our food supply.
- Research exists on dioxin, but information is being suppressed by industry.
- Homes and cars should be safe for children – endocrine disruptors are prevalent in our environment (e.g. flame retardants).

Macro

- We spend considerable amount of time in indoor environments.
- 10% of our national population resides in temporary structures.
- Current economy may be negatively influencing community siting (EJ) and building practices.

Recommendations for NIEHS:

1. Sponsor extramural community health evaluations on impacts of built environment.
2. Provide focus for Healthy Buildings Initiative.
3. Support intramural research on flame retardants.
4. Support integrative research on which dioxins are increasing/decreasing and why.
5. Be a model for built environment best practices.
6. Report on current economic impact on EH/built environment.

7. Emphasize scientific insight regarding healthy buildings and communities because of potential large impact on public health and our behavior of spending the majority of our day in indoor environments.
8. Continue to conduct fundamental research on the health impacts of dioxins and dioxin-like compounds with the goal to assist regulatory reform.
9. Support extramural grants to inform urban planners and architects related to disease prevention.
10. Support interagency collaboration on this topic (eg HUD, HHS/Sustainable Communities Partnerships).

Discussion Participants:

Bruce Androphy

Terrence Collins

Lisa Conti

Howard Frumkin

Andrea Hricko

Christopher Long

Heather Nicholas

Report 32: Indoor Air Quality

Convener: Patrick Breysse

Brief History:

Research and funding for indoor air quality assessments and impacts lags behind the investment in ambient air quality research. Diseases like asthma continue to rise despite improvements in ambient air quality. People spend 80-90% time indoors. Indoor environments have sources and pollutant profiles that are unique in terms of particulate matter (PM) characteristics and gas phase components.

In international settings biomass burning is an important contributor to disease burden. Two-thirds of the world's population cook with biomass and many groups are investing billions (?) of dollars in deploying new cook stove technology in the developing world without evidence that this technology will reduce exposures (PM and gas phase) to result in improvements in health.

Discussion Highlights:

- Important indoor environments include homes, schools and day care/preschool settings
- Women, children, and the elderly are disproportionally impacted
- This is an environmental justice health/disparity issue since poor, inner-city populations are at increased risk
- Indoor environments are readily modifiable and amenable to intervention
- The importance of schools, preschools, and day care environments was extensively discussed. Little information of exposures and health impacts is available.
- With respect to schools, the importance of IAQ and academic performance was noted as an important research gap
- No regulatory agency has responsibility for IAQ and this could be an important area of scientific contribution for NIEHS
- The health impact of the biological component of indoor PM (except for allergens and maybe endotoxin) is not well characterized
- Community interaction and risk communication are important components of studying IAQ
- The combined impact of indoor and ambient air pollution is not well understood
- The neurotoxic/neurodevelopmental effects of indoor exposure to combustion products from biomass burning and indoor pesticide use is not well understood

- Chemical emissions from building products are not well understood. Formaldehyde was mentioned as an example of carcinogen emitted from many building product

Recommendations (not in order):

- NIEHS should place a strategic emphasis on studying indoor air
- Intervention studies need to be conducted. Studies demonstrating the efficacy of intervention to change the environment need to be conducted prior to conducting health outcome interventions. NIEHS should partner with agencies like HUD to move these studies forward.
- Evidence base linking IAQ and school performance needs to be developed
- Evidence base linking cleaning products, IAQ and health needs to be developed. The assumption that "green cleaning" products are safer needs to be tested.
- Cooks stove pollutant toxicity studies (PM and gas phase) need to be conducted
- Health impact of "improved" cook stove technology needs to be evaluate
- The health impact of indoor air quality in poor and rural settings needs to be more actively investigated
- Policies addressing smoking in homes and multiunit dwellings need be developed
- Overall the group though that NIEHS was uniquely positioned to generate the evidence base need to stimulate policy and practice changes needed to reduce the impact of IAQ on health across many outcomes and settings

Discussion Participants:

Claire Barnett
Patrick Breysse
Paul Foster
Dori Germolec
Stephanie London
Frank Mirer
Nuala Moore
David Peden
Tom Sinks
Wendy Thomas
Robert Wright

Report 33: Novel Modeling Techniques in Environment and Health Science

Convener: Wendy Marie Thomas

Brief History:

Many terabytes of Earth's health exist at NOAA, NASA, EPA and other agencies. In the continuum of health—from planet, insect, animal, and human—the well-being of each reflects or influences another. This inextricable link of life on this planet drives the need to better merge physical and biological sciences in order to truly promote health. Reaching this level of understanding, however, is currently hampered by the vastly different modeling techniques between the sciences, ultimately creating many disconnects and gaps of knowledge. The next phase of exploration should involve novel modeling methods that merge the parameterized physical world with the non-parameterized biological world.

Discussion Highlights:

- Merging data in a thoughtful, strategic way will first require partnerships between agencies and their decision-makers. Steps are needed to erase agency-envy or mistrust, and to replace it with transparency.
- Today's fiscal climate was created from old thinking and actions. It's time to think and do differently. Revolutionizing the nexus point between health and environmental sciences requires new thinking and new actions.
- Recognize that the federal policy framework is *not* currently structured to create a purposeful exchange of information, and that a single agency can initiate a paradigm shift.
- More to the point above, the current policy framework rewards agencies that deliver findings or results, and not necessarily the ones that worked to deliver critical information (e.g., temperature, moisture, toxicant data). Creating a sustainable partnership requires addressing this obstacle to progress.
- NIEHS will need to work with other agencies to identify the areas of data intersection and to work together to develop new modeling techniques, as no one agency holds a monopoly on this knowledge.
- Recognize that human health is also a marker for planetary health, and that NIEHS should take the initiative to open channels of communication to help inform environmental science agencies on the possible implications for Earth (e.g., pollutant loads on aquatic systems, heat/cold stress on agriculture, solar radiation stress on life, etc.).

Recommendations: (to be performed in tandem)

(1) NIEHS should initiate a new paradigm of cross-agency cooperation that is built on and cultivates a spirit of genuine partnership. To reach this point NIEHS should consider the following:

- **a.** Address Congress and the Administration on the need to reward agencies that funnel key knowledge to NIEHS for research, this step will support be a visible sign of change. Cross-agency advocacy is more effective than other means of informing federal decision-makers.
- **b.** Work with NGO partners in both the health and environment disciplines, as these organizations can repeat the message to agency-leaders on the need and benefit of cooperation.
- **c.** Write MOUs and Cooperation Agreements with other agencies to open the door for information exchange, and use examples where these agreements have worked well in the past.

(2) Create focused workshop series (over a year-long period, keep it short and focused to maintain momentum and interest) on the following themes:

- **a.** Exploration of current data/data formats
- **b.** Discussion on data/data formats that are useful to environmental health information
- **c.** Investigate Artificial Intelligence and other data mining techniques that might be helpful in joining the physical and biological sciences

(3) Issue joint-agency grants in order to reach a broad audience of talented researchers. (This activity would necessarily connect agency program managers, which also helps strengthen cross-agency collaborations and understanding of data needs).

(4) Celebrate successful agency collaborations with letters of appreciation and thanks (as friends would do to acknowledge each other, and thereby deepen and continue the friendship). This step could also support the continuation of cooperation during Administration changes.

Discussion Participants: Wendy Marie Thomas

Report 34: Commensal Organisms (Microbiome) and Health

Convener: Thomas Vogt

Brief History: Ten times more bacterial DNA exists in our bodies than human DNA. In other words, there are ten times more bacterial cells than human cells in every person. The microbiome and humans have evolved together. There is increasing recognition that the microbiome influences human health, the environment influences the microbiome, and conversely the microbiome influences how we respond to the environment. Important discoveries are often made when new technologies and new concepts in biology are introduced. Study of the microbiome is at this stage and the time is ripe for the NIEHS to explore opportunities in how environmental health sciences can contribute to this field.

Discussion Highlights:

- The human body may be viewed as a scaffold for hosting a wide variety of commensal organisms (microbes, viruses, fungi, parasites).
- There are approximately 10 times more genes in the microbiome than the human genome.
- The commensal relationships are reciprocally influential along the continuum of health to disease. Commensal organisms can alter human responses (eg immune and metabolic) to their environment.
- These commensal populations are highly dynamic and therefore can be envisioned to be early and sensitive readouts of environmental exposures, conditions, and potential health effects.
- Four systems were focused on: skin, respiratory, GI, and urogenital.
- The group acknowledged that these populations are differentially influenced at each life-stage—perinatal was a key example.
- A key opportunity is that contemporary technologies are ripe for application to this field (DNA sequencing, metabolomics, proteomics, etc.) and an interdisciplinary approach is critical.
- The group recognized the microbiome poses a problem of significant complexity with respect to determining a reference dataset. Individual microbiomes are altered by nutritional status, diet, administration of antibiotics, etc.
- The microbiome is believed to represent a very appealing “sensor pad” for environmental sampling (diet/nutrition, ambient environmental conditions, toxicants, exposures, etc.)
- Humans are a particularly approachable population for this type of inquiry. Animal modeling can be leveraged for building on human studies or informing human studies.
- The microbiome is being approached by multiple institutes and groups, e.g. the NIH Microbiome Project, the Metabiome Project but not necessarily with an environmental health focus.

- Interdisciplinary skill sets across a wide range of expertise are required to advance this area: microbiology, ecology, biology, epidemiology, bioinformatics, statistics, genetics/genomics, nutrition, toxicology, etc. This opportunity clearly cuts across all divisions of the NIEHS.
- The group highlighted and real gap and the need for training in the microbiome across a variety of disciplines.
- The group felt that the biological opportunity represented a low to moderate risk with a very significant impact within the time period of the 5-year strategic plan.

Recommendations:

- NIEHS should launch a commensal organism/microbiome program.
- NIEHS should look to partner with other agencies and institutes who have existing commensal organism projects.
- An NIEHS program has significant potential in environmental surveillance and in doing so impact knowledge of the human/environment interaction and to inform policy.
- The NIEHS project has significant potential to better our understanding of the microbiome and its importance or application for prevention, intervention, and management of a variety of diseases.

Discussion Participants:

Stavros Garantziotis, Frank Gilliland, Philip Hanawalt, Bernhard Hennig, Paige Lawrence, Stephanie London, Richard Mural, Craig Newschaffer, David Peden, Jerry Phelps, Jennifer Sass, Ray Tice, David Umbach, Thomas Vogt, Clarice Weinberg, Steven Zeisel, Darryl Zeldin.

Report 35: Moving from the "cure" model to the three "P" ---Predicting, Preventing, Personalized treatment of autoimmune diseases and Cancer

Convener: Virginia Ladd

Brief History: With the human genome project there is now a platform for identifying biomarkers, studying epigenetics and the potential for personalized treatments. Focusing on the three "P'" will engage the public more and lessen the frustration with the lack of promised "Cures."

Although many gene variants are linked to autoimmune diseases, each contributes just a small percentage of overall risk. Disease occurs when many genes act together and even then genetics can't explain the entire risk, indicating that environmental factors are involved to a significant degree. The concordance of autoimmune disease in identical twins is at most 30-50%.

Discussion Highlights:

- There is a need to identify environmental triggers of autoimmune disease by expanding the realms of possible triggers to more than chemical. Other triggers, which should be explored are supposed "safe" substances, stress, hormone, viruses/infections, allergens, diet or even a too clean, parasite free gut environment.
- It is not known what role epigenetics or the microbiome play in the development of autoimmune diseases.
- Why is there a common genetic background but different expression of autoimmune diseases?
- There is a lack of consolidated efforts to coordinate and understand the mechanisms involved in autoimmune diseases and immune mediated inflammatory conditions. Understanding mechanisms may help to focus on targeted treatments.
- Understanding the timing of triggering events during development in multiple autoimmune diseases and cancer is an important research area for NIEHS to consider.
- Autoimmune and inflammatory immune mediated diseases are increasing significantly in the developed world and it is not known what synergistic interactions among environmental factors and disease are at play.
- Only 24 of the more than 130 autoimmune diseases have a good epidemiology study and this inhibits the understanding of the magnitude of the problem and makes health policy development difficult.

Recommendations:

- Epidemiology studies on autoimmune diseases for which there is none.
- Increased collaboration and consolidation among the NIEHS and the other NIH institutes studying biomarkers, epigenetics, microbiome and environmental triggers of autoimmune diseases and cancer.
- Given that environmental factors are a major component in the development of autoimmune diseases, NIEHS should be the lead Institute in the coordinating the research efforts for autoimmune diseases.
- NIEHS should take a leadership role in studying the full range of potential interactions between diseases (cancer, autoimmune disease, etc.) and the much wider Range of environmental triggers than is currently studied.
- Considerable more research into the mechanisms involved in the development of autoimmune diseases and immune-mediated inflammation and how the environment plays a role.
- Understanding the environmental exposures during development (pre- and postnatal) is key to understanding the common links to shared genetic loci among different autoimmune diseases. There is a need to better understanding of why these diseases cluster in families and can manifest as different autoimmune diseases in identical twins.
- More research into the early life exposure to environmental elements and the role of genetic background in the development of autoimmune diseases.
- Better data documenting the frequency and location of autoimmune diseases in the population. Example: a national registry that would allow for tracking disease hot spots and environmental exposures.
- NIEHS should study the synergistic interactions among environmental factors and disease. Example: radon and cigarette smoking individually can trigger cancer; exposure to the combination synergistically increases cancer risk.
- More research into the role of infections, hormone disruptors, stress, and diet should be study as environmental triggers of autoimmune diseases.
- Using a systems based approach to understand differential host responses to environmental exposures is needed.

Discussion Participants: Virginia Ladd, Richard Woychik, Michael Pino

Report 36: Role of environment in neurodegenerative diseases and healthy aging.

Convener: Marie-Francoise Chesselet

Brief History:

- Healthy aging is a general aspiration and an economic imperative
- Healthy aging is severely compromised by diseases that affect the aged; some of these, such as Parkinson's disease, have clear environmental risk factors based on epidemiological studies; others, like Alzheimer's disease have no known/clear environmental risk factors identified in epidemiological studies yet the small role played by genetics points towards an obligatory role of environmental factors

Discussion Highlights:

- Environmental risk factors may not have been identified because they were studied in isolation
- Genetic polymorphisms may have small effects but become a lot more significant in the context of environmental exposures
- Understanding the genetic basis of sensitivity or resistance to environmental toxins can be critical to understand the mechanism of neurodegeneration
- Insights into the role of environmental factors in neurodegeneration is likely to come from a basic understanding of DNA repair mechanisms and other defense mechanisms of the cell
- Resources are generated by various institutes that need to be integrated in the study of environmental effects; these include genetic data but also model organisms
- Exposure is difficult to measure/characterize; better assessment measures and biomarkers will help
- When no clear epidemiological data are available, it may be worthwhile to expose model organisms of the disease to a variety of environmental toxins to determine which ones are most likely to synergize with the mechanisms of disease pathophysiology to guide further epidemiological studies to validate their role in humans

Recommendations:

- The NIEHS needs to play a leadership role in bringing the role of the environment into research on neurodegenerative disorders conducted by other institutes. Many investigators are not aware or do not know how to study environmental factors associated with neurodegenerative disorders.

- Conversely, the NEIHS can play a role in increasing awareness of investigators interested in the role of environment about resources generated by other institutes. For example, concretely, generate an RFA designed to study the effects of relevant environmental exposure on model organisms generated by other institutes
- The NIEHS should promote studies that consider the role of genetic risk factors for neurodegenerative disorders generated by GWAS and other studies in the context of environmental exposure
- Peripheral and central inflammatory cells are likely to be a mechanistic link between environmental exposure and neurodegeneration; the institute should promote research at the interface between environment, inflammation, and neurodegeneration
- The NIEHS should take a leadership role in promoting public/policy makers awareness that environmental factors influence the health of the aging population

Discussion Participants:

Marie-Francoise Chesselet

David Armstrong

Deborah Cory-Slechta

Barry Dellinger

David Miller

Scott Williams

Report 37: Environmental Health Education as an Intervention and Prevention Strategy

Convener: Bono Sen

Brief History: EH education has been done only on an ad hoc basis and through the grants program and EHP. It should be a cross-institute priority.

Discussion Highlights:

Recommendations:

- NIEHS needs to make EH education and engagement a priority, and devote appropriate resources to it. There needs to be a strong commitment from top leadership that education is a priority and an integral part of the NIEHS mission of "dissemination."
- NIEHS needs to define EH education broadly to include K-16, informal education, engagement, internal education (NIEHS staff) and more, which goes beyond the current OSED.
- NIEHS needs to develop an EH education strategic plan that coordinates efforts across the institute, interagency, with local/state and NGO partners and makes use of the successful models of other agencies.
- NIEHS needs to partner with educational experts who are working to create an EH literate society (starting young) and including NIH OSE, Dept. of Ed, and other agencies.
- Internal education needs to be strongly encouraged and supported so that all NIEHS employees understand the mission and broadly the work of the institute so that they can be informal champions/educators/ambassadors outside the institute. This needs to be incorporated into the culture of the institute and incentives given for people to learn what others outside their immediate group are doing.
- Choose several EH topics on which we have a substantial body of knowledge and work with professionals to develop EH education campaigns to a variety of stakeholders and making use of all available technologies (social media, webinars, workshops, direct relationship building), and including evaluation components to demonstrate the effectiveness and for further refinement.
- Important to educate and partner with state and local health and environment officials and their constituencies.
- Develop opportunities/programs/details/rotations in EH education for internal staff, particularly young scientists.
- Leverage models from other agencies for effective education and engagement.
- Work to educate at federal and other levels to get "Health" into the initiatives/considerations of priority activities in sustainability, climate change, global health, environmental protection, public health, economics, etc. Integrate a One Health approach to our education/messaging.

Discussion Participants: Trisha Castranio, Kathleen Gray, Richard Kwok, Christopher Long, George Lucier, Daniel Madrigal, John Morawetz, Ericka Reid, Kimberly Thigpen Tart, Richard Woychik

Report 38: Investing in publicly available resources and computational tools for integrating and analyzing environmental health data

Convener: Carolyn Mattingly

Brief History: Across the environmental health community there is a need for centralizing, accessing and analyzing diverse environmental health data through public resources. Currently there are multiple databases being developed by disconnected groups. Data in these resources could be leveraged more effectively through better integration of these resources in combination with feedback from the community regarding research needs.

Discussion Highlights:

- There is a need to integrate existing resources that are relevant to environmental health to better enable searching across data sets more effectively.
- Integration and centralization of environmental data will improve access to relevant information for hypothesis development.
- This integration must be spearheaded by a "leadership" group that combines representatives from technology, biology, the community and NIEHS. This has been done by other scientific areas (e.g., genomics) and we can learn from their example (one example that was discussed was NIF).
- A particular challenge for integration of environmental resources is the diversity of data, variety of endpoints, study structures (e.g., epidemiology, basic science, pathway studies, etc.).

Recommendations:

- Need for information gathering in the form of workshops that address the following aims:
    - We need to gain a better handle on the research priorities that could be enabled by better integration – this requires feedback from the community
    - In parallel, we need to inventory existing resources and associated technologies and vocabularies/ontologies in order to determine how to prioritize integration and streamlining future development based on community feedback (above).
        - Publication of a data resource inventory in a journal relevant to the environmental health community (e.g., NAR database issue)
        - Request for information issued by NIEHS to the community about research questions that require or would be better enabled by databases as well as about resources that they currently use.
- In order to facilitate integration of resources:

  - Create a multidisciplinary consortia that may function at a leadership level to drive the implementation of integration of resources, development of needed ontologies, standards for data representation etc.

  - NIEHS should invest in providing support for this consortia to be successful (e.g., There is a precedent for this in coordination of NCBI resources and various institutes working together to make genetics and genomic data publicly available).

  - A UO1 mechanism might be appropriate for involving members of the community in this integration process.

- NIEHS should also take a lead role in helping communicate the existence of an integrated environmental health resource to the community. Our recommendation is to work with NCBI, which is already the primary resource among biomedical researchers, to integrate EHS resources (there is significant overlap in individual data points such as genes).

- NIEHS should invest in strengthening their internal informatics expertise, which could contribute to the integration of resources and provide insights into needed research initiatives that could benefit from these resources.

Discussion Participants:

Carolyn Mattingly
David Balshaw
Chris Bradfield
Ken Fasman
Julia Gohlke
Heather Henry
Stephanie Holmgren
Robert Kavlock
Antonio Planchart
Kristina Thayer

Report 39: Global Environmental Health & the changing burden of disease in the developing world

Convener: Joshua Rosenthal

Brief History:

Over the past several decades a dramatic shift has occurred in the burden of disease around the world. While infectious diseases continue to be important in many low and middle income countries, particularly in Africa, mortality and disability has dropped considerably. People are living longer in Asia, Latin America, Eastern Europe and other regions. As a result, chronic and non communicable diseases have grown considerably and in fact, mortality from chronic diseases now exceeds that from infectious diseases on a global basis. Cancers, heart diseases, stroke, pulmonary diseases including asthma, and brain disorders, obesity are growing at remarkable rates in developing countries; applying traditional biomedical approaches to them will be prohibitively expensive. More emphasis on cost-effective primary prevention is essential for the global economy.

The environmental contribution to these changes has received much less attention than "lifestyle" components. This shift poses both and opportunity and a need for enhanced engagement by NIEHS in global environmental health in the developing world than has been the case historically.

Discussion Highlights:

In many developing countries industrial and agricultural pollutants are poorly regulated and standards are slow to develop due to lack of locally relevant science and capacity.

Gradients of exposure for many pollutants occur in less developed countries allowing for study of population effects through "natural experiments" in ways not possible or unethical in the US and more developed countries.

Environmental pollutants including airborne and foodborne contaminants make their way back to the US from overseas. For example in California we can quantify the number of additional days that cities exceed air pollution standards due to emissions in China.

Large populations, sometimes with existing data registries, offer the ability to study the environmental role in relatively rare conditions such as birth defects and autism.

The incredible growth of interest in Global Health in North American Universities (Fastest growing and most popular major in many US and Canadian institutions) has been overwhelming focused on infectious diseases, ironically despite the shift in disease burden toward non-communicable diseases.

There is increasing evidence for some established toxicants (e.g., lead, tobacco, air pollutants and benzene) that the effects are proportionately greater at the lowest levels of exposure. Thus, there is both more potential to benefit by reducing exposures as well as scientific opportunities to examine the risks across a wider range of exposure.

Recommendations:

NIEHS should help create a new vision of global environmental health and should invest more substantially in Global Environmental Health than it has in the past. NIEHS should help move the science and the conversation about chronic disease burden from Lifestyle to include a better understanding of the environmental contribution.

NIEHS should harness the enormous enthusiasm for Global Health at Universities around the country toward Global Environmental Health and engage these students in a new vision and extramural programs with peers overseas.

NIEHS should seize opportunity to study the environmental contribution to disease conditions overseas that cannot be studied cost effectively or ethically in the US.

Partnerships with other components of the NIH, foundations and local governments will help both effectiveness and cost effectiveness.

Investments in research collaborations overseas need to include not only basic and population science but efforts at translation, risk communication, community engagement and policy outreach AND respond to policy needs.

There should be a home for Global Environmental Health at NIEHS but it should not be restricted to one program and should engage both intramural and extramural components.

Cookstoves offer an important opportunity for dose response research but also translational science efforts and engagement of community partnership expertise of NIEHS.

Investments in new diagnostic tools for waterborne disease is critical overseas, as coliform bacteria standards are poor predictors are still the only game in town.

Frequency of spina bifida and other relatively rare birth defects in the US should be studied in developing countries where the frequency is greater.

NIEHS should convene an international conference to examine environmental determinants of chronic disease, with a specific focus on preventing environmentally –induced disease.

NIEHS, in collaboration with other agencies, should help establish a vision for healthy cities in the developed and developing countries.

Discussion Participants: John Balbus, Geraldine Dawson, Richard Finnell, Howard Frumkin, Bruce Lanphear, Mary Wolfe

Report 40: Environmental Epigenomics

Convener: Brad Bernstein

Brief History: disease susceptibility is a function of genetic and environmental influences. Genome sequencing studies have gained increasing insight into the genetic bases of human disease, but in nearly all cases the genetic components explain only a fraction of disease prevalence. Importantly, a large body of epidemiological data has identified diverse environmental exposures that also contribute to disease. However, the mechanisms remain obscure.

Discussion Highlights:

VISION: The participants in this session identified the broad area of connecting environmental influences to disease through the study of epigenomics and epigenetic mechanism as an opportunity and important long-term goal for NIEHS.

ENVIRONMENT → EPIGENOME (+GENETICS) → MANIFESTATION OF DISEASE

TIMING: Experimental and computational technologies have advanced to the point that comprehensive study of human epigenomes is now feasible. Coordinated efforts by Common Fund, NHGRI and international consortia are now mapping human epigenomes and functional genomic elements at unprecedented rate. The technologies and infrastructures developed in these contexts provide an opportunity for expanded synergistic – for example, related technologies have been embraced by the Cancer Genome Atlas to characterize epigenomic aberrations in human cancer.

HOWEVER, none of the ongoing studies are considering the role of environmental perturbagens and how such agents may alter the epigenome. Such information could provide insight into the mechanisms of action of disease-relevant environmental exposures, and identify relevant biomarkers that could be applied more broadly in population-based studies.

The participants sought to define a relatively focused scientific project that would leverage existing infrastructure and resources within NIEHS (DIR, DERT, NTP) and ongoing large-scale epigenome mapping projects.

Recommendations:

- *In vitro* cell assays to identify the influences of toxic exposures on the epigenome. Cell models would include state-of-the-art human stem cell models, derivatives, artificial tissues
- Toxic exposures would be identified with a disease-driven strategy to ensure maximal relevance, and would prioritize compounds deemed likely to confer stable (long-term) consequences. This would dovetail with ongoing projects and vital expertise at NIEHS.
- Readouts would leverage existing high-throughput technologies for DNA methylation, histone modifications, chromatin accessibility, RNAs.

- Key goal will be to distinguish short-term and long-term epigenomic changes; the latter 'stable' markers are of particular interest for understanding environmental contributions and biomarkers of disease susceptibility.

- In parallel, the strategy would be applied to key mouse experimental models of exposure through coordination with NTP. Though lower throughput, these studies will provide critical *in vivo* validations.

- The project could lead to multiple follow-up studies on the mechanisms of action of environmental insults. Such studies would be ongoing and supported in parallel.

- The project will identify biomarkers of environmental insults which would be validated and applied in cohort studies to examine predictive value for disease susceptibility (in concert with genetic analysis)

Discussion Participants:

Karen Adelman, Trevor Archer, Brad Bernstein, Geraldine Dawson, David Fargo, Richard Finnell, Frank Gilliland, Shuk-Mei Ho, John Hollingsworth, Steve Kleeberger, George Leikauf, Stephanie London, David Miller, Sheila Newton, Jonathan Pollock, Robert Sills, Jack Taylor, Fred Tyson, Leroy Worth, Mike Waalkes

Report 41: Partnering with Communities

Convener: Erin Haynes

Brief History: Strong internal interest is recognized; however, EJ and CBPR grants are currently not active. Many of the leading community-based groups started their environmental health capacity and focus from NIEHS funding! PEPH is a broad umbrella including some community partnerships in research.

Discussion Highlights:

Good CBPR does not mean hiring someone from within the University to do outreach.

It would be ideal to connect NIEHS investigators with potential legislation that could affect health in order to evaluate pre and post effects related to a policy decision, for instance, reducing diesel exhaust on school buses.

Recommendations:

Reinstitute EJ and CBPR grant mechanisms and reinforce/communicate NIEHS support for community grants as the perception from the community does not match the perception from within.

NIEHS should step-up and strongly recommend a community partner to improve "good standard of practice" for traditional R01s.

Community partnerships should be evaluated.

Study Section Issues: Increase capacity of study section members to review grants that include community partners. This goal could also be met by revising study membership to include community members and having COEC-types be 1st reviewer on COEC-type sections. Expand focus of study sections to include CBPR-type grants and include CBPR approaches in the scoring.

Increase NIEHS involvement in Dissemination Science across the NIH

Improve partnership between sister Environmental Public Health agencies: CDC, NIEHS, etc. because current partnership attempts from universities to public health agencies have been extremely challenging as some health departments have been resistant to partnering on environmental health issues relevant to the community.

Improve University IRB capacity to handle working with community groups and to review CBPR projects.

Improve recognition of importance and prestige of doing CBPR in the promotion and tenure process for universities and within the NIEHS

Include departments of health on advisory committees

Make the Public Interest Partners Meaningful or Disband

Discussion Participants:

Bruce Androphy

Douglas Brugge

Christie Drew

Julie Brody

Kathleen Gray

Andrea Hricko

George Lucier

Daniel Madrigal

Peggy Shepard

Tom Sinks

Report 42: Develop an integrated, searchable knowledge base on the impact of environment on health

Convener: Deborah Winn

Brief History:

Having authoritative and current research findings on environmental factors and health that are available at a single site and provide summary data and the level of scientific evidence linking specific exposures to health and disease, and other relevant data would be very useful for a wide range of audiences. These users include the general public, advocacy groups, policy makers, journalists, clinicians, scientists in other disciplines, and environmental health scientists who need quickly an up-to-date and accurate summary of scientific evidence. Some types of searchable knowledge bases in other content domains exist such as the Cochrane Collaboration which provides well-curated and documented reviews of evidence from clinical trials and the HuGeNet website at CDC that provides reviews, meta-analyses, and searchable tables of associations between genes and disease incidence related to genetic factors that may influence disease susceptibility. While searchable data bases linking environmental exposures and health exist, they are not comprehensive and are 1) generally too complex for non-scientists or scientists and clinicians not familiar with the content area to use and 2) the evidence is not sufficiently summarized or presented in easily digestible formats. For example, the International Agency for Research on Cancer monographs on carcinogenicity of exposures has the benefit of providing conclusions about whether a substance is or is not or may possibly be a carcinogen, but the reports are presented as long documents and a few tables, and, in addition, the evidence is not updated on a regular schedule. What is needed is an integrated, searchable knowledge base on the impact of the environment on health that includes knowledge synthesis and systematic review with links to population data, communications materials, data sets for analysis, and evidence-based guidelines. In the absence of such an integrated database, this group of users is likely to continue to have to spend a lot of time searching Google or PubMed or trying to navigate through complex websites such as EPA's, digesting information, and making their own interpretations of the meaning of a hodge-podge of information.

Discussion Highlights:

The group noted that developing such a database:

Requires significant curation, which is time-consuming and costly and would need to be done continuously to keep the database up-to-date

Would include evidence from human as well as animal and other studies

Would not contain individual level data from studies or individual publications from the scientific literature, although there could be links to this and to other more detailed information and databases

It might be possible to have a searchable integrated searchable knowledge base website that contains a separate section that provides most current publications, etc. that would not have

been curated (yet) but would be available to the user (e.g., a section of the website for "news and recent articles").

Whenever data is summarized and conclusions drawn, such as the International Agency for Research on Cancer does, people may question or find fault with what information was included and the process of coming to that conclusion. However, the alternative is that persons who may not have expertise in an area have to make their own conclusions based on their own interpretation of the evidence

Because evidence from publications and studies would be summarized or presented as levels of certainty about links between exposures and disease for example, documentation and transparency in how publications were selected, abstracted, summarized, and conclusions drawn would need to be carefully spelled out

Developing the user interface would be challenging, since it cannot be assumed that users would know chemical names, for example

Could incorporate, leverage or be linked to other databases such as the National Biomedical Monitoring program, which contains summary data from NHANES on levels of environmental chemicals in biospecimens from a national probability sample of the U.S. population, the National Toxicology Program, and others.

Could be led by NIEHS, but could be developed jointly with other NIH Institutes, other agencies, academic institutions, etc. and it could be housed at NIEHS, NLM or elsewhere

Recommendations:

NIEHS should lead an effort to develop such as searchable knowledge base of evidence on the effect of the environment on health

Discussion Participants: Michael DeVito, Richard Kwok, Sheila Newton, Jeanne Rizzo, Daniel Shaughnessy, Kristina Thayer, Deborah Winn, Tracey Woodruff, Richard Woychik

Report 43: Is it important to educate the public, and if so, how best?

Convener: Amy Kostant

Brief History:

How to position NIEHS with the media – does the Institute want to raise its profile?

Who is responsible for communicating the science emanating from NIEHS: the scientists, the Institute (communications staff) or a partnership?

Discussion Highlights:

Challenges – institutional comfort level – controlling the message; scientist comfort level; political ramifications; changes to science media – fewer reporters; science literacy – public education needed

Communicating to the public is the cutting edge of translational research - this should be key to NIEHS (BPA is a good example)

Is there value in determining newsworthiness of research?

Journalist needs: two sides to make a good story, plus middle-of the road 'voice of reason' to provide solid science background. NIEHS role might be to provide the highest credibility background info.

Vulnerability of scientists speaking to the press without training. How to prepare for this and lessen the risk/anxiety?

Science literacy: Consumers need to be able to make their own decisions.

NIEHS isn't using modern-day communications technology. Have to move beyond email and static websites to engage with audience and built next generation of science interest.

Recommendations:

Make communication a part of the research culture – not an afterthought. This includes thinking through in advance the public health impact of the research and how to make it accessible.

NIEHS should carve out areas of expertise where science is most excellent and therefore, less controversial.

Streamline process for -- and encourage and train -- NIEHS researchers to provide background to journalists – on the record.

Develop ways to talk about uncertainty in science – without sounding uncertain. Educate the press and the public on the uncertainty inherent in good science.

Internally – for its own staff, NIEHS should provide environmental health-specific presentation/media training so they can be go-to people for the media on given topics. Partner with foundations to fund this training, and also to support broader communications work.

Make use of thought leaders: extramural scientists who are good communicators, communications experts, and experts from complementary disciplines.

NIEHS should re-invest in environmental health science education to increase environmental health science literacy. There is a lack of awareness of what already exists – needs to be built up and disseminated.

Explore appropriate (effective) technologies for communicating with the public.

Discussion Participants: Austin, Collins, Edwards, Germolec, Graedon, Hall, Jung, Moore, Newschaffer, O'Fallon, Schroeder, Walker, Wexler

Report 44: Biomarker Development Using Omic & Systems Biology Approaches for Use in Disease & Injury

Convener: Rick Paules

Brief History: There was a consensus for a need for better biomarkers and a better approach for the development of biomarkers for use in human studies. In particular there was a general agreement for the need of a systems approach with an integration of platforms in biomarker development. In the past there has been a lack of integration of platforms, lack of quantitation, lack of comparisons across species for utility of biomarkers, as well as a lack of informatics resources supporting the development of biomarkers. As a result, biomarkers have not lived up to their initial promise. In addition, biomarkers need to go beyond association derived from population studies to testing in individuals.

Discussion Highlights: There was uniform passion about the power of exploiting a systems biology approach to biomarker development. We need to understand mechanisms of injury or disease for prevention, early detection, treatment and health promotion. Biomarkers need to provide insight into mechanisms. There needs to be an integrative approach using model systems (e.g. mouse), individuals, populations, communities, integrated using systems biology. We need mouse/cell based models to tease out complex effects, to validate effects in humans. Cross species comparisons can reveal important differences in pathways and systems that will inform better biomarker development.

Recommendations:

- Need working group to define approach for platform integration in biomarker development.
- Need new clinic models for identifying risk and rapidly testing potential biomarkers (too many potential biomarkers to test in very large epi cohorts).
- Need mechanistic based biomarkers, not just associations.
- There is a need for bioinformatics support of biomarker development.
- There is need for cross platform validation, quantification, standardization, and integration. Also, there must be transparency within the research community and general public of data collection and results in all stages of biomarker development and data must be place in the public domain.
- There needs to be an integrative approach using model systems (e.g. mouse), individuals, populations, communities, integrated using systems biology.
- Need precise, quantitative exposure information instead of retrospective recall studies.
- There is a need for Private/NIEHS partnerships to leverage resources and advance development.

Discussion Participants: Rick Paules, Victoria Seewaldt, Bill Suk, John Groopman, Mike Holsapple, Chris Kemp, Richard Miller, Frank Mirer, Jonathan Pollock, Robert Rickard, Jim Swenberg, Jack Taylor, Rick Woychik (partial) and Linda Birnbaum (partial)s

Report 45: Training and Mentoring

Convener: Luz Claudio

Brief History: The workforce engaged in public health is aging. It has been estimated that over 25% of the public health workforce will be retiring within 5 years. There is a need to replenish this workforce in public and environmental health. Further, there is a need for more interdisciplinary training to be applied to environmental health sciences. There is a strong need to engage young people from different disciplines to apply those disciplines to find solutions to environmental health problems. This is timely, as the report from Lancet Commission on Education for Health Professionals in the 21st Century has been issued and defines many of the country's needs for training.

Discussion Highlights: Everyone in the group agreed that there is an acute need for support in training and mentoring in EHS and that this is part of the NIEHS mission. Much of the discussion centered about the need to have young people with multidisciplinary training be engaged in environmental health sciences.

Recommendations:

1. NIEHS can partner with existing programs (from other organizations) that engage trainees at different levels in science and medicine. NIEHS can play an important role in supporting the need for multidisciplinary training as a partner to these organizations because of the multidisciplinary nature of environmental health sciences (EHS can reach engineers, chemists, geneticists, etc through their societies). Some examples of existing programs from other organizations with which NIEHS can partner are:

a. SOT Postdoctoral program

b. National Postdoctoral Association

c. Science Ambassadors Program – for training high school teachers in science curriculum development

d. Young Epidemiologists Program

e. American Association for the Advancement of Science fellowship program

2. NIEHS has a new person in education and outreach. Perhaps this person can reach out to the organizations above and others that are already doing innovative training and education outreach programs to attract young people into EHS.

3. Add a "cool" tool to the NIEHS website that would be attractive to engage young people in EHS. Use social media and electronic games to engage young people in EHS and to promote the work of NIEHS

4. Develop incentives for faculty to engage in mentoring including more grants that support PIs to conduct mentoring and training

5. Evaluate existing training data tables (submitted by PIs) to assess which types of training programs are most effective in transitioning trainees into faculty positions and success in obtaining research grants. Add other metrics of success in career development.

6. Issue a "Grand Challenges in Environmental Health" award where young people in different disciplines can be supported to find innovative solutions to pressing environmental health problems

7. Have more grants that are given directly to postdocs in order to improve their opportunities to obtain faculty positions and leave the "serial postdoc" treadmill.

8. Continue to support and expand the K-12 outreach and EHS education programs. Engage graduate students and postdocs in these programs.

9. Support multidisciplinary training in the intramural postdoc program by encouraging multiple mentors for trainees

10. Define the goal for international postdocs. Is the goal for them to return to their home country and increase capacity there or to integrate them into the US science workforce? This is an issue because close to 50% of postdocs in science are international postdocs on work or training visas. How can NIEHS play a role in defining the goals for these trainees?

11. Add a requirement in RFAs for training in communication of EHS research results. This would be similar to the current requirement for ethics training.

12. Address attrition in the training ladder due to family issues. Inform NIEHS grantees of the new policies to take into account family leave in productivity gaps. Provide no-cost extensions for grantees who have gaps in productivity due to their own family responsibilities or family leave of their key staff.

13. Add sessions for young participants in existing NIEHS activities such as Town Hall Meetings.

14. Have the Office of Communication provide training in science communication. There could be a virtual course (web-based) and/or an in-person course available to grantees at different levels.

15. Feature different possible career paths for environmental health scientists. Have EHS career days and have career profiles in the NIEHS website that illustrate what EH scientists do and how they use different disciplines to solve EH problems.

Discussion Participants:

Thomas Begley
Abee Boyles
Douglas Brugge
Jose Cordero
Paul Foster
Laurie Johnson
Michele LaMerrill
Heather Nicholas
James Putney, Jr
Gwen Collman
John Froines

Report 46: Appropriate reporting and analysis of sex differences in environmental research

Convener: Martha Nolan

Brief History: Historical challenges to the inclusion of both sexes in research from basic to human studies. And the lack of reporting of sex in research

Discussion Highlights: Not enough is being done even now. There is a need to do a better job of analyzing – report even no difference. We know sex differences exist and are biologically significant – so how do we make single sex studies rare or require justification even in animals since anyone who tries to follow it up in the other sex hits problem of not being novel or unique.

Focus on women needs to not be so significantly on reproductive health. Expand to lung, autoimmune, cardiovascular, metabolic and other organs and systemic issues. Reproductive organs are only a part of women or men's health. Discussion brought up emphasis on toxicants and xenobiotics not just endogenous E2 and timing of exposure affects disease outcomes (fetal development).

Is regulatory science adequate to identify sex differences? Are the protocols effective? Appropriate? Out of date? Can NIEHS help to improve the quality of this work? Refine/improve the toolbox? Justify inclusion of additional animals needed?

Recommendations:

- Research should be adequately powered to detect sex differences (or justify why not) in both animal and human research. Give weight to sex difference at granting mechanism – recognizing cost factor upfront.
- Make identification/evaluation of sex differences in a study (animal and human) a valid/important specific aim for NIEHS funded research. Communicate to study sections and provide incentives.
- Get beyond reproductive organs (beyond plumbing) to other organs or systems. Include life stages such as puberty as a critical window as well as other significant age points.
- Sex differences research transcends NIEHS and should involve other institutes in a collaborative/integrated approach. NIEHS lead/encourage effort internal to NIH and externally to other regulatory agencies on addresses sex differences in environmental science.
- NIEHS should give value to studies where sex differences is an end point

Discussion Participants: Paul Howard, Mary Lee, Grace LeMasters, Edward Levin, Health Patisaul, William Schrader

Report 47: Exposure Science

Convener: Sacoby Wilson, Ph.D.

Brief History: With the advent of the release of the EPA cumulative risk assessment framework, The National Academy of Science report on risk assessment, coupled with the recently formed Institute of Medicine committee on exposure science; the NIEHS is perfectly positioned to be at the forefront of exposure science.

Discussion Highlights: Although the US EPA and NIEHS have completely different mission, there should be more collaborations between the two towards correcting the lack of good science that EPA is using to set policy on. Since children are considered to comprise one of the most vulnerable segments in our population, NIEHS needs to be at the forefront of discovery in exposure science based on the requirements the charge of the National Children's Study.

There is a need to profile background exposures in susceptible populations via the development of high throughput methodologies. This is necessary for because differential exposure determinations need to be made. We must link exposure to risk assessment for the purposes of conveying risk to the affected community. If NIEHS does this correctly, exposure science will translate the cumulative risk-assessment framework to informed changes in policy in this regard.

Recommendations: NIEHS-sponsored exposure science research will;

1) Model exposures based on real-life situations.
2) Encourage community partnerships that are linked to exposure biology programs aimed at developing techniques and methodologies for monitoring in affected communities.
3) Develop a more robust bio-monitoring program for the purposes of determining total body burden of exposure components (i.e. sensor development)
4) Develop oxidative stress biomarkers that will implicate the affected molecular pathways (i.e. ARE activation)
5) Stimulate the refinement of exposure science training programs
6) Lead to the application of Support Vector Machines to epidemiological study analysis towards identifying previously undescribed associations between exposure and disease.
7) Stimulate an evaluation of the relevant ethical issues involved in determining chemicals in blood

Discussion Participants:

Sacoby Wilson, Darryl B Hood, Secretary, Beverly Wright, Rob McConnell, Aubrey Miller, Cossette Serabjit-Singh, John Bucher, Richard Denison, John Froines and Elaine Hubal

Report 48: Invent new ways to incorporate NIEHS research expertise effectively into disease specific research.

Convener: Cheryl Marks

Brief History: All too often NIH disease-focused ICs fail to appreciate that the environment has a key role in disease etiology, and it is necessary to consider the extent of contributions of environmental factors to poly-morbidities of complex diseases. The expertise of NIEHS-funded investigators is often under-valued by disease-specific research teams, and the environmental perspective is urgently needed to balance the gene-centric view of medicine. Researchers who try to find support for the study of the role of one or a few environmental factors in several diseases are often frustrated by the difficulty of "selling" their project to more than one categorical IC; in other words, NIH does not facilitate the funding of research that crosses the boundaries of categorical diseases.

Discussion Highlights:

- Need to ensure that the leadership of all ICs appreciate the importance of the environment as a co-factor in disease.
- Even if the tools for interrogating the effects of the environment are imperfect, they need to be incorporated into a variety of population studies to ensure their validation for a broad collection of diseases.
- The extent of recent developments in sensors and biomarkers and other environmental measures are under-appreciated and under-utilized by investigators who study human populations for underlying causes of specific diseases.
- The potential that exposing environmental factors as components of disease etiologies has for prevention is under-realized.
- NIH does not utilize funding mechanisms that provide support for research in the collaborative ways that reflect current research practice, or support the long-term studies required to explore the role of the environment in disease manifestations that may take decades.

Recommendations:

- Implement inter-IC and inter-agency panels of outside experts to highlight the opportunities for integrating environmental research expertise and tools into specific disease research.
- Ensure that environmental issues that are pertinent to specific regions and of concern to the US population are rapidly addressed with research.
- Develop mechanisms for partnering among NIEHS-funded researchers and specific disease research communities to leverage their cross-disciplinary expertise.

- Invent facile support mechanisms that enable researchers from several disease research communities to aggregate their expertise and interests in effective collaborations to address the potential of environmental factors as causative for more than one disease.
- Address the limitations of current funding mechanisms that do not permit long-term assessment of environmental factors in disease etiology; incorporate realistic milestones for assessing progress for continued support of such long-term studies.
- Explore effective outreach mechanisms to inform all disease research communities of the environmental research methods, survey tools, and technologies that are available to incorporate into their research.
- Ensure that NIEHS augments its connections to other agencies and entities to incorporate technologies that may be useful to monitor environmental factors; i.e., leverage investments in nano-technologies, sensor technologies, and other novel techniques.
- Partner with disease-centric clinical programs to deploy and validate environmental research methods and survey tools.

Discussion Participants: Janice Allen, Gary Bird, Gwen Collman, Barry Dellinger, Thomas Gasiewicz, Michael Gould, Gina Goulding, James Kiley, Cheryl Marks, Patrick Mastin, Kimberly McAllister, Dale Sandler, Palmer Taylor.

Report 49: Children's Environmental Health Research: Networks and More Bang for the Buck

Convener: Carol Stroebel

Brief History:

When we protect children, we protect others who are as vulnerable as well

To get to healthy adults, you need healthy children.

NIEHS has made children's environmental health a priority, supporting centers of excellence in research in children's environmental health and the National Children's Study.

Why is this topic important now:

The rising prevalence of children's diseases associated with environmental factors: asthma, autism, cancer.

We have activities now, such as the National Children's Study, research centers, PEHSUs. We realize that the structure is very complex, and we need a structure. Based on the experience we've gotten from the existing centers et al, the state of the science, etc., what should be the future role, activities, structure of NIEHS' children's environmental health focus?

Discussion:

NCS anticipates additional studies will be done to leverage the data. NIEHS perhaps should look at that mechanism to see if that's the best way to go. Will the other hypotheses be looked at by other investigators? If you want to study early life events, periconceptual, fetal, newborn, will you still be able to make it through the NCS process to get the additional data you need?

Lots of opportunities for cross-fertilization

Will there be adequate coordination between NCS study sites?

CEH research centers each do their own silo of research of CEH; it's different than NICHD which has linked studies go on in different sites. Is there a role for an EH children's research network?

Given the state of the science now, and what we've learned from current/past activities, do we need a structure so that the complexity of studying children's environmental health can be addressed? How do we build on what we've learned?

Community partnership: should it continue to be required? Yes

How to network communities? It can be done.

What about similarity to MCHB to emergency pediatrics. If, e.g., the PEHSUs or others could capture the children sickened by sick building syndrome, arsenic exposure. Could be source of similar subjects of studies.

Need to identify sick building as a disease.

Need good public communications to let people know about the work and findings.

Even with lead poisoning, you have to do a multi-site study to find enough children.

Not a lot of guidance of how to deal with incoming questions, eg, about problems dealing with exposure/health at schools, child cares, to PEHSUs or study sites.

Concerns about further harm to indoor environmental health due to weatherization and tighter buildings

Neonatal research centers would be a good source of samples; maternal fetal sampling network could be another source

Recommendations:

Children need to remain a priority; the existing programs need to be maintained, even expanded.

Just as other research fields have developed national research networks (eg, COG, NICHD NRN, MFM-RN, PECARN) to move their fields rapidly forward, NIEHS should invest in a national research network, where studies are conducted at multiple sites. PEHSUs could be used as the initial patient identification source. (Other potential high risk populations such as NICUs could be considered as well)

Existing research centers and their partner communities should be continued and networked (researchers networked, community leaders/groups/parents networked)

The Children's Environmental Research Centers are measuring a lot of the same health outcomes, exposures; NIEHS should require that this data be pooled.

Continue to require/expand requirement to partner with community (broad definition of community) in research, above and beyond "communication and outreach."

Require research centers to translate their research findings to the public and create central repository of these public information materials. Outreach should be done to AAP committee on environmental health, NAPNAP, AWHONN, physicians assistants, etc. about these materials and other information.

NIEHS should increase work on defining the exposome of children.

In the NCS, environmental sampling of school and child care facilities should be required.

NIEHS can better partner with other entities (eg, CDC, ATSDR) to assist in issues of notification of exposures, identifying risk

Discussion Participants:

Claire Barnett, Cynthia Bearer, Nuala Moore, Carol Stroebel, Robert Wright

Report 50: Integrating Environmental Health into Medical and Nursing Curricula

Convener: Karin Russ

Brief History: Concepts in environmental health, such as history taking, screening, anticipatory guidance and treatment of environmental exposures, are notably lacking in the basic training of doctors and nurses. Core content within the entry level curricula on environmental exposures mainly focuses on classic examples of toxicants, such as lead poisoning in children, indoor air quality and asthma, and avoiding a limited number of substances during pregnancy: alcohol, tobacco, and mercury exposure through fish consumption. A handful of universities across the US that provide entry-level training in medicine and nursing have electives in environmental health.

At the graduate and post-graduate level, more options for specializing in environmental health exist, but by definition, these programs are populated with students who already have an interest in environmental health issues. The general practitioner and the bedside nurse do not receive adequate preparation in environmental health to care for their patients. Patients are coming to their healthcare provider with questions about substances such as BPA, phthalates, VOCs and pesticide that the provider is not equipped to answer. Patients are needlessly being exposed toxicants and suffering from acute and chronic diseases as a result.

NIEHS needs to address the integration of environmental health content into basic medical and nursing curricula now, so that health care providers can focus on the prevention of chronic and acute diseases associated with environmental exposures. In addition, NIEHS needs to provide opportunities for post-graduate training of doctors and nurses, to strengthen and solidify the pipeline of environmental health researchers for the future.

Discussion Highlights:

In discussion the basic training of doctors and nurses, we agreed that our own initial professional training provided minimal opportunities to learn about environmental health. For example, physicians are not adequately trained to recognize and address chronic diseases that are caused or exacerbated by environmental factors. Training in emergency situations, such as a community oil spill, is also lacking.

Nursing is a discipline that has strong roots in environmental health. Florence Nightingale improved conditions of sanitation, air, water and food quality in army hospitals during the Crimean War. But current nursing education is more focused on treatment, with less emphasis on prevention.

There is a need to make basic training in environmental health a mandatory part of initial training for health professionals. How can we encourage and facilitate the adoption of environmental health contact into medical and nursing curricula? One effective strategy is to work with the licensing bodies that administer the RN and MD certification exams, to insure the inclusion of environmental health questions of the tests. Another strategy is to work with pertinent professional organizations, to integrate environmental concepts as core competencies for doctors and nurses. NIEHS can act as a resource for content development.

In addition to integrating environmental health into entry level training, there is a need to attract healthcare professionals to pursue further training in environmental health. The question becomes: how do we generate interest in environmental health? Currently, environmental health is seen as something tangential to the main functions of nursing and medicine. We need to bring environmental health to the forefront of clinical practice, and to highlight for clinicians the risk reduction messages they are already providing, to redefine their concept of environmental health. For example, if a healthcare provider asks a patient with atopic dermatitis about products around the home that may be exacerbating the condition, that screening and the subsequent recommendation to avoid exposures falls under the purview of environmental health.

Recommendations: We recommend that NIEHS take the following steps to achieve the two goals of basic and specialty training in environmental health for healthcare providers:

1. **<u>Integrating environmental health into entry level training of doctors and nurses</u>**

    - Convene a group of experts in environmental health in nursing and in medicine, as an expert committee to make recommendations for curriculum development.
    - Look at lessons learned from the NIEHS worker training program, and apply similar principles to the development of a health care provider training program.
    - Form public/private partnerships with groups appropriate for the creation and dissemination of environmental curricula. For nursing, that may include: American Association of Colleges of Nursing (AACN), American Nurses Credentialing Center (ANCC), American Nursing Association (ANA), Alliance of Nurses for Healthy Environments (ANHE). For medicine, that may include: American Association of Medical Colleges (AAMC), American Medical Association (AMA), Council on Graduate Medical Education (COGME), American College of Preventative Medicine (ACPM), Physicians for Social Responsibility (PSR).
    - Make a recommendation to colleges of nursing and medicine to integrate environmental health into entry level training.
    - Provide opportunities to 'train-the-trainer', in order to bring existing faculty up to speed on environmental health.
    - Create a PR campaign to promote incorporating environmental health into practice. This might include re-framing the existing curriculum content on environmental issues, to highlight the importance of the work. Another strategy may be to link concepts clinicians can relate to with concepts in environmental health that may be new. Examples are: "Heart disease is not just about cholesterol- it's air pollution. Diabetes is not just sugar- it's about endocrine disrupting compounds."

2. **<u>Providing opportunities for post-graduate training in environmental health</u>**

   - Partner with local area universities such as UNC or Duke, to offer an environmental health rotation at NIEHS.
   - Sponsor a post-doctoral elective course in environmental health, to generate interest in the field.
   - Create an NIEHS Fellowship program for doctors and doctorally prepared nurses, to increase future research capacity. A mechanism similar to the T32 may be useful.
   - Promote NIEHS funding opportunities to schools of medicine and nursing. A persuasive way to frame the opportunities might be: "Apply to two agencies- double your chances". A direct communication from the NIEHS director to the Deans would be especially effective.
   - Write editorials in professional journals, to highlight environmental health as an emerging subspecialty within traditional medical fields. Pertinent groups to target include preventive cardiologists, pulmonologists, immunologists, and allergy specialists.

Discussion Participants:

Michael Fessler

Nadine Gracia

Paul Jung

Karin Russ

Report 51: One Health

Convener: Lisa Conti

Brief History: One Health is a concept to address "wicked problems" that require collaborative solutions from multiple disciplines. A One Health Task Force was convened by the American Medical Association and American Veterinary Medical Association to develop partnerships. The timing for this integrative work is critical as, for example:

- The next major human pandemic is likely to come from animal origins.
- The growing need for animal protein is setting the stage for an enormous expansion of factory farming globally.
- Antibiotic-resistant genes are environmental pollutants (they can be bioaccumulated) – "Gene Toxicants".

Discussion Highlights:

A working definition of One Health: The inextricable linkage between, human, animal and ecosystem health, demanding cross disciplinary collaborations to achieve optimal health in human and animal clinical medicine, training and applied public health.

- Animals can serve as sentinels for human and broader ecosystem health (eg, canary in the coal mine, endocrine disruptors, West Nile virus). We can sample pets as an indicator of household exposures to infectious diseases and toxicants. (eg, 55% of pet cats are indoor only animals)
- We have created artificial barriers between specialties.
- We share the same environment as our companion animals (pets' health can indicate home health), and as consumers of farm animals, we are indirectly exposed to their environments.
- The infectious disease community has embraced the concept of One Health, this is not as evident among in environmental health.
- Sustainable farming practices take advantage of natural animal behaviors and obviate the need for interventions that may ultimately be hazardous. (Judicious use of manure from non-industrial agriculture is 'Black Gold' where huge concentrations become 'Toxic Waste').
- A number of small, animal disease databases exist, largely supported by NGO efforts, but a comprehensive and integrative surveillance system is lacking.
- Laboratory based research can benefit from a One Health approach.
- From a public perspective, NIEHS can benefit from embracing One Health.

Recommendations for NIEHS:

1. Support a workshop on integrating One Health and the Environment to review new developments and potential opportunities.
2. Embrace the concept of "Genes as Toxicants" – resistance and virulence genes in the environmental pathogen pollutants.

3. Extend opportunities for DVMs to benefit from existing NIH fellowship awards and build other support for research training for DVMs.

4. Support research of companion animals as indicators and sentinels of the built environment (eg lead levels, obesity).

5. Support partnerships and collaborations for a One Health Surveillance System including companion animal, agricultural animals and wildlife disease biomonitoring similar to NHANES.

6. Through a partnership with USDA, compare impacts of sustainable farming practices with industrial practices.

7. Consider the One Health aspects of nanotechnology.

Discussion Participants:

John Froines, Howard Frumkin, Claude Hughes, Aubrey Miller, Andrew Rowan, Ellen Silbergeld, William, Stokes, Lisa Conti

Report 52: Opportunities in Translational Animal Models

Convener: Tom Vogt

Brief History: Animal models represent a powerful experimental approach across a range of research questions in environmental health. The choice of which animal models to pursue is driven by the specific biological question to address. The questions posed were: 1) does the NIEHS have a comprehensive and integrated approach to the selection and use of translational animal models, 2)are there opportunities for new approaches to improve relevance to environmental health, and 3) is there opportunity or value to broaden a focus on traditional animal approaches to animal population type approaches.

Discussion Highlights:

- An important health research area is understanding genetic variation to risk susceptibility and health and disease
- The rodent models represent a rich source of historical data, advanced experimental manipulation, well characterized profiles, and cost containment.
- The group championed that there is a valuable opportunity to broaden the use of emerging mouse genetic reagents to mine the value of genetic variation and to look to relate the genotype: phenotype response to the understanding of human variation in risk, response, and health. Specifically the group championed investment in the mouse *genetic diversity outcross* and the *collaborative cross* as enhancements to gaining understanding to the efforts focused on an inbred strain or F1 strain for screening and testing.
- In consideration of the potential resource ramifications of multiple strains by multiple experimental tests (single agents, dosing regimens, complex mixtures etc.) the group suggested there needs to be consideration of use of higher throughput screens in simpler model organisms, increased effort in modeling and simulation, and increased efforts in integrating human variation data with the model organism variation to prioritize experiments with highest human health impact.
- Outside the traditional experimental model discussion explored the potential value of “eco-toxicity” in natural populations to explorations of companion animal studies as a correlative read-out for shared living environment with humans. One exploration was regarding companion animals in common environment with similar health responses (allergies). There was a strong sentiment that the value proposition would best focus resources on human and experimental translational model research.
- It was unclear to the group what is the level of coordination and communication between NIEHS activities in translational animal models with the strategies and activities of ex-USA efforts (Western Europe etc).

Recommendations:

- Strategically explore and exploit the emerging datasets on correlating human variation to health by an increased use of genetic diversity in the rodent model to address questions in environmental health. Grapple with the real value and the challenge of looking to develop new approaches against the inertia of large data sets collected in single species and/or strains.
- For translatability in the rodent model in addition to leveraging genetic variation fully explore the use of genetically engineered approaches to "humanize" the response to xenobiotics by germline engineering of Phase 1 and Phase 2 metabolizing genes in the rodent model.
- Strategically develop an overarching approach across the span of experimental model organisms (from bacteria to nonhuman primates) so that the information, infrastructure, communication, and governance are in place to efficiently and effectively address the questions of highest importance.
- Seek a strategic approach that has the NIEHS divisions to work in an integrated fashion in the translational animal models approach to addressing questions in environmental health—shared goals and shared datasets.
- Seek a strategic approach that is maximizes the efforts of other groups in advancing the strategic translational animal models capability (e.g. Computational Toxicology at EPA, rodent genetic resources and uses, systems biology data, etc.)

Discussion Participants:

Christopher Bradfield, Gina Goulding, Michele LaMerrill, Richard Mural, Robert Sills, Thomas Vogt, and Richard Woychik

Report 53: Effects of the Environment on the Immune System

Convener: Darryl Zeldin/Paige Lawrence

Brief History: Recent studies have emphasized the importance of environmental factors in immune system development and function; however, this has been an understudied area at NIEHS and at NIH overall.

Discussion Highlights:

- The role of environmental exposures in allergic diseases pathogenesis has historically gotten lots of attention, but there has been limited focus on other areas of importance including autoimmune diseases, infectious diseases and host defense mechanisms. Research involving animal models and human studies are both critical.
- There is a disconnect between what epidemiologists and basic researchers are studying with respect to environmental exposures; research efforts need to be better coordinated.
- Both human and animal research efforts need to focus on measuring endpoints that relate directly to immune system function.
- A barrier for research in humans is accessibility of relevant tissues/cells; some tissues (e.g. nasal washes) are more easily accessible than others, but may not be suitable in some situations.
- The inherent memory of the immune system is an untapped resource that may provide a biomarker of past environmental exposures.
- There is a gap in knowledge about how environmental factors impact innate immune system function, especially at mucosal sites, to affect disease onset and/or progression including diseases that develop in non-immune locations (e.g. brain).
- The emerging role of the microbiome – immune system as a bridge between host and environment.
- The role of genetic susceptibility and how this needs to be factored into research on environmental influences on immune function.
- The impact of the environment on immune system development needs more attention with an emphasis on epigenetic regulation and vulnerable windows; there was extensive discussion on this topic.
- Need to develop cross-species translational biomarkers
- Tox21 could be used conceptually to study immunotoxicity of environmental agents. Blood or cultured cells could be used as tools to answer key questions and/or validate human biomarkers of exposure.

- Better marketing is needed for immunotoxicology and host susceptibility.

Recommendations:

1) Expand research on how the environment impacts immune function and health in human populations; expanded use of existing human databases to focus the research questions.

2) Strengthen NIEHS' niche as leaders in understanding how early life environmental exposures (i.e. in utero and early post-natal) affect the development and function of the immune system.

3) Extend research on vulnerable windows throughout the lifespan – from conception to adolescence to aging – as these either are susceptible windows in time or represent especially susceptible populations of individuals.

4) More research on how the environment influences host defenses (how the environment serves as a modifier of host defense mechanisms) and how infections modify how the host responds to environmental exposures (e.g. bidirectional interactions).

5) More mechanism-based studies on how environmental chemicals perturb immune system function.

6) Develop PPG mechanisms (e.g. cooperative agreements, U01) that pull together scientists in three arms of NIEHS (NTP, DIR, DERT) to work collaboratively/cooperatively on studies related to environmental influences on the immune system.

7) Improve publicity of NIEHS' and NTP's research capabilities and contributions to this area of research.

8) Hold a series of workshops to develop ideas for research opportunities and foster more research in this area.

Discussion Participants: Darryl Zeldin, Paige Lawrence, Karen Adelman, Janice Allen, Patrick Breysse, Geraldine Dawson, Mike Fessler, Dori Germolec, John Hollingsworth, Michael Holsapple, George Leikauf, Grace LeMasters, Pat Mastin, Rob McConnell, Dave Peden, Jim Putney, Ellen Silbergeld, Claire Weinberg

Report 54: Public Private Partnerships for Advancing Environmental Health Sciences

Convener: Jonathan D. Pollock

Brief History: Public Private Partnerships (PPP) have been used to accelerate research and product development in pharmaceutical, nano electronics, orphan disease research, and by NIH for development of biomarkers and medications for tobacco dependence. In addition has proven effective for working with NGO and community outreach. Another of a PPP is the partnership between EPA and Industry through funding an institute at MIT.

Discussion Highlights:

Why is it needed?:

1) Controlling cost by eliminating duplication of effort
2) Augmenting research capabilities
3) Promote technology development and products
4) Bring different expertise to the table and enable industrial technology to be exported to academia and government.

Recommendations:

PPPs could accomplish the following goals for Environmental Health Science:

1) Promoting data integration and creation of federated and centralized databases
2) Speeding up the development of new toxicology paradigms
3) Developing new technologies both highput tools and hand held monitoring tools and wireless technology. Engage industry develop the next generation EHS tools.
4) Promote access to new tools and resources
5) Getting researching into action; communicating findings in to practice.
6) Identifying problems; identifying solutions
7) Creating public private partnerships to address food deserts in impoverish neighborhoods

Possible strategies and obstacles:

Seed start-up company and step away
Work with FNIH.
Need to protect I.P. while evaluating a product to be commercialized.

Discussion Participants: Jonathan Pollock, Thomas Begley, Claire Barnett, Robert Rickard, Andrew Rowan, Kimberly Thigpen Tart, Mary Wolfe

Report 55: Cross-Disciplinary Training Of Environmental Health Scientists

Convener: Dale Sandler (Abee Boyles)

Brief History:

The pool of environmental health scientists needs to be larger in order to move questions on the role of environmental factors in disease and public health to the forefront.

Future generations of environmental scientists need to be able to work collaboratively and across disciplines to tackle complex problems.

Discussion Highlights:

Barriers

- Breadth of the field makes "core competencies" challenging
- Common language needed
- Funding opportunities are limited – need to get other agencies to recognize the role of the environment.
- It is difficult to get funded under current mechanisms for research outside narrowly defined disciplines
- Difficult to retain and attract trainees because jobs in EHS careers are hard to come by

NEEDS

- Need to bring HEALTH to undergraduate training in Environmental Sciences
- Need to bring young researchers into the NIEHS Intramural Programs, Extramural Programs, and NTP
- Need to bring understanding of environmental health into medical subspecialty training
- Need to bring people with training in other basic scientific disciplines (physical, applied, etc.) into EHS research
- Need to attract the best and brightest into EHS and keep them in EHS research endeavors
- Need to broaden the definition of a "successful" EHS career

Recommendations:

- Increase support for a variety of creative training programs that attract the best and brightest. Models could include
    - Year 3 MD training opportunities in EHS
    - Using Harvard business case model to develop an intensive experience for cross disciplinary problem solving (both Intramural and Extramural)
    - Epidemic Intelligence Service model from the Commissioned Corps

- NIEHS should have a more visible presence in existing NIH wide training programs that can bring expertise to EHS, e.g. ORWH program
- Support training programs for Medical subspecialists that include EHS, e.g., environmental cardiology, environmental gastroenterology, etc.
- Explore mechanisms to bring people from other disciplines to public health; e.g., Create postdoc and other training programs for people that come from other disciplines
- Recognize that NIEHS is training a broad range of experts in EHS fields that go on to non "laboratory" focused careers. Support opportunities for trainees to learn about communications, policy, administration, public health, etc.
- Support young investigators through professional development, mentoring, grant support, etc.
- Actively develop and coordinate opportunities for workshops and symposia on the role of the environment in other disciplines
- Peer review structures for training programs should include the breadth of the science that trainees are exposed to
- Capitalize on existing Environmental Science programs to build competencies for undergraduates and others
- Fostering more cross-disciplinary interactions by modeling plain language communication throughout NIEHS
- Support doctoral training programs that require an NIEHS component, where classwork occurs at top Universities, and the dissertation work occurs in the intramural program at NIEHS
- Extramural and Intramural programs should encourage cross disciplinary research through targeted program announcements (e.g. IRA's intramurally)
- NIEHS should encourage/improve mentoring of established scientists as a strategy for bringing new/early stage investigators into EHS fields. Evaluate the quality of the mentoring.

Discussion Participants:

Archer, Austin, Bearer, Birnbaum, Boyles, Cidlowski, Dolinoy, Drew, Gasiewicz, Hall, Johnson, Kwok, Lee, McConnell, Patisaul, Reid, Sandler, Schrader, Schroeder, Sen, Silbergeld, Sinks, Walker N, Woychik, Zeisel

Report 56: Mechanisms of Resistance, Resilience and Recovery: Learning from Success in Dealing with Environmental Stressors

Convener: Ed Levin

Brief History: Typically attention has mostly been paid to mechanisms of susceptibility to the adverse effects of exposure to environmental toxicants and other stressors. Little attention has been paid to those individuals who do not show adverse effects after exposure, but it is those who can adequately deal with the environmental stress who may best direct us to how we can help the vulnerable to better respond.

Discussion Highlights: There are numerous examples of how physiology maintains homeostasis including accommodation of neurotransmitter receptors in the face of chronic agonist or chronic antagonist treatments, induction of liver catabolic enzyme systems, epigenetic modifications, DNA repair mechanisms, and induction of superoxide dismutase that help organisms cope with toxicant stresses without phenotypic impairment. These and other response systems such as induction of immunologic response for eliminating invading microbes or precancerous cells and neurobehavioral reactions to minimize further toxicant exposures can help minimize the functional impairment from toxicant exposures. Evolutionary adaptation has provided organisms with numerous systems which help maintain homeostasis. Indeed it is the exercise of these systems that can help with further response in thriving in a complex environment. The idea of achieving an idealized pristine environment without toxic challenges is unrealistic. We can decrease the toxicant load but not eliminate it. It is important to understand the mechanisms by which organisms can cope with toxicant challenges ameliorating their effect before they produce a functional toxic impairment.

Recommendations:

Pay attention to the reactions of the exposed groups in our studies who do not show functional toxic effects to determine the mechanisms by which they avoid such effects. This will help determine how endogenous mechanisms of homeostasis can protect from functional damage and provide leads into how to develop effective treatments for those who are vulnerable. Use of outbred lines to provide diverse response can facilitate this effort to understand diversity of response.

Discussion Participants:

Ed Levin, Claude Hughes, Deborah Cory-Slechta, Julia Gohlke

Report 57: Healthy Buildings and Communities

Convener: Howard Frumkin

Brief History:

The group identified several factors that make buildings and communities timely and important topics of environmental health research and capacity-building:

1. People spend the vast majority of their time in buildings, transportation infrastructure, and community settings.
2. The depressed economy has resulted in a great deal of deferred maintenance and substandard building conditions, which may threaten health.
3. The depressed economy has created a backlog of building demand; with economic recovery, there will be a substantial increase in building.
4. Similarly, the growing population (an estimated 100 million more Americans in the next 40 years) will create the need for extensive new building.
5. The advent of "green" building techniques, including new energy technologies, new building materials, and other innovations, will pose new exposures, which may have health implications.
6. Organizations active in design and building are eager to access health expertise, to enable them to reduce liability and create healthy places.
7. Major causes of morbidity and mortality, such as heart disease, cancer, asthma, and mental illness, all have plausible links to the built environment. If NIEHS places a priority on high-impact conditions, then the built environment is an essential focus of attention.

Recommendations:

Definition and scope

1. NIEHS should move toward a **broad, integrative view of human health** and well-being, using a contextual and systems approach. This means supplementing conventional biomedical, toxicological approaches with consideration of the whole person in the whole environment. The environment should be defined to include far more than the chemicals to which people are exposed; it should include the settings in which people spend time, and the infrastructure (buildings, roads, parks, etc.) that form those settings.
2. Similarly, NIEHS should consider not just toxic hazards, but also **environmental approaches to health promotion**, such as the design of healthy places.
3. Because architecture, building science, city planning, transportation planning, and landscape architecture create the environments that people inhabit, NIEHS should define these fields as

highly relevant to environmental health, and should support research and capacity-building that extend to these domains.

4. The "built environment" should also be considered to include **contact with nature** e.g. access to natural daylighting, parks, and greenspaces, since data suggest that these features may offer health benefits.

5. In addition to design and construction of the built environment, NIEHS should define **operation and maintenance** as part of its environmental health approach. Examples include cleaning materials and procedures, and HVAC system maintenance, which have clear potential impacts on human health.

6. The **economic impact** of the built environment on health is likely to be considerable, but needs much more study and quantification. NIEHS should include economic analysis in its approach to buildings and communities.

Programmatic recommendations

7. NIEHS should take a **leadership position** in studying health implications of building and community environments.

8. Understanding that large-scale funding and program-building are not feasible, NIEHS should establish a **focal point** within the Institute to lead this work, to identify collaborative and leveraging opportunities, and to guide program development over time. The small but effective Climate Change effort was cited as an example.

9. In pursuing this work it is essential that NIEHS **partner with other entities** to develop this research and capacity-building. While no other agency is in a position to lead, other agencies do have much to contribute—CDC's National Center for Environmental Health its applied public health approach, HUD its housing and urban planning expertise and industry partnerships, DoT its transportation expertise and industry partnerships, and NGOs and associations such as the American Institute of Architects and the US Green Building Council their extensive hands-on experience and expertise. In particular, NIEHS should lead HHS engagement with the Sustainable Communities Initiative (HUD, EPA, and DOT) since health considerations are regrettably absent from this effort.

10. Within NIH, NIEHS leadership should involve **partnering with other Centers and Institutes**. For example, NIEHS could partner with NIMH to explore mental health impacts of building design, with NCCAM to explore the benefits of nature contact, and/or with NHLBI to explore the health benefits of community design that promotes physical activity.

11. NIEHS should consider requiring involvement of researchers with design and construction expertise in certain grant-funded projects, analogous to the way the Children's Environmental Health Research Centers require basic science expertise.

12. NIEHS should focus on building materials that may expose occupants to chemical hazards, including both conventional materials and emerging new materials (an especially important category given the emergence of innovative "green" materials). NTP should prioritize chemicals that are found in substantial quantities in building materials, given the large potential for exposure.

13. NIEHS should prioritize those buildings and community settings in which at-risk populations spend considerable time, such as child care centers, schools, old-age homes, health care facilities, and low-income housing. Environmental hazard identification and control, and environmental health promotion, can yield considerable population health benefits in such settings.

14. NIEHS should consider awarding prizes or other forms of recognition to researchers who produce important findings that advance health at the scale of buildings or communities, and to buildings and communities that effectively incorporate health promotion and protection into their design and operation.

Discussion Participants:

Barnett
Brody
Hubal
Kostant
Long
Nicholas
Rosenthal
Schroeder

Report 58: Develop novel technologies and methodologies to detect and analyze (real-time) multiple exposures and their human health effects

Convener: Stavros Garantziotis

Brief History:

Multiple exposures are the reality in human biology. However, we do not really know what we are exposed to in daily life. We need to have accurate information on the multitude of exposures that may in aggregate affect human biology and development, even though they may be innocuous when viewed in isolation. The NIEHS has already developed an Exposure Biology Program which is piloting multi-exposure sensors. This panel would like to expand on this program in order to address the next generation of environmental exposure questions.

Discussion Highlights:

1. Exposures may be vastly different depending on geographic location and period of life
2. Real-time sensing is important for short-term exposure effects, but usually not as important for long-term effects (exceptions apply). Integrated exposures are sufficient for the latter. Technology for this may be more feasible.
3. Non-real-time exposures should therefore be the initial target of a development effort
4. Strategy will need to be guided by first attacking problems which have a finite exposure-effect window (e.g. prenatal/postnatal exposures on childhood development)
5. Understanding of biology will inform sensor development, but hypothesis-building data mining is also very valuable. In all, this will need to be an iterative process with a mix of biology-driven targeted sensing of specific toxicants, and non-targeted sampling of data.
6. Existing databases (such as NHANES) can be used to mine biomarkers of exposure, so that sensor development can be strategically guided to target the environmental toxicants associated with these biomarkers
7. Statistics and IT tools are currently available to handle the mass of data likely to result. Therefore, from the development perspective this seems to be more of an engineering problem.
8. Cross-pollination and interaction between disciplines (engineers, biologists, biostatisticians etc.) needs to be fostered.
9. Research initiatives need to be designed so that multiple questions can be answered with similar approaches, and that follow-up projects can be developed.

Recommendations:

1. Identify next generation of questions that are not answerable with currently available technologies and would be answerable within reasonable period of time.

2. Try to find combinations of problem areas and platforms that may be answered with similar technology

3. Panel identified child development issues as such an example (e.g. autism, childhood asthma), but other mechanisms such as RFI can be used to develop set of targets

4. Develop cross-discipline teams to design best approach (e.g. based on best knowledge of biology, available technology, etc.)

5. Promote process of refinement of pilot systems

6. Build upon existing Exposure Biology Program expertise and experience

Discussion Participants: Archer, Balshaw, Bird, Fargo, Fasman, Garantziotis, Nicholas, Serabjit-Singh, Weinberg, others on drop-in/out basis.

Report 59: The National Prevention Strategy: Integrating Environmental Health Research to Focus on Disease Prevention and Health Promotion

Convener: Dr. William Stokes

Brief History: The National Prevention Strategy was released by the National Prevention, Health Promotion, and Public Health Council on June 16, 2011. The National Prevention Council consists of the heads of 17 departments, agencies, and offices across the Federal government and is chaired by the U.S. Surgeon General. The Strategy is a cross-sector integrated national strategy that identifies priorities for improving the health of Americans. The of The Strategy's vision is "Working together to improve the health and quality of life for individuals, families, and communities by moving the nation from a focus on sickness and disease to one based on prevention and wellness." The overarching goal to increase the number of Americans who are healthy at every stage of life.

To realize the vision and achieve this goal, the Strategy identifies four Strategic Directions and seven targeted priorities. Healthy and Safe Community Environments is one of the four strategic directions. The Strategy recognizes that clean air and water, safe foods, and safe homes, schools, and workplaces are necessary to support good health and prevent disease and injuries. The Strategy recognizes that research is necessary to understand the extent of exposures to environmental hazards, the risks of these hazards, the impact of exposures on health, and to identify how to reduce exposures, especially among vulnerable populations (e.g. , infants, children, the elderly).

Discussion Highlights:

1. The need to evaluate the level of evidence needed to take regulatory and public health policy actions
2. The necessity of early involvement of all stakeholders in environmental health research.
3. How do we evaluate the impact of NTP and NIEHS research and reports, such as changes in NHANES biomonitoring levels?
4. There are multiple levels of prevention: Primary (prevent exposures), secondary (chemoprevention), tertiary(medical treatment)
5. The definition of lifestyle choices is overly broad and often inclusive of environmental exposures; these need to be identified and more appropriately addressed in prevention strategies and research
6. Other discussion points are summarized in recommendations

Recommendations:

1. Incorporate "Prevention Science" into the mission statement of NIEHS
2. NIEHS should be the hub/coordinator for NIH prevention research
3. NIEHS should develop a strategic (high impact) research program focused on prevention science (i.e., RFAs, PAs)
4. NIEHS should develop research programs to support the National Prevention Strategy to address the Strategic Priority for healthy and safe community environments (homes, schools, workplace)
5. NIEHS should, as a component of prevention science, measure the effectiveness of prevention strategies to demonstrate their value
6. NIEHS should adopt public health research goals aimed at preventing major diseases and conditions related to environmental exposures
7. NIEHS should review the lessons learned from 50 years of public health advances and effective interventions (e.g., removing lead from gasoline and paint) that focus on environment, and apply these to current environmental health issues
8. NIEHS should expand and enhance translational communications on prevention and effective interventions for a broad audience: affected communities, policymakers, clinicians, journalists, the general public. NIEHS should partner with NLM and others to accomplish this.
9. NIEHS should expand research to identify toxic exposures associated with adverse effects, and research on how to reduce/avoid exposures and to promote health and prevention
10. NIEHS should enhance interagency partnerships to support the National Prevention Strategy
11. NIEHS should Continue to focus on developing, validating, and gaining regulatory acceptance of improved safety testing methods that can be used as prevention tools to more accurately identify hazards ***before*** humans are exposed to such substances
12. NIEHS should improve environmental health literacy for the public, healthcare providers, and others
13. NIEHS should address issues raised in the President's 2010 Cancer Panel Report: *Cancer and the Environment: What We Can Do Now*, during the NIEHS strategic planning process

Discussion Participants:

Douglas Brugge, Geraldine Dawson, Michael Gould, Erin Hayes, Bruce Lamphear, Kimberly McAllister, Aubrey Miller, Jeanne Rizzo, William Stokes, Philip Wexler

Report 60: Advocacy

Convener: Nuala Moore

Brief History: At this time of reduced federal budgets, it is critical to increase advocacy to support NIEHS and maintain/increase federal funding.

Also a critical need to educate policymakers and the public on the importance of NIEHS's work to improve public health.

Discussion Highlights:

NIEHS's role in advocacy

- NIEHS cannot advocate directly but can disseminate information to advocacy organizations including the Friends of NIEHS
- Discussion of NIEHS's Office of Translation and usefulness of this information including factsheets on diseases. Conclusion that these factsheets are very effective tools for educating policymakers.
- Friends of NIEHS and other organizations can use NIEHS's research findings and information to educate/lobby policymakers
- With advocacy restrictions, how can NIEHS advocate for the best science?
- Long discussion of the need for NIEHS to build relationships with other federal agencies such as Dept. of Trans. so that these agencies follow science in their policy

Recommendations:

1) NIEHS should continue to build relationships with organizations such as the Friends of NIEHS, healthcare assoc., etc to disseminate their public health research findings.
2) NIEHS should be a spokesperson for environmental health science.
3) NIEHS should find new ways to disseminate science to regulatory agencies, including EPA, OSHA and others.
4) NIEHS should continue to do policy-relevant research
5) NIEHS should seek ways to build relationships and an ongoing forum with other federal agencies (such as Dept. of Transportation) that are/should be impacted by NIEHS's research in order to achieve better policy practice results.
6) Require industry to contribute to an emergency fund for new environmental threats, to include supplements to environmental health centers.

Discussion Participants: John Balbus, John Bucher, Lisa Conti, John Froines, Joe Graedon, Andrea Hricko, Paul Jung, Martha Nolan, Jennifer Sass, Kristina Thayer

Report 61: Basic Research on Mutagenic Mechanisms Using Model Systems

Convener: Phil Hanawalt

Brief History: Fundamental study of the mechanisms of genomic maintenance has been a subject of world-class research across NIH, but especially through the NIEHS intramural and extramural programs. Discoveries using model systems have led to, for example, the role of mismatch repair in colon cancer, the mechanism of triplet repeat expansions in neurological disease, and in general, the development of screening tools and test systems for identifying genotoxicants. Molecular structures are being determined for relevant enzymes to reveal mechanisms and to yield crucial information for intervention (e.g., through small molecule inhibitors). Model systems promote understanding of the factors involved in response to damaging agents and may help to simplify the assessment of environmental risks to humans. New sequencing technologies can now be applied to single cells and simple organisms used as models for repair. Mechanistic research facilitates the understanding and interpretation of sequence changes and "mutational fingerprints" of environmental exposures.

Discussion Highlights:

- Our current understanding of how cells respond to environmental genotoxicants (for example, development of the Ames test) are only possible because of fundamental research in DNA repair.
- There are still great untapped opportunities for understanding the function of genes in model organisms that respond to DNA damage. For example, in *E. coli*, the recN gene is the most highly upregulated gene in response to damage. Yet, the function of this gene is not currently known.
- Research on effects, for example, of unusual secondary or alternative structures (non-B DNA) point to increased susceptibility to damage from toxicants as well as reduced repair in these sequences. Although some effects are likely subtle, all contribute to overall disease risk.
- Model systems permit the application of single and multiple gene knockdowns to dissect the genetic contributions to damage response and to understand basic mechanisms.
- Fundamental research in DNA damage/repair related to environmental exposures supports studies of cancer etiology, neurological disease and aging.
- Basic research should encompass studies at multiple layers of complexity, from studies with naked DNA through chromatin organization in higher organisms.

Recommendations:

- NIEHS should continue to promote cutting-edge, mechanistic research that maintains the Institute as a world leader in understanding environmental genetic toxicology and disease.
- We should take advantage of new sequencing technologies and other novel tools for single cell genomic sequencing to obtain mutational fingerprints from environmental exposures and to

understand repair mechanisms that are operative. Information from these efforts will be crucial for advances in intervention and prevention.

- Among systems for mechanistic studies, we should not overlook the importance of bacteria, yeast, and other model systems. Basic research gives us insights into the limitations of various test systems (including rodent models) as surrogates for humans. Comparative analysis of different systems is therefore critical.
- We should continue to explore potential translation of fundamental discoveries to environmental health issues.

Discussion Participants: Hanawalt, Worth, Adelman, Williams, Shaughnessy, Tyson, Mural

Report 62: A systematic evaluation of alternative model organisms for understanding the effect of environmental exposures on human development and health.

Convener: Antonio Planchart

Brief History: Currently, there are two favored approaches to understanding toxicity: in vitro, cell based models (low level) and in vivo rodent models (high level). However, the power of other comparative models, including vertebrate and invertebrate models, has not been adequately exploited to understand environmental health effects in humans despite their long and valued history in other scientific disciplines that have recognized their importance in understanding mechanisms that are fundamental to human biology, including development and disease. Embracing alternative models for toxicological studies can contribute to many aspects of environmental health research, including augmenting our understanding of critical stages during human development that lead to structural birth defects or set the stage for fetal origins of adult human diseases when perturbed by environmental exposures.

Discussion Highlights: It was acknowledged that a more systematic approach to developing and using alternative model organisms for use in environmental health studies would accelerate the pace of understanding the adverse outcomes on human development and health resulting from environmental exposures.

Recommendations:

- There is a real need to move away from treating model organism studies as purely ecological studies and instead focus on understanding why they are good proxies for understanding human biology. Other biological disciplines, (e.g., genetics, developmental biology, physiology) have long recognized the relevance and importance of multiple model organism systems in understanding the molecular bases of heredity, embryonic development and systems biology. There is much to be gained in the field of toxicology by embracing multiple model organisms to address specific questions related to the environment and its role in human development and health.

- There is a need to perform comprehensive evolutionary analyses among diverse model organisms (e.g., C. elegans, zebrafish, sea urchin, flies, Daphnia, Medaka, Tunicates) in order to determine the degree of biological pathway conservation and the degree to which these pathways are affected by environmental exposures. This knowledge will facilitate identifying the most cost-effective and efficient system in which to deploy strategies for:

    - Developing “green” chemicals that do not pose substantial teratological, developmental or adult health risks;

    - Evaluating which chemicals pose the greatest risk to human health, and establishing sound biological reasons to prevent their commercialization;

    - Understanding the biological outcomes of exposure to environmental stressors, toxins and toxicants;

  - Evaluating the role of candidate genes/proteins in the mechanisms leading to toxic outcomes;
  - Validating in vitro studies using in vivo systems that are cost-effective, genetically tractable, and result in rapid knowledge acquisition.

- Use of alternative models with rapid generation times can be valuable for understanding the role of parent-of-origin contributions (epigenetics) to the development biological risk factors leading to the onset of disease later in life.

Discussion Participants:

Terrence Collins

Carolyn Mattingly

David Miller

Antonio Planchart

Ray Tice

Report 63: Integrating community outreach and translation into research

Convener: Daniel Madrigal

Brief History: There are several permutations of the community outreach, engagement, and translation cores that are attached to NIEHS projects. For simplicity, they will be referred to as engagement cores. Across these engagement cores there are variable levels of prioritization/ importance placed on the communication and outreach work done. Some NIEHS projects highly value community engagement, others do not.

Discussion Highlights:

Importance

- NIEHS is at a place where it can move forward community outreach efforts. In the past community outreach had been deprioritized (defunded).
- Opportunity to demonstrate relevance.
    - To public health.
    - Especially important in the current fiscal environment
- Moral imperative.
- Growing uncertainty of the public of the impact of environmental health exposures.
- NIEHS needs visibility.
- There are many grantees, now is the moment to build the network. Let's not reinvent the wheel.

Other highlights

- Encourage current efforts of community engagement that are successful.
- Important to differentiate between engagement, education and partnerships. All have a specific role. Partnerships should be encouraged.
- Discussion as to what level of community engagement is needs to be a part of every project. It was agreed that a plan for communication should be included for every project, as long as "community" can be broadly defined. For bench science, the relevant community may be restricted to other researchers.
- There is a lack of clarity as to the distinction between the different engagement cores. A discussion was had as to whether a future recommendation would be to have these cores work together more effectively. It was noted that historical structure of these various cores may present an obstacle to working together across engagement cores. Currently PEPH is one effort

to build a network between these groups of engagement cores (community outreach and translation core vs. community outreach and engagement, and others).

  - Another need is for the grantees of engagement cores to have a better understanding of the network of engagement cores funded by NIEHS. Who is doing what, where?

- Link March meetings of the PEPH to hill visits (to educate congress members of environmental health research).

Recommendations:

- Find ways to elevate dissemination of research in the NIEHS mission statement.
  - There should not be "token" dissemination, sending something out just to check off the dissemination box.
- Increase public health relevance and communication in the grant scoring process.
- All NIEHS funded projects should consider public health relevance. It should be written into the grants.
- All NIEHS should include a communication plan. Communication to the relevant stakeholders.
  - All "center-like" programs should have a community engagement component.
- Simplify engagement cores. Phase out distinctions between the different types of engagement cores. One name so that the general public can have a better understanding as to what these cores do.
  - This could be done through the PEPH meetings, if the grantee community engagement meetings (such as COTC or COE) occurred at the same time as the larger PEPH meeting.
- If the several engagement cores remains, there should be a clear explanation as to how they are different.
- Support PEPH goals of building network of engagement cores
  - A section of contacts of coordinators/directors of engagement cores across NIEHS so there may be more instances of collaboration/ center-to-center communication.
  - Success stories.
  - Lessons learned (what didn't work out so well, sharing these stories so others may learn). This may be more effective in a space that is only open to grantees.
- Support formal training of community outreach and engagement skills.

- A place to do this is at grantee meetings or the PEPH conference. There could be a training at the beginning or at the end of these meetings that can build the skill sets of those doing community engagement work.

Discussion Participants: Jose Cordero, Kathleen Gray, Erin Haynes, Liam O'Fallon, Banalata Sen, Carol Stroebel

Report 64: Protecting our investments by providing infrastructure and support to biorepositories, cohorts, and datasets to expand our ability to study new and emerging hypotheses

Convener: Gwen Collman

Brief History: Many clinical and population studies have been supported over the last decades which enrolled large populations and accumulated massive amounts of data and specimens. There is the potential to use these data and specimens to answer new and emerging scientific questions on hypotheses not yet defined. Specimens are being stored in freezers in various formats with varying methods. Technologies are now available to more effectively track, organize and retrieve samples and link them to databases in order to expand the universe of scientific questions that can be addressed. Databases are currently unconnected and not readily open to new users. Now is the time to build an infrastructure that will support data sharing and discovery science and maximize the utility of data that has been collected in the past. With the recognition of the importance of the effects of early life exposures on adult diseases and health outcomes, it is critical to maintain cohorts and other population resources in order to study emerging hypotheses in the future.

Discussion Highlights:

Biospecimens

Need to build biorepositories in a way that saves a diversity of tissues and specimens collected and processed in ways that allow for and not limit future analyses on known and emerging analytes. There is a new to create or apply standards for EH repositories to assure responsible stewardship.

Need for guidelines for specimen storage for EH research and 'how to' resources for investigators

Promote ways to use clinical samples which might be discarded for EH research

Broaden the use of core facilities to support the long term storage of specimens for EH research. Promote EH research within the CTSA network and become part of the CTSA programs in order to utilize CTSA resources to protect study investments (specimens, cohorts, data)

Create and incentivize opportunities for specimen and data sharing within collaborative groups and give access to new investigators. Reduce barriers to sharing specimens by simplifying Material Transfer Agreements, consider consent and IRB issues, and confidentiality and privacy issues

Create new models for collaborations around existing study resources. One example is an auction which would reward bidders with access to specimens and study materials based on collaboration parameters (bids)

Encourage new/young investigators to use already collected specimens and data to test emerging hypotheses by granting access to study resources

Cohorts:

Create study framework with long term goals and needs for preservation of resources for study follow-up, specimen storage, data preservation over the appropriate time frame (Don't just think in 5 year cycles)

Tie maintenance of cohorts to relevant study goals and prepare for active and passive follow-up. Provide support for both types of follow-up irrespective of hypothesis testing.

Utilize creative funding mechanisms to keep study infrastructure intact in order to pursue long term scientific questions. These can include community partnerships, passive or active follow-up, critical data collection not tied to main hypotheses but tied to possible future questions. Find ways to fund additional data collection at time sensitive windows

Data:

Change the paradigm from local use to use by the greater EH community. Identify barrier and solutions to assuring privacy and confidentiality and the responsible use of EH data

Promote secondary data analyses and create incentives to use datasets beyond initial hypotheses by a single study team

Support the creation of datasets available for sharing and provide financial support for data sharing activities.

Recommendations:

NIEHS can provide leadership to support the increased use of investments to answer new and emerging scientific questions within study populations that have been previously created. They can do this by supporting long term support for biorepositories, long term maintenance and tracking of study populations, and by promoting more open access to properly created data sets (with privacy and confidentiality protection assured).

NIEHS should think strategically about study populations and resources that would be needed to answer emerging scientific questions in the future and should actively plan to support and maintain those resources.

NIEHS should create financial and resource incentives to promote sharing of study resources by the wider community in order to maximize its investments

NIEHS should catalogue study resources (cohort characteristics, specimens, and data), advertise them, and actively promote their use throughout the wider EH community. This can include web-based catalogues of information, presentations about resources, and other notifications about the availability of resources.

Discussion Participants: Gwen Collman, George Leikauf, Craig Newschaffer, Marie Lyn Miranda, Tracey Woodruff, Julia Brody, Chris Bradfield, Marie- Francois Chesselet, Stephanie Holmgren

Report 65: Early life exposures in childhood and adult disease: role of susceptibility factors

Convener: Bill Suk and Steve Kleeberger

Brief History: From a mechanistic standpoint, evidence suggests that exposures to environmental agents during early life have adverse impacts on childhood and adult disease, as well as susceptibility to additional exposures. In addition, disease prevalence data indicate a dramatic increase in complex/chronic diseases, which may be the result of exposures to environmental agents in early life. These observations have led to questions regarding mechanisms of susceptibility and/or predisposition to this important disease etiology.

Discussion Highlights:

Parallels were drawn between challenges and opportunities in the role of epigenetics and genetics in this environmental disease process.

Exposure assessment is critical

Need for incorporating exposure in GWA studies

Need to build upon NIEHS GEI/Exposure biology investment

Which environmental exposures are important to measure (e.g. particulates, metals, infectious agents, endotoxin, etc.)

Biomarkers of exposure, development, and link of these exposure development markers to adverse outcome(s).

Primary outcomes that were discussed included complex diseases such as cancer, diabetes, asthma, autism, and neurodevelopmental/neurocognitive deficits. A secondary outcome that was discussed was growth stunting.

Interaction of early life exposures and childhood and adult disease is a global health concern.

Consideration of microbiota and microbiome signatures as important factors in disease susceptibility and progression.

There is a necessity to put in place as soon as possible mechanisms to intervene and/or prevent early life exposures to environmental agents. This could include putting in place interdisciplinary centers for research and prevention/intervention in maternal and child health.

Importance was stressed on the development of animal models to identify genetic and other mechanisms of susceptibility to tease out windows of opportunity to link exposures to adverse outcome.

Discussion regarding early life exposures and latency of disease onset (i.e. short- and long-term) and the ability to study and model/understand the link between exposure and disease: in addition to being an exposure and disease interaction, there is also an important temporal component.

Recommendations:

Need to identify and develop state-of-the-art methods and capabilities in analytic chemistry for measurement of 1) biomarkers of response and exposures, and 2) various environmental agents in the individual.

Develop interdisciplinary models for research, i.e. development of research programs to address this complex and important susceptibility by environment interaction in the development of disease.

Need to develop tools to understand the interaction between susceptibility factors, exposure modalities, disease outcomes, and time to disease onset.

Exposures should be inclusive to incorporate environmental chemicals, infectious/parasitic agents, and other biologics during early exposures. These are global health concerns and must be addressed within that context.

Develop a large prospective study to investigate early environmental exposures and multiple primary and secondary outcomes. This study should leverage resources from partner ICs. There was also identified a need for biobanking, miniaturization of samples, and bioinformatics expertise.

Need to

Discussion Participants:

Dawson
Edwards
Fargo
Finnell
Gilliland
Groopman
Hennig
Kiley
Kleeberger
Suk
Taylor, J
Taylor, P
Umbach
Waalkes
Wright

Report 66: Science-based Risk Assessment

Convener: James Swenberg

Brief History: Our knowledge base of toxicology and environmental health has increased dramatically in the last 25 years, but risk assessment frequently reverts to using "default" approaches rather than a strong science-based approach. The NIEHS is positioned to champion the use of detailed science-based approaches to improve the risk assessment process. This is seen as a critical element for the Strategic Plan of the NIEHS.

Discussion Highlights:

- The Framework Mode of Action (MOA) approach outlined by Sonich-Mullin (2001) provides an excellent approach to evaluate and incorporate scientific research on MOA into the risk assessment process so that decisions are transparent.
- A major factor that drives the use of "default" approaches is insecurity associated with uncertainties. Research on MOA, dose-response and PBPK modeling can reduce uncertainties. As such, it represents an important area deserving high priority in the Strategic Plan.
- Likewise, Systems Biology of the underlying pathways and dose-response leading to disease are both supported by NIEHS and highly relevant to risk assessment.
- The NIEHS should support the development of tools and data to facilitate the use of in vitro assays to predict in vivo effects in a quantitative manner.
- The Report on Carcinogens should evolve from a "Strength of evidence" to a "Weight of evidence" approach to incorporate our improved scientific understanding of exposure and dose-response in chemically-induced diseases in order to move from Hazard Identification to Hazard Characterization.

Recommendations:

- The NIEHS should strongly support research that provides better and high quality information to fill knowledge gaps relevant to risk assessment, such as better data on MOA, improved PBPK models and vastly improved information on human exposures.
- NIEHS should support scientific meetings to examine the risk assessment process and identify where scientific data were or were not well used, where data disagree, and how the risk assessment process could be improved by better incorporating scientific data.
- NIEHS should return to offering RO3 grants to enhance interactions between researchers and the NTP to improve our understanding of the MOA.
- The NTP needs to increase the number of studies on mixtures to enhance knowledge our understanding of MOA and cumulative risk.

- The NTP is encouraged to contrast the cost of their toxicology and research studies with the costs of remediation and human health.
- Training of graduate students and postdoctoral fellows in science-based risk assessment should be an important feature of NIEHS training grants.
- The ROC should enhance the incorporation of MOA and dose response information to support a weight of evidence approach leading to Hazard Characterization.

Discussion Participants:

Berry Dellinger

Michael DeVito

Paul Foster

Julia Gohlke

Heather Henry

Robert Kavlock

Christopher Kemp

George Lucier

Richard Miller

Frank Mirer

Michael Pino

James Swenberg

Report 67: Informatics partnerships, services and infrastructure for intramural and extramural EHS research

Convener: Ken Fasman

Brief History: As with many other areas of science, the pace of data generation in environmental health sciences (EHS) has outstripped the existing resources for information acquisition, management, analysis, visualization and dissemination. There seems to be a broad consensus in the community that more informatics expertise and resources are required to support both intramural and extramural NIEHS research.

Discussion Highlights:

- Relationship with NCBI and other organizations/groups with significant informatics expertise
- Promoting EHS informatics – building on existing bioinformatics and cheminformatics disciplines but taking into account particular needs of EHS research, such as the role of GIS information
- Education and training – how to create the next generation of EHS informaticians, how to spread these skills and techniques throughout the community to address broad needs
- How best to provide EHS informatics services to both intra- and extramural research? ("There's a great bioinformatician down the hall from me, but he's only interested in his own research questions. I need a consultant – even better, a scientific collaborator -- to help me organize/analyze/visualize my data.") There are a number of models to choose from:
    - NIEHS intramural informatics group supporting intramural research only
    - Intramural informatics group supporting both intramural and extramural research
    - Contracting with commercial informatics companies to provide service to intramural and/or extramural activities
    - Funding a network of one or more academic groups as national centers of EHS informatics (e.g., as the biomedical imaging community have done) – look for groups that are already doing this well at the local, institutional or regional level
- Creating registries for EHS data resources, informatics tools, and services so that the community can be aware of, and effectively utilize, already existing resources
- Advising and guiding both intramural and extramural investments in IT hardware (storage, high throughput computing, networking, etc.) about in-house investment vs. cloud computing. Individual NIEHS grantees shouldn't have to answer these questions again and again on their own.

- Creating the infrastructure for an "EHS network" sharing data, storage and computational capacity, along the lines of caBIG for NCI research -- without repeating the specific mistakes of the caBIG program!

- Improving NIEHS's ability to connect, collaborate and leverage related activities in other NIH institutes and peer organizations (EPA, CDC, FDA, etc.) despite the Institute's geography

Recommendations:

- NIEHS should make environmental health science informatics a priority to make the most of its research investments. Investment is required in order to foster the development and expansion of this discipline to meet the needs of the scientific community.

- This investment needs to take the full life-cycle of scientific data into account. Once we fund scientific studies to generate new data, we should consider how the data will be organized and disseminated, visualized, and integrated with other related information. We must also consider the useful life span of the information, and provide for its maintenance during that lifetime.

- Please don't reinvent the wheel. Leverage the existing NIEHS intramural informatics service model, as well as the considerable expertise of NCBI and other organizations and academic groups with significant informatics expertise. Don't "go it alone."

- Successful partnerships among (EHS) informatics, traditional Information Technology, and Library and Informatics Sciences are difficult to achieve; many organizations have stumbled here. There are various models for implementing this, but success usually depends on active sponsorship from the organizational leadership as well as strong, mutual respect among the disciplines.

- These and related informatics issues seem to run through many of the topics over the past two days. These threads could be braided together to create a unifying informatics theme for NIEHS.

Discussion Participants: Stephanie Holmgren

Report 68: Bottled water: where is the science, are we wasting resource and needlessly anxious

Convener: Cosette Serabjit-Singh

Brief History: Bottled water represents a fairly recent change in US beverage consumption that contributes to waste, a return to dental caries seen in the absence of fluoridated water and may represent a belief that tap water represents a health risk.

Discussion Highlights: Budget for health care and research is constrained and focus on the important health concerns can be eroded by concerns that are unfounded. Is the scientific knowledge about real vs. imagined health risk informing consumer choice, bottled water being representative? Is it the responsibility of agencies like NIEHS to assure consumers when there is little risk?

Recommendations: Determine whether there are community concerns (such as health benefit of bottle water) that can be addressed with available evidence, especially those concerns that impede moving environmental health sciences forward.

Discussion Participants: Cosette Serabjit-Singh, Joellen Harper Austin

Report 69: Infectious Diseases and the Environmental Health Portfolio

Convener: Ellen Silbergeld

Brief History:

Over the past 50 years, infectious disease has moved out of the environmental health portfolio of research, clinical medicine, and public health practice – for a variety of reasons. As a result, the NIEHS research portfolio has relatively little intra- and extramural investments in this area. It was generally agreed that this situation has opened up "holes" in knowledge and missed opportunities for understanding and predicting disease risks as well as designing interventions and preventive health programs.

Much of the gap concerns understanding the importance of the environment in transmission and in population response. Examples: understanding how the environment may influence pathogens (persistence, virulence and infectivity); understanding how environmental exposures may affect host response and variations in host response within populations.

History: NIEHS used to be involved in the EID program at Fogarty, but not so much at present (info from FIC) and not in a way that integrates the NIEHS "take" on EH into ID research.

Earlier discussions on immunotoxicology are relevant to this discussion as well, and participants from that workshop were present at this meeting.

Discussion Highlights:

Discussion recognized the importance of a strategic approach in terms of resource constraints and "turf" among NIH institutes.

Immunotoxicology and its relevance to infectious disease could be a critical handhold in such discussions.

Also, interest in the environment and microbiome (see workshop) is relevant, as this area of research is considering how exposures (nutrients, pathogens, and chemicals) may modify human microbiomes and how the microbiome may modulate presentation of environmental exposures (e.g., metals, organics).

Other discussion topics: knowledge base on exposures to air pollutants and ID; could go both ways (ID as an effect modifier of response to air pollutants, or air pollutants as modifiers of response to pathogens) Examples were: air pollutant and RSV; cookstoves and early respiratory infections in children (including TB), possible activation of dormant pathogens and changes in viral latency may be associated with environmental exposures (note: some of these exposures include nutrients, and "beneficial" chemicals should also be considered).

Much discussion on building the case for valuing integration of EH perspectives and knowledge into ID in order to reduce burdens of disease. This focused on two directions: building case from toxicological and mechanistic data on specific environmental agents (such as ozone or mercury) and utilizing existing

large cohort studies to insert methods to assess associations between environmental exposures and immune status or disease risk. Examples included utilizing existing sources, such as the Agricultural Health Study or NHANES (which include biosamples as well as extensive annotation on participants in terms of exposures); seeking to participate in longitudinal studies to include appropriate sampling and information (ex: study vaccine "take" in the NCS, being sure to include a sample of the vaccine administered); the MADGC study on persons with multiple autoimmune diseases; drawing in opportunities from research in the developing world where both environmental exposures (e.g. e-waste) and infectious diseases may be significant in terms of risk.

Recommendations:

1. We need momentum to energize this conversation by developing an agenda that builds the case for the importance of integrating ID and EH
2. We also need to find ways to bridge the research gaps in existing research portfolios by conversations among NIH institutes and others
3. Convene a workshop to discuss opportunities for exploiting existing population studies such as NCS, including both large environmental health studies as well as large ID studies with equal weight and potential value.

Discussion Participants:

Ellen Silbergeld, Paige Lawrence, Christopher Long, Jerry Phelps, Joshua Rosenthal, Kimberly Thigpen Tart, Linda Birnbaum, Lisa Conti, Michael Fessler, Virginia Ladd

Report 70: The role(s) of ncRNAs in environmental health

Convener: Frederick Tyson

Brief History: A number of functional roles in cell biology are emerging for classes of RNA transcripts that are not translated. These non-coding RNAs (ncRNAs) appear to contain a hidden level of internal signals that: control gene expression in development and help determine cell/tissue specificity; are involved in maintenance and establishing chromatin architecture; involved in development of epigenetic memory; and regulate alternate splicing and RNA editing. ncRNA regulatory networks may be involved in the determination of complex characteristics and play a significant role in disease pathogenesis. There are programs such as the NHGRI funded ENCODE that are cell specific ncRNAs but these are being examined in static situations, or the absence of environmental toxicants. Questions have been raised about how exposures might induce SNPs that alter ncRNA function or non-genotoxic agents may alter binding of ncRNAs. There is emerging data indicating that ncRNAs can be modified by environmental stressors but much of this is preliminary. Exploration of how exposures interact with ncRNA function represents an opportunity for the NIEHS to practice **proactive toxicology**, taking advantage of novel biology and exploiting exposures to inform both normal biological processes associated with ncRNAs and elucidate the role of exposures and ncRNAs in disease pathogenesis.

Discussion Highlights:

- Environmental agents trigger cascades of signal transduction networks via ncRNAs.
- ncRNAs (tRNAs) can serve as sensors of exposures, tRNAs have modifications associated with stress responses.
- Determine the extent of exposure responses to ncRNA regulated editing and generation of splice variants.
- How does the subcellular localization of miRNAs contribute to polarity.
- What is the role of miRNAs in cell migration.
- How do exposures contribute to RNA turnover/decay factors/termination factors.
- Do exposures impact ncRNA chaperones or ncRNA repair.
- How might exposures influence genome instability through ncRNA mediated stress responses.

Recommendations:

- NIEHS support development of novel technologies to discover unknown miRNAs; improve on currently used mass spectrometry technologies for the detection of modified RNAs;
- Invest in the elucidation of the roles of ncRNAs and responses to environmental stressors in disease etiology and pathogenesis;
- Incorporate the study of ncRNAs in defined model systems with coordinate epigenomic and underlying genetics analysis;
- Include the study of ncRNA exposure responses in the broader exposome program.

Discussion Participants: Karen Adelman, Tom Begley, Linda Birnbaum, Chris Bradfield, John Cidlowski, Traci Hall, George Leikauf, Fred Tyson, Rick Woychik

Report 71: Environmental pressures over space and time—taking advantage of novel technologies

Convener: Julia Gohlke

Brief History:

Compared to other biomedical fields, environmental health deals with complex spatial and temporal components to link exposure to outcomes. Technologies to evaluate space and time dimensions of the environment, such as remote sensing datasets, are currently being underutilized and are particularly important for looking at environmental aspects of complex diseases, health impacts of climate change, and health disparities. On longer time scales, evolutionary approaches to tease apart adaptive responses to the environment are key to understanding gene-environment interactions (i.e. environmental pressures on previous generations shape the genomes, behaviors and hence health outcomes today) and predictions for limits of adaptation to climate change. In 2005, NIEHS convened a workshop on global earth observations applications to air quality and human health, and findings from this workshop could serve as a basis for expanding this topic further.

Discussion Highlights:

Particularly for epidemiological studies, geospatial datasets are key to understanding composite exposures. Spatial data architectures can provide environmental exposure estimates through integration of census, land use, hydrology, community resources, health care access, green space, built environment, crime, air pollution, water quality, product purchasing demographics—when cohorts are geo-referenced relationships can be tested. This will be particularly useful for integration with medical records datasets. Evolutionary biology is particularly important for looking at environmental justice and health disparities research. For example racial differences in vasculature may be explained by environmental conditions at locations of origin. GIS datasets are particularly useful for determining disproportionate exposures across communities and relevant for environmental justice. EWAS studies will be able to use these technologies. In terms of climate change and health, studies of relative fitness across temperature and hydrological parameters across different model species will be useful for establishing estimates for limits and mechanisms of adaptation.

Recommendations:

1. Explore the possibility of joint RFAs or programs with NASA and/or NSF using remote sensing and evolutionary biology to answer environmental health questions.

2. Leverage resources in CTSAs by enhancing with environmental datasets—linking medical records will provide spatially referenced cohorts to examine environmental health questions.

3. NIEHS should develop intramural and extramural programs in GIS, remote sensing, and spatial statistics.

4. Develop spatial data architecture on a regional basis (e.g. pick one state from NE, mid-Atlantic, Deep South, Mid-West, SW etc.) to explore differences in exposures—this is particularly relevant for health disparities and climate change research programs.

5. Prioritize mixtures exposures most relevant for testing by NTP via use of spatial data architecture outputs.

6. **Support research in ecologically relevant model systems to look at time/space interactions over multiple generations to determine evolutionary pressures.**

Discussion Participants:

Marie Lyn Miranda

Ray Tice

Julia Gohlke

Report 72: Infrastructures for the Environmental Health Sciences

Convener: David Balshaw

Brief History:

Over the past decade numerous technologies have emerged, and continue to emerge, that hold the potential for fundamentally altering the way environmental health sciences research is conducted. Many of these technologies have either been slow to be adopted broadly or are inherently not suitable to wide-spread adoption. This session was focused on identifying strategies and topics for establishing centralized clearing houses for these technologies

Discussion Highlights:

The discussion focused heavily on technologies for exposure assessment and the varying needs of studies in terms of the analytical capacity of exposure assessment technologies in terms of the temporal resolution, number of analytes, complexity of the device and the cost of analysis.

A sentiment was voiced that tools that can be utilized by the lay public would be particularly powerful.

For more traditional analytical capacity such as biomarker detection the ability to certify laboratories as providing 'true' values was advocated. Two models were discussed, one was the use of a licensing protocol where certain labs would be certified, the other was the publication of standard procedures and certified quality metrics that could be more widely utilized.

Recommendations:

Establish a clearing house for exposure assessment capacity. This would span scales of analytes and technologies and be applicable to a range of studies from panel to mega populations of more than 50,000 subjects. It could also include an iTunes type infrastructure for mobile apps that could measure noise exposure or provide geospatial analysis of exposure and integration of diet and physical activity. This could also support validation of exposure metrics.

A second clearing house could include biomarker detection and validation including large scale mass spec expertise.

A third infrastructure would be an animal studies facility that would provide behavioral assessment, phenotyping and moderate to high throughput screening.

A fourth infrastructure would be a centralized database curating and adjudicating literature information on exposure and response that would allow imputation of exposure disease relationships.

A fifth infrastructure was discussed that is not limited in scope to NIEHS but is of critical importance; centralization of IRB assurance and informed consent for multi-center clinical studies.

Discussion Participants: Armstrong, Balshaw, Bird, Hricko, McConnell, R. Miller, Peden, Sandler

Report 73: Genome/Environment Interactions

Convener: Richard Mural

Brief History: The genome is shaped over evolutionary time by the environment and an organism's genome determines how it interacts with the environment. The interaction of the genome and the environment leads to the observed phenotype. Since the completion of the human genome 10 years ago the cost of whole genome sequencing (WGS) has dropped to the point that it is now, or soon will be, possible to use WGS as a method for discovery of genetic variants that are associated with phenotypes of interest to NIEHS. It is also possible to generate very complete data such as complete genetic variation within and between populations, the intergenerational mutation rate, estimation of the selective pressure on various alleles, etc. The use of WGS and the use of data generated by WGS that illuminates basic human biology should be a central focus of the NIEHS five year plan.

Discussion Highlights: A number of interesting point were discussed:

WGS shows promise in extending and expanding the results of Genome Wide Association Studies (GWAS) which have often been disappointing to those studying the genetics of responses to environmental factors.

GWAS often lack data on environmental exposures of the study populations.

Family studies using WGS to study effects of environmental exposures may be powerful and useful.

In addition to powerful new tools for WGS or resources such as the mouse diversity plan and the mouse strains generated by the Collaborative Cross will provide substrates for proof of principle studies for populations based studies of the effects of various environmental exposures.

Recommendations:

NIEHS should leverage data from WGS studies that give new insights into human variation, population structure and critical parameters of human biology such as intergenerational mutation rates in the design of future studies.

NIEHS should support the use of WGS methodologies to discovery human variation associated with response to environmental exposures.

NIEHS should support the use of WGS for family studies to understand the genetics of response to environmental exposures.

In addition to using various WGS technologies, NIEHS should leverage new mouse resources like the diversity panel and Collaborative Cross as models for studies of the role of variation in human population responses to environmental exposures.

Discussion Participants: Richard Mural, Marie-Francoise Chesselet, Kimberly McAllister, Clarice Weinberg

Report 74: Integrated Assessment and Testing Approaches (IATA)

Convener: Robert Kavlock

Brief History: The topic was based on two assumptions: (1) it is a fundamental mission of NIEHS to provide information on the hazards and risks of environmental chemicals and (2) the current approach to hazard and risk determination is neither efficient nor effective as it needs to be. There are too many chemicals with too little data, and the data to reduce uncertainties in the risk assessment process even for data rich chemicals is less than optimal based upon recent experiences. The emerging transformation of toxicology is posed to change both the methods used in (1) and the approach used in (2). In order for this transformation to occur, it is necessary for a strategic plan by which the knowledge of human disease processes are discovered and how these discoveries can be applied in the conduct of chemical safety assessment studies

Discussion Highlights: The IATA approach has been proposed by a number of organizations (e.g., IPCS, the Canadian Council of Academies, EPAs Office of Pesticide Programs) as a way to intelligently integrate the information coming from various data domains (e.g., in silico models, computational chemistry, high content and high throughput bioassays, genomics (broadly defined), human exposure, pharmacokinetics, etc,) in order to better understand the likely biological targets of chemicals which in turn will inform the design of specific animal bioassays to define critical dose-response information. For example, screening results may point to a chemical to possess activities that suggest potential impacts on cardiovascular function, and animal bioassays would be specifically designed to explore this lead at a higher level of biological organization. Conversely, this chemical would be de-prioritized for effects on cancer because the screening results showed a low probability of cancer mechanisms being triggered.

To date, however, there has been no broad scale effort to bring all the components needed for IATA to occur and it remains largely a theoretical construct (although components of IATA are being employed in NIEHS and regulatory organizations across the globe). This is despite all the potential benefits that might occur by its full implementation and use. If successful, the IATA approach would allow for a transparent and uniform way to integrate the information flow from various sources, target animal use appropriately, and address the key uncertainties normally present in contemporary chemical risk assessments. For this to happen, it is important that the field not develop in a haphazard process, but be guided by strategic planning and implementation. The challenges to implement IATA are broad, and it will take a coordinated effort to realize the potential. NIEHS has the capabilities and capacity to be the leader in moving the IATA approach forward and bringing us closer to the vision of toxicology in the 21st century.

Recommendations:

- IATA could become a unifying concept by which research on chemical safety is conducted at NIEHS and should be guided in its development at the Institute level.

- NIEHS should become the institute that leads the transformation of development of the knowledge bases for human disease etiology caused by environmental chemicals (and other influences) and their application for disease prevention.

- NIEHS should become the leader in transforming the process of chemical safety assessment by developing broad scale proof-of-concept studies that show the potential of IATA in resolving key toxicological issues

- There are complementary roles for the DIR and DERT with the NTP in moving the science forward. Basic discovery of causes of diseases would be the responsibility of the DIR and DERT (and other NIH institutes) and this knowledge would be actively transferred to the NTP for application of proof of concept. Conversely, the NTP could advise the DIR and DERT about significant gaps present in the ability to characterize the broad spectrum of biological interactions of concern to guide basic biological discovery. NIEHS is uniquely positioned to foster this activity as a core part of its mission.

- There is also a role for broader cross-NIH interactions to mine the information on basic biology of disease pathways and to bring that information into the context of environmental health. The multi-disciplinary expertise available within the NIH is an extremely valuable resource to be tapped.

- Implementation of IATA will require a strong biomathematical/computational contribution for synthesizing the large volumes of various information flows. This will likely require development of both an intramural capacity, as well as support for the extramural scientific community. This is key component will need careful fostering to develop the appropriate capability and capacity.

- System model development inherent in IATA must develop in an iterative fashion between the computational/information scientists and the biologists developing the data. New approaches must be done in parallel with traditional approaches so that the added value is apparent.

Discussion Participants: Michael DeVito, Michael Holsapple, Claude Hughes, Christopher Kemp, Ed Levin, Cheryl Marks, James Putney, William Stokes, Tracey Woodruff

Report 75: Environmental Health Economics

Convener: Bucher/Balbus

Brief History: In an era of shrinking resources, providing economic justification for resource expenditures, including those for environmental health interventions, will become increasingly important. To date, there has been very little development of either methods or data for valuing environmental health impacts and/or the cost savings provided by interventions. This gap contributes to a lack of focus and emphasis on environmental health in major policy initiatives like the Affordable Care Act and the National Prevention Strategy.

Discussion Highlights:

- Valuation has been well worked out for air pollution impacts, lead impacts on IQ/income loss, to certain extent asthma
- Both federal and state government representatives endorsed the importance of this issue in their work for being able to discuss environmental health in more general health policy contexts.
- There are several areas of need
    - Increasing analyses of economic impacts using established methods and datasets (e.g.,. local analyses of air pollution impacts)- could be done by a contractor
    - Building the community of researchers in environmental health economics. There are health economists and environmental economists but very few to no environmental health economists.
    - Funding methodological research to develop new and better ways to do analyses
- Rob McConnell wanted to include economic analysis of burden of disease associated with roadside air pollution. He was able to find funding not from NIH but from SCAQMD and sponsored a workshop to facilitate finding an economist with interest and skills needed to assist. This underscores the current challenges in expanding the knowledge base in this field.
- Partnerships with business schools, economics departments, foundations, insurance companies, social scientists will be necessary
    - Business schools provide internships and student projects, but still a need for qualified mentors
    - Insurance companies have actuarial tables and massive amounts of data, not linked to environmental exposures in general
- There is a major need for inter-disciplinary dialogue for several issues
    - Definitions of outcomes (e.g., school absence has strong meaning for economists, less for public health professionals)

  - Terminology
  - Incorporation of personal/societal values into cost-benefit analyses and decisions

- Translating environmental health information into personal economic terms, such as loss of lifetime income of a child from an environmental exposure, can be powerful in terms of communicating with both the public and policy-makers
- Serious concerns were raised about investing in expanding knowledge base on economic aspects
  - Decisions about value of interventions will be made narrowly on simplistic cost-benefit information, not taking into account other values
  - There may be an expectation that only interventions that save money are worthwhile, lack of recognition that all interventions have associated costs that often exceed benefits but are made for societal goods
  - Questions about how economic effectiveness information would drive the NIEHS research agenda, including governmental review of research programs
- Important to analyze costs and impacts up front in a variety of processes, including building design, green chemistry, rather than always comparing benefits to costs of remediation and cleanup.

Recommendations:

  - Hire senior economist/social scientist to provide internal expertise/advice on program development
  - Sponsor workshop or series of workshops to begin to frame the issues and identify the relevant experts
  - Explore partnerships with academic institutions (e.g., Frank Ackerman at Tufts) for joint training opportunities
  - Explore incorporation of incentives for adding in economists and economic analyses as supplements to grants or other funding opportunities

Discussion Participants:

Bruce Androphy, John Balbus, Douglas Brugge, John Bucher, Trisha Castranio, Lisa Conti, Mike DeVito, Christine Drew, Lynn Goldman, Nadine Gracia, Kathleen Gray, Erin Haynes, Bernhard Hennig, Shuk-Mei Ho, Andrea Hricko, Laurie Johnson, Paul Jung, Bruce Lanphear, Pat Mastin, Rob McConnell, Joshua Rosenthal, Jennifer Sass, Jane Schroeder, Bono Sen, Peggy Shepard, Kimberly Thigpen Tart, Wendy Thomas, Mary Wolfe, Robert Wright

Report 76: Healthy Environments for Children: IEQ

Convener: Claire Barnett

Brief History: Children are 100% of our future, and 98% of all children attend schools and/or child care facilities every day. Public schools disproportionately enroll children with health and learning problems, disabilities, and children in poverty; about 40% of all 50 million public school children are children of color. Poor env conditions deeply impact health and learning. Two NAS reports have documented major concerns and opportunities for improving indoor environments in these settings. IOM (2011) reported that poor indoor env quality was already impacting health and learning. While children outnumber adults in these settings and they are more vulnerable than adults to exposures, there is no system of research, surveillance, tracking, or interventions to improve their environmental health, attendance, learning, and behavior. US EPA is launching a Healthy Schools Initiative

Discussion Highlights:

~ NCS is not set up to assess exposures in child care or school settings; PEHSUs are not adequately supported or authorized to address hazards

~ there is no surveillance system or baseline on children's env health in schools

~ Risks to children's health include: lead, radon, CO, CO2, pests and pesticides, hazardous cleaning products, chem spills, chem mismanagement, poor ventilation, poor drinking water, growing molds, outdoor air pollution sources and vapor intrusions, lack of adequate plumbing and sanitation, and other numerous problems (NAS, EPA, GAO, NCES)

~ children are not covered by OSHA or NIOSH nor by bargaining contracts

~ parents/communities often may not know about hazards until a child is sick or may have trouble associating the illness with exposures

Recommendations:

Schools – and child care facilities - should be a platform for health and healthy children. The topic includes school buses/vehicles and school grounds.

- Note the recommendations below link with similar recommendations from other break out groups- including IAQ, Built Environment, Healthy Buildings, Children's Env Health Research-Bang for the Buck, Public Private Partnerships, Disasters and Vulnerable Populations, Exposure Assessments, EJ-CBPR, and Communications

NIEHS should identify priority needs for research into risks and exposures where children spend their time

NIEHS should invest in developing scientific evidence base for measuring effectiveness of environmental interventions, i.e., cost-benefit of mitigating hazards

NIEHS can invest in biomonitoring and other exposure studies of children enrolled in these facilities and in documenting health outcomes of interventions in improving indoor environments – possible partnerships with EPA and ED and/or CDC/ATSDR and CDC/NIOSH

NIEHS should invest in a survey of child care and school hazards, partnered with HHS and EPA/ED, similar to but expanding on topics in the housing survey of lead and allergens conducted with HUD (IOM: NIEHS 2011)

NIEHS should research gaps in children's env health research in indoor environments and actively participate in the Federal Council on IAQ coordinated by EPA. NIEHS goal should be to build a base of evidence sufficient for NGOs to advance IAQ-IEQ regulatory standards for these settings.

NIEHS should seed the development of environmental health histories on children enrolled in child care and in k-12 schools and the resulting work shared with AAP-COEH, PEHSUs, ATSDR and other agencies, as well as the Children's Research Centers. NIEHS should also research the cost-effectiveness of EH histories and their recommendations for actions

NIEHS should research what constitutes a healthy indoor environment

NIEHS should research the impact of health and learning outcomes of increasing 'greenery' – trees, shrubs, grass (natural turf) - outside schools as buffers to outdoor sources of pollutants

NIEHS should advance with other agencies and with states an expanded definition of 'sentinel event' in public health, including CO poisoning (eg, among school bus drivers or school custodians which suggests that children are having undiagnosed exposures), food anaphylaxis, fatal asthma attacks in schools

NIEHS should advance with other agencies and with states a surveillance system for pediatric environmental health in schools

NIEHS should develop an animal model of children in child care or schools to facilitate research into exposures, exposures to complex chemical mixtures, and effective mitigations/ interventions

NIEHS and EPA shared child care on RTP campus should be a model of environmentally healthy learning place

Discussion Participants:

Barnett, Breysse, Claudio, Edwards, Gray, Sinks, Stroebel

Report 77: Emerging research areas and technologies at the interface of DNA repair and environmental health

Convener: Scott Williams

Brief History:

Our genomes are continually damaged as cells duplicate their chromosomes, and as a consequence of oxidation, environmental exposure to chemicals and DNA-damaging radiation. Oxidative DNA damage from reactive oxygen species, during inflammation, or upon exposure to environmental agents poses threats to all cell types. Ionizing radiation and non-ionizing radiation from external sources such as diagnostic X-rays further mount a constant assault on our genomes. As a first line of defense, the cellular DNA repair machinery recognizes perturbations and responds to DNA damage with initiation of multifaceted responses. We aimed to identify research priorities and emerging areas to maintain the NIEHS at the forefront of the integrated study of DNA repair and genome maintenance, and its impacts on environmental health.

Discussion Highlights:

- The cellular DNA repair machinery is a critical modulator of environment induced disease. Perturbations in DNA repair can contribute to susceptibility to exposures. Also, environmental factors have the capacity to modulate DNA repair, and are poorly understood.

- DNA damage responses to environmental exposures are multi-level. These involve not only the recognition and enzymatic repair of damaged DNA, but complex and poorly understood cellular signaling, epigenetic modifications to chromatin, and dynamic assembly and disassembly of multi-protein repair and signaling complexes. The impacts of epigenetic marks on DNA repair, and the establishment of marks in chromatin are ill-defined.

- Non-coding RNAs in regulation DNA damage response was mentioned as a possible unknown.

- Many DNA repair genes are impacted by mutations that increase cancer risk and are linked to neurodegenerative disorders, but the roles for DNA repair capacity variation in complex diseases (eg Autism, PD) is unknown.

- There are possible undefined links between nutrition and aging and their impacts on cellular energetics (e.g. ATP and nucleotide pools) on the efficiency of DNA repair.

Recommendations:

- It will be key to promote multilevel studies, from basic molecular mechanisms to understand DNA repair enzymology, to utilizing systems biology and proteomic studies to better define global cellular DNA damage responses.

- The DNA repair response in the context of chromatin and the impacts of epigenetic (eg Histone modifications) is in its infancy. A detailed understanding DNA repair in global chromosome architecture is needed.

- Support of enabling technologies (next gen sequencing, quantum dot technologies mentioned) will be required to support integrated approaches.

Discussion Participants: Geraldine Dawson, Philip Hanawalt, Richard Paules, Thomas Vogt, Scott Williams, Daniel Shaughnessy, Leroy Worth

Report 78: How can Environmental Health Sciences Help Chemists Create Benign 21st century materials – Creating a protocol for green chemists to design out endocrine disruption

Conveners: Terry Collins and Karen Peabody O'Brien

Brief History: In recent years the environmental health sciences have revealed profoundly important information on the mechanisms behind chemical toxicity, especially on the issue of endocrine disruption. Since the goal of Green Chemists is to create inherently benign chemicals, having access to this science is crucial, yet the majority of chemists have no training in basic toxicology or an understanding of the more recent science around EDCs and other cutting edge tox issues.

Discussion Highlights: The group agreed that enhanced communication across the scientific disciplines is critical, both around the issues of EDC and other tox issues.

The group also agreed that there should be better communication to chemists and companies of what testing tools are available.

There was disagreement about whether EDCs is the most pertinent tox issue to focus on; but framing EDCs as a test area in which to begin cross-discipline communication was agreed to be a good and necessary step.

It was argued that there are already enough assays on EDCs and enough educational materials exist so no additional work on this area is needed. The reply was that chemists and companies cannot negotiate the thicket of information around all available assays on EDCs. Chemists need a vetted and reliable shortcut for navigating through available tools, and a clearly delineated suite of tests that would be necessary and/or sufficient to establish confidence that a new compound is not an EDC. Moreover, there is a need for clear scientific principles by which companies and chemists can evaluate the reliability of assays and tools as well as the practices of the many research and testing companies offering these services.

Toxcast and TOX21 and other HTS tools were discussed, as potentially useful tools for a quick and relatively inexpensive wide net to test to toxicity. Their shortcomings were also noted in that they still turn up both false negatives and false positives and miss some important end points. A tiered testing protocol designed to catch missed endpoints was discussed, moving from broader, cruder tools up the ladder to more refined and specific assays. The one thing that must be kept in mind in such an approach insofar as chemists are concerned in that the testing system be actionable, economical, and transparent. Lastly, the protocol should allow for periodic review and updates

Recommendations:

NIEHS should play a role in convening scientists from multiple disciplines (namely chemistry and environmental health sciences) to meet and educate one another of both their needs and capacities.

NIEHS should help develop educational materials on toxicology and EHS for chemists (this could be both for university and industry research chemists).

NIEHS should develop fora to inform research chemists of the latest testing and assaying tools available (running the gamut from HTS through cell and whole animal based assays).

In addition to EDCs, nanotech is an emerging area in which both chemists and environmental health scientists need to share information and testing tools.

Discussion Participants:

O'Brien, Collins, Denison, Henry, Patisaul, Rizzo, Schrader, Walker, Wexler

Report 79: Exposure Science and the Exposome

Convener: Julia Brody, Aubrey Miller, Elaine Cohen Hubal

Brief History:

We know that exposure and disease are complex. The concept of the exposome captures this complexity and recognizes the need to develop measurements that integrate multiple exposures across domains and incorporate a temporal component. It provides a conceptual framework for strategic development of biologically relevant exposure metrics and systems-based exposure models. Developing this framework will advance understanding of exposure-response relationships and toxicology.

Exposure science has not been well addressed by NIEHS or NIH and lags behind GWAS. A large fraction of chronic disease is due to environment, so poor characterization of exposure is a barrier to progress. Exposure is a weak link in environmental health science that is impairing progress in gene-environment science.

Discussion Highlights:

National Academy workshops have discussed the exposome and opportunities to harness technology to characterize the exposome. That discussion needs follow-up.

The exposome concept creates a framework for discovery of exposures we don't know to look for rather than "looking under the lamppost."

We are not adequately using existing tools and we also need new tools.

A strength of the exposome concept is that it focuses attention on the need to measure the entire pathway from exposure to disease, developing measures that are early markers of the effects of exposure. For cohort studies, it is desirable to develop measures that are markers of exposure years ago and to develop low-cost measures that can be collected repeatedly in large numbers. Measurements are needed to integrate exposures over many years and to measure exposure in critical windows of development. Currently there are cost and technology barriers to environmental exposure measures that are not questionnaire-based in cohort studies.

The exposome concept is needed to move us from linear to complex network approaches consistent with systems biology.

A critique of the exposome is that it seems unbounded. In addition, regulation is chemical by chemical, creating a tension with conceptions of multiple exposures.

NIEHS is a good place to explore the exposome because it is not engaged in regulatory issues.

Advances in bioinformatics will be needed to deal with data generated in exploration of the exposome.

In parallel to the exposome concept, we need to move beyond old models of disease diagnosis to a more complex, molecular definition of disease. Exposome measurements are needed to evaluate perturbation in a biological pathway that may lead to disease.

Observing biological perturbation in a population with unique exposures, such as after the Gulf oil spill, can lead to back-analysis to identify the responsible exposure source.

Interdisciplinary skills, including informatics and toxicology, are important and require training and incentives for investigators to work together.

Development of the exposome must be "open sourced," with shared databases that don't wait for publication.

Recommendations:

NIEHS should use the exposome concept to frame a research agenda that (a) elevates characterizing exposure to an end point rather than an ad hoc adjunct to other ends, (b) supports discovery science, and (c) reflects coordinated strategic priorities.

NIEHS should fund the development and validation of cost-effective exposure measurement technologies (platforms) for population surveillance, epidemiology, and emergency response.

NIEHS should fund proof-of-concept studies in existing cohorts or add-ons to cohorts.

NIEHS should facilitate data sharing, development of repositories for environmental and biological samples and data, repositories for measurement standards, and bioinformatics support to encourage rapid advances in understanding of exposure. Development of guidelines to ensure quality and consistency will enhance these shared resources.

NIEHS should promote the concept that exposures that perturb a biological pathway should be considered relevant to health, with the understanding that we must also investigate long-term meaning.

NTP should develop a program of pilot-testing in animals for biomarker discovery. Metabolomic and genomic profiling in exposed animals can lead to discovery of biologically-relevant metrics and disease pathways. These can be targets for human biomarker development and feed into high-throughput screening programs.

NIEHS should serve as a convener of workshops to develop a coordinated, strategic approach to the exposome concept and should explore collaborations with NSF, DOD, NASA, and NHANES.

NIEHS should work to ensure that the National Children's Study contributes to understanding of health effects of environmental chemicals and understanding the exposome.

Discussion Participants:

Trevor Archer, Joellen Harper Austin, Linda Birnbaum, Julia Brody, Gwen Collman, Michael Fessler, Richard Finnell, John Groopman, Erin Haynes, Elaine Hubal, Richard Kwok, Aubrey Miller, Craig Newschaffer, Michael Pino, Joshua Rosenthal, Robert Sills, Jack Taylor, Deborah Winn, Steven Zeisel, Darryl Zeldin

Report 80: Preventing Prenatal Exposures to Toxicants

Convener: Karin Russ

Brief History: The problem of prenatal exposures to toxicants is of the utmost concern to our society today. The effects of prenatal exposures range from the short term, evident in infants and children, to long term effects that may not be seen until adulthood. Birth defects affect 3-4% of all babies, and some 2/3 of those are of unknown etiology. In addition to the pain and human suffering associated with short and long term effects of toxicants, the economic impact of birth defects and chronic diseases is a substantial burden to our society.

NIEHS needs to take steps to ensure the prevention of prenatal exposures to toxicants. Studying the causes of birth defects, neurodevelopmental and functional disabilities, and adult diseases of fetal origin will advance environmental science in many ways. Studying prenatal exposures will provide insight on genetics, epigenetics, mechanisms of action, and effects of complex chemical mixtures. It is crucial to know the associative or causative relationships of toxicants and prenatal outcomes, because the prenatal period is a vulnerable window of development, and a period in which interventions that prevent or limit exposures may yield the greatest cost/benefit ratio. In addition, now is the time to undertake studies at the cellular and molecular level, because emerging technologies make such research possible.

Discussion Highlights: Birth defects are a major public health concern, and have not improved much in the last few decades, despite efforts to improve maternity care. Some types of birth defects that may be associated with environmental exposures, such as hypospadias and neurodevelopmental disabilities, have risen sharply over the last 20 years. The main factor that limits the ability to assess trends in birth defects is the lack of a national birth defects registry. Currently, 30-40 states have birth defect monitoring programs that capture only the major structural defects evident in the first year of life, such as cardiac anomalies, defects in limb development, cleft lip and palate, and hypospadias. One birth defects research group, funded through the CDC, is endeavoring to collect data on congenital anomalies in a more comprehensive way. The birth defects research group gathers information from 6-7 states via birth certificates (which describe only about 10% of the defects eventually found), and also from records from cytogenetic labs, surgical records, and ICD-9 codes from hospital admissions. This is a start in understanding the scope of the birth defect problem, but still does not represent the entire US. A better example of comprehensive reporting is the National Childhood Cancer Registry, through the Pediatric Oncology Group at the NCI.

Assessment is the first step in working toward prevention of prenatal exposures to environmental toxicants. Education of prospective parents on environmental risks is an important component of prevention. Finally, studies in teratology and clinical interventions can begin to evaluate which measures are most effective in reducing negative pregnancy outcomes.

Recommendations: NIEHS should take the follow steps to ultimately prevent prenatal exposures to toxicants:

Assessment

- **From an Inter-Agency Task Force on Birth Defects and Functional Outcomes.**
  Multiple agencies are involved in the tracking and study of birth outcomes in the US. Recommended members of the Task Force include: NIEHS, NICHD, ATSDR, CDC, EPA, NCI and OSHA. In this way, a coordinated effort at assessing, tracking and conducting research, without gaps in research or duplication of effort, can be advanced.

- **Create multidisciplinary research teams, to better understand the multifactorial nature of prenatal exposures, birth defects and later life diseases.**
  Team members may include toxicologists, teratologists, developmental biologists, epidemiologists and clinicians.

- **Promote cross-agency collaboration between the NIEHS and NCI.**
  This partnership will allow for identification of childhood cancers that may have origins in fetal exposures to toxins. Suggested activities include: recommend that NCI collect an environmental exposure history from families of childhood cancer patients, recommend that NCI collect tissue for banking from registry patients, conduct GIS mapping of cancer incidence. These actions can inform the direction for future areas of study at NIEHS.

- **Promote improved screening of pregnant women for environmental exposures, including an occupational health history.** A primary activity within this action would be the identification or creation of a prenatal environmental health history screening tool, and the broad dissemination of this tool to health care professionals. Collaboration with professional organizations of healthcare providers delivering OB care, such as ACOG, ACNM, and NPWH is a critical step toward this goal.

- **Create an electronic environmental health assessment tool for the coming of Electronic Health Record (EHR)**
  The EHR, mandated by the Healthcare Affordability Act of 2009, will provide an unprecedented opportunity to assess, track, monitor and analyze environmental health exposures. A standardized environmental health assessment tool for prenatal patients will greatly facilitate the collection and utilization of environmental health data, and will allow for early detection and a clinical guidance on risk reduction strategies.

Health education

- **Maintain a repository of health education materials for pregnant women.**
  There is a vast array of health education material available for women of reproductive age, designed to help them reduce their risk of exposure to environmental hazards. NIEHS would be the ideal agency to collect and house this information on one webpage.

- **"Tweets for Teens".**

Adolescents are a group at high risk for unintended pregnancies, and also for high risk behaviors that may expose them to toxicants. Utilizing Twitter technology to deliver prevention messages would be an effective way to reach this population. An exemplar that is already in place, delivering general messages about prenatal care, is the Text4Baby program.

- **Engage in studies to determine what methods of environmental health education are the most effective in changing behavior.** Traditional methods rely on pamphlets for distribution at health care providers' offices, website materials, or live presentations to groups of learners. Evidence of the efficacy of these vs. newer technologies such as Twitter or social marketing would help guide future health education efforts.

Areas for future research

- **Revive programs that fund studies on teratology.**
  Funding for basic research on teratology has dwindled in recent years and needs to be restored.

- **Promote and fund intervention studies.**
  Potential examples include: adverse effects of herbal preparations and complementary medicines, supplementary dietary choline to prevent neural tube defects, alcohol and smoking intervention for youth at high-risk for pregnancy.

Discussion Participants:

Cynthia Bearer

Jose Cordero

Geraldine Dawson

Paul Foster

Gina Goulding

Joseph "Chip" Hughes

Mary Lee

Grace LeMasters

David Miller

Nuala Moore

Karin Russ

Tracey Woodruff

Report 81: Environmental Epigenomics and Complex Heritable Disease

Convener: J.W. Hollingsworth

Brief History: There is considerable evidence that many complex diseases are heritable and have a genetic basis. However, current evidence suggests that genetic code do not account for all risk of disease. Furthermore, many common complex diseases have alteration in prevalence over decades (for example asthma and obesity) suggesting lifetime environmental exposures (or experience) could modify disease risk. Environmental exposures during vulnerable periods of development can modify the likelihood of development of disease or severity of disease. Emerging evidence supports that epignomic marks can be modified by exposures (or stress) and are associated with altered disease risk. However, there are limited evidence supporting the mechanistic link between exposure, epigenomic marks, and disease. The NIEHS is uniquely poised to lead the effort to better understand this important relationship between environment, epigenome, and complex human disease.

Discussion Highlights: There are considerable interest in the emerging field of epigenomics and disease risk. The NIEHS should lead this effort to understand the important role of environment on modifying epigenomic marks as they relate to disease burden.

Epigenomics for the purpose of this discussion was **defined** as transmissible modifications in DNA and DNA-associated molecules that influence whether genes are turned on or off. These changes include CpG methylation and chromatin/histone modification.

Environmental exposures should be **defined** broadly to include; psycho-social stress, diet, toxicant exposure, obesity, etc.…

There are **vulnerable windows** of susceptibility to environmental stress associated with modification in epigenomic marks.

There are limited good mechanistic studies to link exposures with modification of epigenomic marks and disease risk. Basic understanding of this link is required.

Studies of the epigenome require an appreciation for specific tissues and cell types contributing to disease pathogenesis.

The epigenome can be somatically transmitted and could contribute to heritable risk of disease. Further studies should focus on heritable transmission of disease.

Proof-of-principle studies are necessary to move the field forward.

While there is technology available to study epigenetics, this technology should be further developed to facilitate meaningful studies of epigenetics. These include platforms for global methylation and novel technologies that could include in vivo imaging.

Bioinformatics is probably adequate but need to facilitate training of scientist.

A systems biology approach is required to integrate environment, epigenome, genetic code variation, and disease risk.

Timing and dose of exposure are important considerations. There can be considerable lag between relevant exposure and development of disease.

Translational studies should be encouraged but may require further mechanistic insight into targets from mechanistic basic studies from either cell culture or animal models of disease.

Important to integrate studies initiated at the NIEHS with ongoing studies (if possible). Identification or development of adequate human cohorts to study the link between environment, the epigenome, and disease are required (for example, the National Children's Study).

Recommendations:

1. Basic mechanistic studies of relationship between environment, epigenome, and disease are necessary. Studies should link the functional consequences of modification of the epigenome on regulation of gene expression.
2. Improved technology will facilitate the field moving forward.
3. Emphasis should be placed on vulnerable windows of susceptibility.
4. Translational studies should be designed to better understand the relationship between environment, epigenome, and disease.
5. A systems biology approach should be encouraged to integrate the environment, epigenome, genetic variation, genomic expression, and disease risk.
6. Biobanks should be established with appropriate protocols to study epigenomic marks. Tissue/cell collection should be protocol-driven.

Discussion Participants: Adelman, Bernstein, Boyles, Cidlowski, Cory-Slechta, Dolinoy, Fargo, Garantziotis, Gasiewicz, Gould, Hollingsworth, Kiley, London, Miller (David), Peden, Pollock, Tyson, Umbach, Vogt, Woychik, Waalkes, Zeisel

Report 82: Environmental Light: Is NIEHS research focused enough on environmental light and its interaction with chemicals, compounds and organisms in the environment?

Convener: Paul C. Howard (FDA)

Brief History: There are points to consider why role of sunlight and other light sources (it is more than sunlight and more than UVB!) in the human interaction with the environment is important at this time and for the next several years:

- Sunlight is not homogenous in the environment and human interaction is altered by sunlight latitude, season, time of day, atmospheric conditions; other light sources are quite diverse;
- Sunlight is known to have biological activity that is dose and wavelength-dependent, and examples are induction of human and animal skin cancer, induction of human skin photoaging, support of photobiology (*e.g*. plants and photosynthesis), biological development of vision and photoreceptors, and induction of human diseases (*e.g.* seasonal affective disorder);
- Sunlight is known to have chemical/photochemical activity, examples are photoactivation (or photodecomposition) of atmospheric pollutants or bioactive compounds (such as pesticides), photobleaching of plastics and other chemicals, photovoltaic cells;
- Human exposure to sunlight and other light sources is changing, with concomitant increases in adult leisure time (demographics; kids indoors) and skin cancer rates, but at the same time altering patterns of youth time outside in sunlight.

Discussion Highlights: There was discussion regarding the evidence that environmental light does affect biological and chemical systems, and the rationale or reasoning that NIEHS should emphasize (where appropriate) controlling for environmental light in studies. Topics that were discussed were:

- Approximately 25% of the genome oscillates with light exposure;
- Asthma and multiple sclerosis rates are latitude dependent, raising the question whether these are affected by environmental light;
- Some toxicities are chronologically-dependent, for instance, acetaminophen toxicity is greatest during fasting states (lower GSH) than following caloric consumption (higher GSH), and feeding is driven by circadian rhythms, which is driven by light-dark cycling;
- There has been considerable research on circadian biology, but is this translating into environmental health research?;
- There is considerable interest in the circadian rhythms and health effects on shift workers, which could be light-dependent or light-codependent;
- Vitamin D is an essential vitamin, is produced in skin as result of environmental light, and there are questions regarding adequate dosing of children (especially indoor-dwelling children);
- Light and photoproducts (*e.g.* DNA photodimers) are immunosuppressive, yet is this role of light controlled for in environmental health studies?;
- Sunlight is a powerful source of energy catalyzing oxidation/reduction reactions of organics and transition metals;

- Since we know that animals respond to environmental light to control circadian rhythms, are our animal models that use nocturnally-active animals, representative and/or translational to humans?;

- Photochemistry of pollutants and other chemicals is widely published.

Recommendations: It is felt that the possible role of light in quantitative environmental assessments may be underestimated or under-appreciated. More attention should be programmatically placed on:

- controlling for environmental light* in environmental fate studies (*e.g*. PAH in gulf);
- controlling for environmental light in epidemiology studies, and experimental studies (are the light considerations adequate);
- light as risk or confounding factor in occupational risk, especially shift-workers;
- understanding of role of light in disposition of environmental chemicals or pollutants (some is known but not in all areas);
- research on light pollution (*i.e.* major metropolitan centers never truly reaching darkness) and effect on environment (fauna and flora);
- enhance research on the possibility of light as a green catalyst in environmental mediation (*e.g.* expand on green light-based photo remediation)

** environmental light being defined as sunlight and other light sources, and recognizing that light sources differ by wavelength and dose.*

Discussion Participants: Bruce Androphy, Chris Bradford, Barry Dellinger, Andrea Hicks, Paul Howard (convener), Richard Kwok, Martha Nolan, Michael Pino, Kris Thayer

Report 83: Health Impacts from Disasters with Emphasis on Vulnerable Populations

Convener: Beverly Wright

Brief History:

The expectation that the impact of climate change will increase extreme weather events will result in more frequent and intense natural disasters with climate justice implications and the political climate supporting lacked enforcement of regulations will result in increased man-made/ industrial accidents requires that public health ply a stronger role in response.

Discussion Highlights:

A major deterrent to the establishment of a response protocol that protects the public health is the lack of historical data to inform the rational design of an appropriate response. It seems that the action plan after a natural/man-made disaster or industrial accident occurs after the incident occurs. The discussion focused on the development of capacity at NIEHS to address these issues.

Recommendations:

Build mechanisms for the purposes of conducting rapid response assessments in response to natural and man-made disasters.

A. Perform evaluation of previous disaster preparedness and response outcomes in order to determine needs and data gaps for development of protocol for future use by NIEHS
B. Interagency workgroup w/ NIH, CDC, FEMA, NOAA, DOD w/ intramural and extramural for disaster research response
C. Create MOUs focusing on communities that are susceptible and vulnerable that require rapid response capacity. This will necessitate both NIEHS interagency working group, intramural and extramural program working with these communities (i.e. PARTERSHIPS-HBCUs/MSIs, 501 (c) community organizations)
D. Extend the reach of NOAA and NASAs capacity to local/community levels towards enhancing disaster preparedness
E. Funding of regional centers modeled after National Hazard Centers (i.e. risk communication)

Conduct vulnerability assessments to determine probable risks for disaster response

GIS mapping of risk data.

Discussion Participants:

Beverly Wright	Darryl B. Hood	Wendy Thomas	Richard Dennison
Sacoby Wilson	Tom Sinks	John Balbus	Richard Kwok
Joseph Hughes			

Report 84: Workplace Exposure to Particulate Agents

Convener: Frank Mirer

Brief History:

Human health effects from exposure to particulate agents at prevailing exposure levels has emerged with considerable force in recent decades, with health effects including mortality and hospitalization from cardiovascular and respiratory causes, and cancer. Agents which are common between workplace and community include particulate NOC (PM2.5), diesel particulate matter, metal oxides (welding fume), environmental tobacco smoke, among others. Agents with limited health effects information, such as emissions from compressed natural gas engines and directed fired gas heaters are expanding. An anchor in human health effects permits a laboratory research program which will inform low dose potency by comparing effects in model systems for agents known to pose a hazard to novel agents such as various engineered nanoparticles.

Discussion Highlights:

The locus for sponsorship of this research was discussed as problematic. NIOSH supports the regulatory mission of OSHA (which itself conducts no research) with research intramural and limited extramural research, while both EPA and NIEHS support work on possibly similar agents outside the workplace. The NTP division of NIEHS is responsible for “testing” of agents.

Recommendations:

1. Laboratory testing of particulate agents including combustion particulate and metal oxides should have an increased priority at NTP
2. Studies of behavior in sophisticated laboratory test systems of agents anchored in human health effects or already conducted bioassays should be conducted in parallel such experiments with related but untested agents to illuminate relative potency.
3. Health effects research on particulate agents by NIEHS should expand in priority because of the demonstrated effects of these agents at prevailing exposure levels.

Discussion Participants:

Mirer, Allen

Report 85: Tissue Engineering and Toxicology

Convener: Jonathan Pollock

Brief History: Toxicological assays have been problematic in cell culture assays. Cells line have deletions, duplications, and mutations that have adapted to growing in culture. There is a clear need for tissues that accurately reflect normal physiology for use in high throughput assays. Tissue engineering using stem cells offers an opportunity to better model normal physiology.

Discussion Highlights:

Need to define cell type in term of molecular phenotype and epigenome to provide a standard to recreate tissues that exist in the organism.

Understand mechanisms needed to recapitulate the desire cell type for toxicological screening.

Needs to be adapted to high-throughput screening platform

Question concerning using homogeneous population of cells derived from stem cells is better than trying to recreate organ.

Develop tissue engineering to ameliorate the consequences of environmental insult.

Leverage IKMC resources and gene traps to engineer tissues to examine gene environment interactions.

Create iPS cells from susceptible/affected individuals to identify mechanism affecting susceptibility

Create ES and iPS cells from Collaborative Cross and Diversity Cross mouse strains for tissue engineering to examine interactions among genome, epigenome, and environmental insult.

Recommendations:

See above.

Discussion Participants: Stavros Garantziotis, Jonathan Pollock, Rick Finnell

Report 86: Promoting Technology Development in Environmental Health Sciences

Convener: Tom Begley

Brief History: New technologies that include deep sequencing, mass spectrometry tools, the internet and hand held PDA's have not only transformed research but everyday life. Technology development has previously played an important role in the growth of environmental health research.

Discussion Highlights: Why technology development is needed:

1) To decrease the cost of research; To increase the speed and throughput of research.

2) To help integrate diverse scientific disciplines and scientists under the NIEHS umbrella.

3) Technology development has the potential to interface the environmental health sciences with industrial partners and lead to research commercialization and EHS products for the public.

4) To promote new discoveries that improve our understanding of human health.

What types of new tools are needed:

1) Technology development to generate cheap, robust and highly reproducible tools for epigenetic research.

2) Mass spectrometry developments to bring proteomics, lipidomics, RNAomic and small molecule analysis to the masses.

3) Miniaturization of basic laboratory equipment, population testing, sensor, environmental medicine and field testing tools.

4) New and readily accessible resources for population studies, as this will speed the translation of new findings to preventions, interventions and policies.

Recommendations:

1) Embrace technology development, utilization and access as component of the strategic plan.

2) Mandate technology development as a component of some new RFA's or intramural research programs.

3) Promote public-private partnerships to develop new technologies and platforms for EHS research.

4) Develop workshops on technology development for EHS scientists, to address needed technologies, team building components, intellectual property, cost and perception issues associated with technology development.

Discussion Participants: Tom Begley

Report 87: Making environmental health-related laboratory assays robust and cheap enough for use in large human population research studies

Convener: Deborah Winn

Brief History: There are many existing laboratory assays that assess biologic levels of environmental agents or their metabolites in human biospecimens or early effects of these agents that were developed for testing scientific hypotheses in small studies in carefully controlled settings; often highly skilled staff are needed to perform these assays correctly. However, it often takes a long time for these assays to be useable in epidemiologic and other field studies (or for health surveillance) because the assays are too expensive, take too much biospecimen or biospecimens that are difficult to obtain, or are too sensitive to the procedure for acquiring the specimen, how it is transported, and analyzed. Often there are few incentives for principal investigators to scale up existing assays to be more robust, cheaper, and easier assays. This is because existing funding mechanisms reward discovery and hypothesis testing research, not the types of methods research needed to solve these technical methodologic problems. In addition, sometimes existing assays are not adequately described in the published literature making it difficult for scientists who want to take and improve the method for use in large human studies. Reference materials are usually not available to make sure that any new method that is purportedly cheaper or more robust meets the standards of original assays. Some existing types of funding opportunity announcements, such as Small Business Innovation Research grants have been used in the past to help address some of these problems; however, much more needs to be done to facilitate and speed the process and provide the tools to perform assays cheaply and easily enough for use in large human population studies. Finally the scientists who do the large population studies usually don't have the expertise to develop these robust assays, and scientists who develop the assays for use in smaller discovery studies aren't aware of the constraints of large population studies.

Discussion Highlights:

Develop more assays that are robust enough to be done "in the field". This is sometimes necessary due to human subject issues, rapid deterioration of the analyte involved, transportation problems, and mandates in some countries that biospecimens cannot be sent out from that country.

Assays used in large population studies need to be able to be completed as quickly as possible in order to be able to get another biospecimen if the original one is compromised, insufficient, lost, etc.

Speeding scaling up and ramping up of assays will require fostering partnerships with businesses and academics with the capacity to do this type of methodologic work.

Assays used in large scale studies typically need to either require very small quantities of biospecimens or the assays need to be heavily multiplexed because specimens are hard to get and must be used for to detect multiple environmental exposures and early effects in addition to use in assessing nutrients, inflammatory biomarkers, immunologic biomarkers, etc. Tools and methods developed have to measure as many analytes as possible.

Recommendations:

NIEHS should develop the infrastructures and incentives needed to ensure that laboratory assays for environmental health-related analytes that show promise for understanding exposure levels and early health effects in human populations are rapidly and efficiently scaled up to be cheap, easy, and robust enough for use in human population research.

NIEHS should ensure that reference materials are developed and maintained that can be used to determine the analytical validity of newly developed laboratory procedures that have the desired properties of being cheap, easy to do, are multiplexed and/or require smaller biospecimen samples.

NIEHS should ensure that the methodologies used to do the original assay and the better, cheaper, more robust assay are properly and extensively documented

NIEHS could consider using CRADAs, Small Business Innovative Research methods, and FOAs such as NCI's IMAT (Innovative Methods for … and Technology or something like that) that can incentivize and foster this type of important methodologic research.

Discussion Participants: Deborah Winn, Dori Germolec, Craig Newschaffer, Palmer Taylor

Report 88: Next Steps for Exposure Biology

Convener: David Balshaw

Brief History:

Wild (2005) defined the concept of the exposome as the accumulation of exposures over a lifetime; the concept integrates a continuum of exposure, susceptibility and response. In 2007 NIEHS lead a trans-NIH effort to establish the concept of Exposure Biology which was intended to provide measures of chemical exposures, dietary intake, physical activity and psychosocial stress in time and space and to enable a linkage of those measures of the personal environment to alterations in biological pathways. In principle the measures from the Exposure Biology Program provide a snapshot of the exposome. The current EBP tools exist as functional prototypes suitable for pilot testing in focused epidemiological studies but as of yet have not been integrated to provide a complete glimpse of the personal environment.

Discussion Highlights:

Exposure Biology provides a potentially very powerful tool for discovery in environmental health that can aid in teasing out the interaction between external factors, internal factors and response that underlie human disease. The concept of a suite of tools that integrate external contact, internal exposure and biological response remains a novel idea which is becoming reality thanks to the leadership of NIEHS.

Recommendations:

While an excellent start, the current EBP tools are very limited. An effort needs to be made to increase the chemical space covered. This could potentially include an emphasis on functional identification of exposures (based on biological activity rather than chemical identity). It is also recommended that sensors be developed with a modular format that would allow adaptation to emerging chemicals of interest or tailoring to epidemiological study design. A particular weakness of the current EBP effort is in the focus on airborne analytes and effort should be made to measure dermal exposures. More importantly, an effort to measure internal exposures is needed which would allow quantitation of oral route of exposure and of compounds with mixed route of exposure and provide a strong linkage between contact and response.

An effort is needed for integration of the EBP (and similar) tools to provide the complete view of the exposome at that snapshot. This includes the need to establish a proof of principle for the concept that integrating chemical exposures with lifestyle factors provides additional biological insight.

An effort is needed to facilitate data handling and analysis, particularly for real time-spatially resolved data and to facilitate interpretation of how pathway-based response relates to exposure.

The devices developed need to be made scalable so that they can be applied to large scale cohorts such as NHANES and the National Children's Study. A critical aspect here is the continued validation of the prototypes and the establishment of commercial partnerships to make them more broadly available.

Finally, the effort to increase awareness of the tools needs to continue. In addition to the currently implemented strategies such as sessions at major meetings, web presence and publications we can use strategies such as blanket mailings and social media avenues such as Tweeting.

Discussion Participants:

Austin, Balshaw, Bradfield, Haynes, Hubal, LeMasters, Pino, Rickard, Swenberg

Report 89: Can NIEHS Support and Foster State and Local Environmental Health Infrastructure?

Convener: Lisa Conti, Aubrey Miller, Kathleen Gray

Brief History: Historically there has not been connectivity between states and NIEHS on environmental health issues and ongoing research. CDC has been a traditional partner for state and local programs, but there is a lack of ongoing coordination and awareness between CDC and NIEHS on environmental health concerns. Current challenges for state and local health programs require collaboration to meet environmental health needs.

Discussion Highlights: The group discussed existing partnerships, both NIEHS-led and CDC-led, and discussed ways that successful efforts in of other agencies could be adapted by NIEHS. The recent NIEHS-led outreach around the Gulf oil spill demonstrated the opportunities for and value of such collaboration and that NIEHS is positioned to lead such efforts/partnerships.

Recommendations:

1. NIEHS should designate a liaison/office to partner with state health agencies. This person could participate in monthly state environmental health directors' calls.
2. NIEHS should convene an exploratory working group to develop strategic goals of partnerships. Also need to convene an inter-agency group to facilitate communication about existing efforts and potential to leverage.
3. NIEHS should compile information on NIEHS activities in each state and share it with the states. Also require that health directors are notified of RFAs that could support collaboration with their agencies.
4. Include state and local health departments in Town Hall Forums in addition to current community-based organizations. Successful examples of this approach include Wisconsin and New Orleans sessions.
5. CBPR should engage state and local health programs (by definition).
6. Survey states to learn about needs and best ways to connect with their environmental health efforts. Have a process for facilitation of dialogue and responsive action.
7. Would like NIEHS to consider supporting additional training/fellowships/direct assistance with respect to environmental health. These efforts should be bi-directional (state staff coming to agencies and agency staff going to states). Would like to see co-sponsorship of Environmental Public Health Leadership Institute by NIEHS.

Discussion Participants: Janice Allen, Bruce Androphy, Chip Hughes, Kimberly Thigpen-Tart, Heather Henry, Peggy Shepard, Tom Sinks, Trisha Castranio

Report 90: Implementing integrated systems based approach for environmental health sciences

Convener: Karen Adelman, Stephanie London, Rick Woychik

Brief History:

Environmental effects on disease are complex and understanding these effects requires an integrated, comprehensive approach.

Emerging technologies allow for transformative analysis of genome structure and sequence, gene expression, methylation, the metabolome, proteome, phenotypes, etc. but there is currently no coordination between these experiments. Strategies that facilitated integration of such data in the context of environmental exposures would permit greater synergy between EHS researchers, and improve our basic understanding of environmentally associated diseases.

We propose a paradigm shift in the way that this data is collected and integrated to allow a broad systems biology approach for studying the effects of the environment on human biology.

Discussion Highlights:

Identify useful exposure models, bring together stakeholders with pre-existing interests and/or data, and identify gaps in data. Work within DIR, DERT, etc. to fill in those gaps.

Involves building a framework to build a standardized data set (agreed upon conditions, quality control, format, genetic background), and a collaborative effort to populate this with different kinds of 'omic data. Could kick start this initiative using current interests/ strengths within NIEHS, and build upon this with targeted extramural funding and intramural hires.

Develop new tools for integration of databases as well as optimized methods for statistical analysis and mining data in order to maximize utility and ease of access to data generated. If the data is of high quality and easy to mine, others will opt to use the standard conditions and our database will continue to grow.

Initial framework can be built upon in a flexible manner as new technologies are developed and new models are added.

Recommendations:

The NIEHS should take a leadership role in connecting the people studying environmental exposures and the various systems biology data sets, and facilitate synthesis of the wealth of data being generated. In addition, we should help direct new research toward further developing these comprehensive strategies and their accessibility.

Develop an overarching framework for how comprehensive analyses of effects of exposures of both model organisms and humans can be conducted, including sequencing of genomes, methylomes, epigenomes, metabolomes, microbiomes, etc.

This framework would entail collaboration across the NIEHS, involving DIR, DERT and the NTP, as well as leveraging the infrastructure and knowledge present at the other ICs.

Discussion Participants: Adelman, Bernstein, Fasman, Holsapple, Mural, Pollock, Taylor, Umbach, Archer, Fargo, London, Fessler, Gilliland, Gould, Hall, Hanawalt, Kiley, Ladd, McAllister, Nicholas, Paules, Tice, Vogt, Worth, Zeisel

Report 91: The Role of Public Health Prevention in Environmental Health Research

Convener: Richard Kwok, Paul Jung

Brief History: A lot of the research that NIEHS participates in is broad and disparate. Sometimes it's not clear why we do what we do. How does NIEHS distinguish ourselves among the other research and regulatory organizations? How do we incorporate public health and prevention into what we do?

Discussion Highlights:

Should NIEHS focus on policy relevant research or investigator initiated research?

How does NIEHS coordinate with other institutes and federal agencies to avoid duplication and improve coordination?

The research project is the entity of concern, not the PI – someone should shepherd the research project from beginning to end but bring in necessary multidisciplinary team members as the project progresses from planned idea to policy implications.

We need good science in order to effect policy.

Need to have other partners at the table when making funding decisions; e.g. NAEHS council for DERT brings together other federal agencies so that funding is coordinated. This decreases duplication, increases collaboration and aligns priorities.

Prevention isn't the only thing that NIEHS does – we need to communicate the whole spectrum from basic science to intervention to prevention to direct public health impacts.

All NIEHS staff including scientists and administrators should be able to quote NIEHS mission statement / tag line and how it relates to their work.

Need feedback at multiple levels and stages of research (from development to execution) to scientists from policy makers, key decision makers and other stakeholder groups regarding the policy implications of NIEHS research.

Recommendations:

1. To encourage collaboration and coordination among federal partners, invite federal partners (e.g. NIH, CDC, NCEH, FDA, EPA, NIOSH, ATSDR, NOAA, FWS, etc.) to actively participate in NIEHS advisory committees

2. Improve communication by changing the composition of NIEHS advisory boards to include policymakers, stakeholders, end-users and decision makers so that relevant policy considerations are incorporated into scientific decisions throughout the scientific process, from planning to execution. Need to have broad stakeholder input to scientists at the beginning of research prioritization / design so that science is relevant to policy-makers.

3. Consider an “office for scientific policy implications” to help both intramural and extramural researchers understand the potential impact of their work (e.g. scientist / policy maker in residence program) and sustain a dialogue between scientists and policy-makers.

4. All individuals involved in creating the NIEHS mission statement should review the mission statements and strategic plans of all other NIH Institutes and relevant federal health agencies.

5. NIEHS should determine how it prioritizes research and make this process transparent to the public and stakeholders.

6. NIEHS should coordinate its priorities with other NIH Institutes and federal health agencies to avoid duplication and increase coordination and collaboration.

7. Create a tagline so that all NIEHS staff including scientists and administrators can quote NIEHS mission statement / tag line and how it relates to their work.

8. Tagline: “Science for Public Health”

Discussion Participants:

Austin, Joellen Harper; Boyles, Abee; Cordero, Jose; Hall, Traci; Johnson, Laurie; Jung, Paul; Kwok, Richard; Long, Christopher; Nolan, Martha; Stokes, William; Thomas, Wendy; Walker, Nigel

Report 92: How do we connect studies on basic biological mechanisms, toxicology, clinical studies and epidemiological studies to synergistically (I hate that word) solve important problems.

Convener: David Miller

Brief History: The organization of research institutions often provides barriers to collaborations broadly across disciplines. Because of those barriers, interdisciplinary collaborations tend to be limited in scope, not utilizing the full potential of programs with basic, tox, clinical and epi components. Larger groups of investigators rarely self-assemble, even when they share an interest in specific problems. How can particularly fruitful larger-scale efforts be organized and focused around critical issues? Are there different drivers for extramural and NIEHS intramural programs?

Discussion Highlights: Intramural investigators can learn from the experiences of the extramural world, where such approaches have been successful. Teams of investigators are assembled around a critical problem. Collaboration should be highly valued by the institution's power structure. The NIEHS center at U. Rochester was considered as a first model. It was clear that collaborations are valued and multiple lines of communication and multiple mechanisms (meetings, seminars, pilot projects) are used to assemble and guide teams.

Recommendations:

1. Defining the target biomedical problem is the key to assembling a team. Each member contributes ideas, techniques, subprojects based on their strong investigator-initiated research programs.
2. The team must have excellent scientists who are motivated and are willing to participate in the process. Fruitful collaboration is a carrot in itself, that should be encouraged by the institution. Within NIEHS, involvement of DIR, DERT and NTP is needed; all divisions can contribute to the statement of the problem, team assembly, data collection, interpretation. Mechanisms are needed to facilitate involvement of extramural collaborators
3. Essential to the assembly process is clear communication among scientists with potentially different takes on a common problem. Well-organized, science-based meetings, retreats (large and small scale, irrespective of sponsoring division) are one key to getting started with the science.
4. Work out incentives to promote collaboration and grease the skids.
5. Study design needs to be iterative and flexible.
6. Proper advance planning and leadership can reduce logistical problems related to publication, resources, etc.

Discussion Participants: D. Miller, R. Miller, P. Lawrence, J. Phelps, J. Putney, C. Weinberg, D. Zeldin, M. Waalkes, D. Armstrong, G. Bird, J. Cidlowski, G. Dawson, T. Gasiewicz, R. Sills, N. Walker

Report 93: Remotely-Sensed and GIS data

Convener: Balbus

Brief History: Information on land cover, land use, airborne pollutants, and other environmental parameters is often not available from ground monitors and observations and is obtained from satellite-based instruments. Applications of this remotely-sensed environmental data to the study, modeling and prediction of diseases and health outcomes are growing. At present, most of these applications are conducted and funded by agencies other than NIEHS/NIH, including NASA, NOAA and NSF. There is a need to determine the value-added of these sources of data for NIEHS science and the role of NIEHS in the national and international activities surrounding remotely sensed data.

In addition, there is growing interest and technological developments in the collection and analysis of geospatially organized data. There is currently no central expertise or program in the analysis of geospatial data at NIEHS, but such institutional capability may be desirable.

Discussion Highlights:

- NASA and NOAA are eager to engage with NIEHS and the public health community on the types of data they collect with their satellite and monitoring instruments
- There is a separate operational discussion as to what activities NIEHS might undertake using those data
- A group combining satellite science and public health experts from Johns Hopkins led by Bill Pan has recently moved from Johns Hopkins to Duke. This group might provide expertise to consult with NIEHS on potential use of remotely-sensed data within the Institute.
- Other experts to consult include Alan Strahler of BU, Rita Colwell, John Haynes (NASA), and Jan Ming Xiao (OK U)
- New technologies like use of Ipads to complete questionnaires with geospatial information automatically recorded will greatly expand geospatial analyses and studies

Recommendations:

- Analyze the NIEHS portfolio for research that might have added value from incorporation of remotely-sensed data
- Hold a workshop bringing together experts in remotely-sensed data and NIEHS scientists to explore applications; focus on what the capabilities of satellites and other remote sensors for health studies
- Convene a group within NIEHS with potential interest, including DIR/Epi branch, GEI – biosensors, and population studies branch of DERT.

Discussion Participants: John Balbus, Julia Gohlke, Josh Rosenthal, Bill Schrader, Ellen Silbergeld, Wendy Thomas.

Report 94: Toxicants as potential metabolic disruptors

Convener: Michele La Merrill

Brief History: There is a high prevalence of obesity and diabetes.

The rapid change in this prevalence is consistent with an environmental etiology.

Some experimental and human evidence indicates toxicants may be a part of this environmental etiology.

Discussion Highlights:

Could toxicants help to explain why some obese persons are otherwise 'healthy' while others are diabetic, dyslipidemic, and/or insulin resistant?

Changes in childhood prevalence of obesity and type 2 diabetes are particularly striking. Basic science indicates metabolic programming occurs in the pre- and peri- natal period, and is modifiable by the environment. The toxicant environment is under-examined as a modifier of metabolic programming.

The pharmacokinetics of obesity complicates the dose response curve in individual potential target tissues of metabolic disruptors. Pharmacokinetics along with toxicant effects on lipid homeostasis also complicate epidemiologic analyses, particularly with respect to cross-sectional studies and to adjusting toxicants by blood lipid levels.

Physiologic mechanisms and/or causal partners of metabolic disruption may include maternal environment, epigenetics, stress, gut flora, inflammation, insulin action, as well as the quantity and quality of micro- and macro-nutrients. Multiple tissues, e.g. liver, muscle, adipose, CNS, and organelles, e.g. mitochondria and endoplasmic reticulum, may be the sites of these mechanisms.

Metabolic disruption may include diminished thriving and states of under nutrition. Consideration of this concept is of particularly relevance to global health.

Biomarkers of metabolic disruption are available for human studies-for instance one can conduct clinical studies with metabolic tracers in combination with exposure assessments.

Recommendations:

Consider the potential of metabolically dysfunctional states (e.g. obesity, insulin resistance, diabetes) as outcomes of toxicant exposures as well as toxicant effect modifiers/susceptibility factors.

Examine the role of early life exposure in metabolic disruption.

Conduct prospective human studies to test the metabolic disruption hypothesis.

Add a metabolic component to high throughput screens and reproductive toxicology tests already in place.

Foster interdisciplinary approaches to metabolic disruptor research through the inclusion of toxicologists, epidemiologists, endocrinologists, nutritionists, and microbiologists.

Leverage the NIDDK Mouse Metabolism Phenotyping Cores to conduct state of the art whole body animal studies.

Utilize metabolomics technologies to examine metabolic disruption.

Discussion Participants:

Androphy, Bruce

Dolinoy, Dana

Gohlke, Julia

Hennig, Bernhard

Kwok, Richard

LaMerrill, Michele

Lee, Mary

Leikauf, George

Wright, Robert

Report 95: Environmental Health Literacy

Convener: Carol Stroebel

Brief History:

We have a long way to go for people to understand environmental health.

Why is this topic important now?

There is a critical need to educate the public about environmental health. Conveying environmental health information is more challenging than others; no smoking gun, no trail of blood.

Media doesn't know how to cover science.

Public doesn't understand probability; doesn't understand science; doesn't understand risk.

Discussion:

A lot of databases @ NLM exist and are used by the public; NLM also has materials for kids.

General public doesn't have a basic understanding of environmental health and there is a range of definitions.

NIEHS has some tools, has office of communications.

Should be a simple model that should be adopted by NIEHS to convey to the public, the exposures and health outcomes studied by NIEHS; something like a food plate for environmental health; has a brand, a long-term impact. And will help increase visibility of NIEHS

NIH has a health literacy study section; very few environmental health proposals that go thru it. Been around for 3-4 years; lots of health literacy research projects. Very few in the area of environmental health. Another question is: If they went thru the study section, would NIEHS fund them? Such projects would be more in the social science realm.

Infectious disease would be the low-hanging fruit; chemical toxicity in the environment is difficult to understand.

Difficult to work on occupational health unless it's acute.

Birnbaum has been very good at educating policy makers.

NIEHS could coordinate, collaborating with other agencies (CDC, EPA) and groups (SOT, etc.) that could contribute.

Targeted development of educational programs and materials.

It's easy for people in scientific community to talk to each other. Outside of NIH, CDC, needs to be some sense of how to communicate and how to understand it.

Need to reach out as broadly as possibly to different groups, different partners; that's the long term goal.

Policy makers also need to be an audience.

Possibly some grants from PEHP that looked at how you educate the political slice of the pie. They are supplemental grants to a larger grant.

Messages really need to be tailored to the specific audiences. Communications, training, etc., all come under definition of health literacy.

Not a systematic approach of what are the priority audiences, the most effective ways, and how to measure how successful we are, don't know how well we're enhancing health literacy.

EX-Tox-net came out of toxicology extension to help workers and others exposed to pesticides. Funding for that dried up years ago. Is still a Website with a caretaker; it's a valuable resource. May be a prototype.

NJ DOH has great fact sheets on certain substances; we need more of them.

Getting the public, journalists, policy makers, etc., to understand studies, interpret studies, etc.; would make a big difference.

Are there educational programs, fellowships? Student groups do come in to visit; tour the labs, understand what EH workshop is about. Teacher's workshop that lasts a day; curriculum focused. . .

What about journalists, policymakers, Congressional staff

Things have been periodic, not that structured, could perhaps that should be more structured, more frequent

More town hall meetings?

Taking science to different communities, not just having NC audiences come in.

SOT had a program (Smithsonian Resident Associate Program); a full day program; very successful.

Next SOT meeting in SF is toxicology and the media, toxicology and journalists

How to improve science journalists? Trade journals have been doing a better job covering environmental health; since Birnbaum came on board, seeing increased mention of NIEHS in the media and increased quality of reports.

Leadership at NIEHS has increased visibility thru op-eds. In past, have not pro-actively sought the limelight. It could be a double-edged sword. . .

Recommendations:

NIEHS increase sessions at scientific meetings (SOT, APHA, ATS, ISEE, ISES, etc.), and at relevant meetings such as the Society of Environmental Journalists, on environmental health.

Create partnerships at universities around the nation for eg., NIEHS director to speak at public health schools and elsewhere in academic communities

Participate in "science cafes" – support scientists speaking at those.

Support environmental health programs at exploratory and science museums, children's discovery museums, etc.

Continue efforts to engage with the media.

Support/foster a network (eg. including NIEHS grantees) to generate a list of best practices on increasing environmental health literacy, and having others help to get the environmental health concepts out.

Use the Institute's worker health and safety training program as a model for, eg., children's environmental health worker training for, eg., school administrators and facility managers, child care professionals, etc.

Should be a simple model adopted by NIEHS to convey environmental health concepts to the public, the exposures and health outcomes studied by NIEHS -- something like a food plate for environmental health; has a brand, a long-term impact

Participants:

Barnett, Claire

Bearer, Cynthia

Holmgren, Stephanie

Madrigal, Daniel

Morawetz, John

Moore, Nuala

Stroebel, Carol

Wexler, Phil

Report 96: Reframing the Societal Narrative so that Environment is the Default for Prevention

Convener: Bruce Lanphear

Brief History: Americans have high expectations that biomedical technology and drugs will cure chronic disease, but they are largely unaware that the most dramatic reductions in child mortality and increases in life expectancy over the past century were largely due to environmental modifications, such as water treatment, housing quality, pasteurization and enhanced nutrition.

With the decline in communicable diseases, chronic disease has emerged as the leading cause of death and disease worldwide. There is now considerable evidence that industrial pollutants, environmental chemicals, poor nutrition and the built environment are major risk factors for chronic diseases. As such, there are tremendous research and public health opportunities to quantify and prevent environmentally-induced disease if we can convince the public to invest in environmental research and interventions, such as regulations to reduce pollutant and environmental chemicals, as well as efforts to modify our environments in ways that are conducive to health.

Discussion Highlights:

We need to identify low-hanging fruit to illustrate the impact of environmental research and interventions on disease outcomes, such as hospitalizations or the impact of smoking bans on asthma and heart attacks. In absence of such data, public assumes health benefits are “medical”.

We need to point out the fallacy of lifestyle choice as the primary reason people develop chronic disease. Our tendency is to blame people for their lifestyle choices, but environmental influences (e.g., living in lead-contaminated housing, lack of affordable healthy foods, smoking in movies) often “cause” lifestyle choices.

We need to redefine the level of evidence that is necessary to justify action. This might be operationalized as the proportionately principle. We also need to distinguish the level of evidence necessary to *remove* or *reduce* exposures to an environmental hazard versus *introducing* a drug or potential hazard.

We need to find ways to enhance research to test synergistic or additive effects of exposures to multiple chemicals or stressors.

We need to enhance use of mechanistic pathways to evaluate the impact of environmental risk factors on a disease or disorder.

We need to recognize that, in contrast with medical interventions (i.e., drugs, procedures) which result in short-term privatize profits or individuals benefits, environmental regulations (i.e., reduce tobacco use, airborne pollutants, blood lead concentration) result in public benefits and costs averted. We need to use different metrics to evaluate environmental hazards and find ways to promote them.

Medical interventions are focused on individuals; environmental interventions (prevention) must focus on populations that affect large numbers of people with only some people benefiting.

Under current model, we wait until an environmentally-induced disease emerges before attempt to identify risk factors rather than require cost-benefit analysis on potential impact of introducing a chemical or industrial pollutant and requiring industry to prove product is “safe”.

Recommendations:

Increase cross-disciplinary research awards with non-traditional disciplines, such as economists, city planners, sociologists and engineers.

Increase partnerships with other federal agencies to conduct research on sustainability (e.g., US EPA), housing (US D of HUD), and Superfund remediation (e.g., ATSDR).

Write narrative as part of first 50 years of NIEHS focusing on lessons learned from lead, asbestos, tobacco, air pollution and other key examples about how to prevent exposure and benefits of reducing exposures on human health, including costs of reducing death, disease and disability. This should include a catalogue of benefits and profiles of environmental scientists who led innovative research with public health impact.

Support cost-benefit analysis of environmental health interventions or regulations including impact of environmental hazards on violence, hospitalizations, crime, neurobehavioral problems, cardiovascular. These models should also examine the impact of newly introduced chemicals or hazards and their potential impact, including estimates of remediation.

Develop an intramural program and fund extramural programs in environmental health economics, focusing on impact of environmental interventions on health care costs, disease and disability or death. These models should also examine economic benefits of alternatives, such as Green Chemistry.

Find ways to communicate impact of environment to public and interested groups, including results of biomonitoring data and impact of environmental interventions. Interested groups might include journalists (e.g., Society of Environmental Journalists).

Discussion Participants: David Peden, Debbie Cory-Slechta, Dale Sanders, Richard Dennison, Gina Goulding, Sacoby Wilson, Terry Collins, Joshua Rosenthal, Christie Drew, Ed Levin, Bruce Lanphear

Report 97: Environmental Health Communication Research

Convener: Liam O'Fallon

Brief History: NIEHS has a long history of supporting projects that communicate environmental health information, but has not engaged in communication research (the science of communicating science). In addition, the theme of communication has been reflected throughout the meeting. Reports 6, 22, 37, 41, 43, and 49 have all recommended that communication be a part of the NIEHS research culture. Communication research could help to improve this work by providing insights on how audiences understand and act upon environmental health messages.

Discussion Highlights:

Partnerships are essential: Behavioral and Social Science Researchers, Sociologists/anthropologists, Schools of Journalism, Other federal partners (NCI, CDC, EPA, NASA, etc), risk communication programs, Marketing organizations.

Gap in environmental health (EH) Communication Research – where information exists, it tends to be outdated. There is plenty of basic communication research information, but not specifically focused on EH topics. Need to provide EH content to inform communication research work.

Need: Disseminating research for prevention and public health is central to the NIEHS mission, EH Communication Research will enhance and inform this part of the mission. It will improve the effectiveness of EH messages, inform better/tailored messages, could be used as part of communication intervention/prevention strategies.

Communication research is part of *primary* prevention strategy.

Key to communication success:

- Trusting relationships (CBPR), communication strategies need to be developed up front.
- Partnerships with advocacy groups to get messages out
- Cultural understanding

Challenge:

- Information overload – communication research can help in understanding of how to tailor and target messages to reduce information overload.
- Organizational challenges – study sections will likely require education of communication research

Communication research can help to move EH communication forward light years. Simple and complex approaches

Simple = focus groups – How do people interpret messages? Understanding of EH? Precautionary principle? **Prevention?** What is the public really interested in??
Complex = hire in outside consultants, imaging (more $$)

There needs to be a process to get people to use information. How do you make it useful? People have their own ways to make info useful. Role of US Gov't is to provide research in 'Plain Language' for public use. In context. Communication research can help to address these issues.

Communication research can show impacts better.

Recommendations:

Increase resources to support communication of research – must ensure community/stakeholder engagement in process of identifying issues.

Build off past NIEHS investments – communication research strategies should use existing frameworks as foundation, leverage existing partnerships

Communication research should be a part of the whole institute

EHP should have a dedicated section on communication science

Convene a workshop of experts in communication research to identify research questions and then act upon those recommendations… develop an FOA.

Discussion Participants:

Brody, Claudio, Edwards, Froines, Haynes, Kostant, Madrigal, McConnell, O'Fallon, Rizzo, Sen

Priority Topics

The 97 discussion reports were voted on by participants as to which they had the greatest personal energy (5 votes per person). The reports that received the most votes became priority topics around which participants clustered the remaining reports. Thirteen clusters were formed. A participant volunteered to convene a breakout discussion for each of these emergent priority clusters and to create a report including discussion highlights and identification of a "recommended strategic goal." Thirteen reports were submitted from these breakouts, which follow in this section.

Priority Topic 1: Training Environmental Health Scientists

Convener: Abee Boyles

Discussion Participants: Gary Bird, Abee Boyles, John Cidlowski, Luz Claudio, Paul Foster, Laurie Johnson, Karen O'Brien, Erikca Reid, and Dale Sandler

Subtopic Report Numbers from Days One and Two:

45 Training and Mentoring

50 Integrating Environmental Health into Medical and Nursing Curricula

55 Cross Disciplinary Training of Environmental Health Scientists

Recommended Strategic Goal:

Recruit, train, and retain the next generation of environmental health scientists and professionals

Potential Beneficiaries of this Strategic Goal:

By insuring the pipeline of new scientists in environmental health by attracting them early in education, pulling from a variety of disciplines, and continuing their involvement as they progress into a variety of career paths, this Strategic Goal will benefit:

Educators (K-12 and universities)

Medical communities and health departments

Policy makers

Rest of NIH and federal partners

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

K-12 education departments and science enrichment programs such as Science Olympiad

NSF, AASC, and similar science foundations

Undergraduate universities (including ones without dedicated environmental science programs)

Medical and public health schools

Other NIH training programs

Professional societies (consider developing a dedicated, cross-disciplinary Environmental Health Science society to foster communication, networking, training, and promotion of EHS)

Priority Topic 2: Connecting environmental influences to disease through the study of epigenomics and epigenetic mechanisms

Convener: Brad Bernstein, John Hollingsworth

Discussion Participants: Bernstein, Dolinoy, Gilliland, Hall, Hanawalt, Hollingsworth, Kemp, McAllister, Taylor, Worth

Subtopic Report Numbers from Days One and Two:

3 Moving beyond the conventional notion of 'bad' substances causing disease while 'safe' substances do not.

12 Early Life Exposure(periconceptual through adolescence) leading to later life impacts

18 Acquired DNA modification(both DNA sequence and epigenetic modifications) may provide an integrated dosimeter of environmental exposure and be a useful predictor of disease

22 Research translation/communication

24 Nutritional modulation of environmental insults (or interplay of nutrients with toxicants to modulate health and disease)

31 Healthy buildings and communities

34 Commensal Organisms (Microbiome) and Health

36 Role of environment in neurodegenerative disease and healthy aging

40 Environmental Epigenomics

41 Partnering with communities

46 Appropriate reporting and analysis of sex differences in environmental research

49 Children's Environmental Health Research; networks and more bang for the buck

70 The role(s) of ncRNAs in environmental health

79 Exposure science and exposome

81 Environmental epigenomics and complex heritable disease

94 Toxicants as potential metabolic disruptors

Recommended Strategic Goal:

Connecting environmental influences to disease through the study of epigenomics and epigenetic mechanisms is an opportunity and important overarching goal for NIEHS.

ENVIRONMENT → EPIGENOME (+GENETICS) → MANIFESTATION OF DISEASE

NIEHS should be a leader in the field of acquired genetic/epigenetic changes from exposure and diet across the lifecourse. A broad goal is to link patterns of epigenomic modifications to environmental exposures. This represents a key step towards (i) linking environment to disease and susceptibility; (ii) attaining mechanistic insight into the underlying pathophysiology; and (iii) identifying biomarkers that quantify exposure and could be combined with genetic information to predict disease risk. These areas have enormous opportunity for human health given the potential reversibility of epigenomic changes by targeted therapeutics.

A number of key areas and opportunities were identified in this regard.

- Systematic study of epigenomic changes induced by specific environmental exposures in multiple contexts, including stem cell models, model organisms and human populations.
- Technology development to enable environmental epigenomics.
- Increase understanding of the stability and plasticity of specific types of epigenomic changes.
- Understanding interactions between genetics, epigenomics and environment.
- Careful consideration of vulnerable windows of susceptibility to the environment and their relationship to epigenome (trans-generational, *in utero*, chronic, etc.).

Potential Beneficiaries of this Strategic Goal:

Potential outcomes of this effort include improved biomarkers, strategies for intervention/prevention, risk assessment, early detection, and basic mechanistic understanding of human biology.

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

NTP, DIR, DERT, NHGRI, Common Fund Epigenomics, International Human Epigenome Consortium, Biotech/Pharma target epigenome

Priority Topic 3: Health Disparities and Environmental Justice

Convener: Peggy M. Shepard

Discussion Participants: Chris Long, Beverly Wright, Aubrey Miller, Peggy Shepard, Darryl Hood, Doug Brugge, Chip Hughes, Jennifer Sass, Bruce Androphy, Erin Haynes

Subtopic Report Numbers from Days One and Two:

8 Environmental justice, climate justice and vulnerable and susceptible communities: how NIEHS can help build capacity towards understanding the role of the environment

27 Environmental justice and health disparities strategy and grant program

41 Partnering with communities

59 The National Prevention Strategy: integrating environmental health research to focus on disease prevention and health promotion

60 Advocacy

83 Health impacts from disasters with emphasis on vulnerable populations

89 Can NIEHS support and foster state and local environmental health infrastructure?

Research Agenda Focus:

Minority and low-income populations

Climate Impacts/Natural and Man-Made Disasters

Funding Mechanisms

Environmental Justice/Health Disparities Centers and grants

Partnerships

- Community-Academic Partnerships that build capacity of all partner and translate research to interventions and policy
- NIEHS partnerships with local/state governments, DOHs, other NIH institutes, and other federal agencies

Recommended Strategic Goal:

Increase understanding of how environmental factors impact health disparities in minority and low-income populations.

Potential Beneficiaries of this Strategic Goal:

- Low income and minority populations,
- people of color,
- seniors,
- children,
- disadvantaged populations and communities
- Reduced lost work time, reduced missed school days

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

- CBPR should be core component of all NIEHS research
- Explore new methodologies
- Aforementioned partnerships

Priority Topic 4: Communication Research

Convener: Liam O'Fallon

Discussion Participants:
Brody, Edwards, Graedon, Gray, Haynes, Lucier, Madrigal, Moore, Morawetz, Nolan, O'Fallon, Stroebel, Walker, Woodruff

Subtopic Report Numbers from Days One and Two:

4 What is the environment? What is the scope? Is there a box?

6 How can NIEHS better disseminate information?

10 Define translational research and its role in EHS

22 Research translation/communication

37 Environmental Health Education as an intervention and prevention strategy

41 Develop an integrated, searchable knowledge base on the impact of environment on health

43 Is it important to educate the public, and if so, how best?

46 Appropriate reporting and analysis of sex differences in environmental research

51 One health

59 The National Prevention Strategy: integrating environmental health research to focus on disease prevention and health promotion

63 Integrating community outreach and translation into research

89 Can NIEHS support and foster state and local environmental health infrastructure?

91 The role of public health prevention in environmental health research

95 Environmental health literacy

97 Environmental health communication research

Recommended Strategic Goal:

Provide Leadership in Translating[1] and Communicating Scientific Knowledge on the Role of the Environment on Human Health

[1] "Translating" in this context does not mean drug discovery.

Rationale:

This strategic goal will:

- Improve environmental public health policy decisions
- Engage vulnerable communities
- Prevent and reduce harmful environmental exposures
- Empower/enable the public to make informed decisions
- Increase visibility of NIEHS
- Sustain support of NIEHS
- Enhance accessibility and usability of environmental health research
- Integrate environment health knowledge into relevant professions and practice (such as health care, education, and occupation)
- Advance, promote, and apply communication science

Potential Beneficiaries of this Strategic Goal:

- NIEHS
- Legislators
- Patient groups
- Exposed populations
- WHO
- Media
- Grantees
- Clinicians
- Science-based NGOs
- Schools of Public Health
- Educators
- Regulators
- State/Local agencies
- Federal, interagency partners
- Communities
- Medical Unions
- Policy/decision makers
- Public health professional

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

- Funding Opportunity Announcements should prioritize communication
- Support Training (NIEHS Staff, Grantees, All partners)
- NIEHS needs to show institutional Leadership (Prioritize within NIEHS)
- Strengthen interactions at Federal, State and local levels for communication (provide resources and coordinate eh messages)

- Specific grants for communication and communication research
- Build off past and current investments:
    - Internally: NTP, PEPH (all aspects), EHP
    - Externally: NCI, CDC, EPA, NLM
- Environmental Health Education – build the capacity of educators to bring EH messages into the classroom
- New communication technologies—communication research and social media
- Evaluation of effectiveness
- Partnerships required – see “Beneficiaries” listed above.
- Partnerships required –
    - transdisciplinary scientists (behavioral and social scientists)
    - communication researchers,
    - marketing organizations,
    - schools of Journalism

Priority Topic 5: National Prevention Strategy

Convener: William Stokes and Jeanne Rizzo

Discussion Participants: Cheryl Marks, Robert Rickard, Jeanne Rizzo, Dale Sandler, Tom Sinks, William Stokes, Philip Wexler, Douglas Brugge, Gwen Collman, Laurie Johnson, Paul Jung

Subtopic Report Numbers from Days One and Two:

28 Clearest and most present dangers from occupational and chemical agents

29 Moving environmental research findings into policy

51 One health

59 The National Prevention Strategy: integrating environmental health research to focus on disease prevention and health promotion

89 Can NIEHS support and foster state and local environmental health infrastructure?

91 The role of public health prevention in environmental health research

96 Reframing the societal narrative so that environment is the default for prevention

Recommended Strategic Goal:

Identify NIEHS as the "Prevention Institute" within NIH through research, training and education that leads to exposure reduction and disease prevention.

Potential Beneficiaries of this Strategic Goal:

- NIH – all Institutes
- NIEHS Intramural
- Extramural researchers and staff,
- Vulnerable Populations and including Environmental Health and Justice communities
- policy makers
- tax payers
- media
- Local and state governments
- Global Health diplomacy

- Health care systems including providers, Medicare and Medicaid
- Safe alternative and green chemistry developers in private sector

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

Capabilities

- Strengthen the evidence vase to understand human environmental exposures that impact human health
- Strengthen the investigator and staff understanding of how the research connects to the prevention mandate
- Provide new tools to assess safer alternatives

Partnerships:

- Disease based IC's
- Professional societies including APHA, AMA, AVMA, ANA
- One Health communities: human, animal and ecosystem scientist
- Economists
- Planners
- Risk Assessors
- Other Federal Agencies: EPA, CDC, National Prevention Council members etc.
- Health Communicators
- Media
- Community partners and non profit organizations

Priority Topic 6: The Effects of the Environment on the Immune System

Convener: Darryl Zeldin and Paige Lawrence

Discussion Participants: Janice Allen, John Cidlowski, Mike Fessler, Tom Gasiewicz, Dori Germolec, Michael Holsapple, Virginia Ladd, Paige Lawrence, Pat Mastin, Jerry Phelps, Michael Pino, Ellen Silbergeld, Darryl Zeldin

Subtopic Report Numbers from Days One and Two:

22 Research translation/communication

31 Healthy buildings and communities

34 Commensal organisms (microbiome) and health

35 Moving from 'cure' model to the three 'P'—predicting, preventing, personalized treatment of autoimmune diseases and cancer

36 Role of environment in neurodegenerative diseases and healthy aging

53 (main) Effects of the environment on the immune system

76 Healthy environments for children

Recommended Strategic Goal:

To make investigation of the interactions between the environment and the immune system, and its relationship to human development, health and disease, a major research priority for NIEHS

Potential Beneficiaries of this Strategic Goal:

1) This research agenda will have a major impact on the global health community because the development, function and regulatory balance of the immune system underlies numerous prominent diseases (e.g. infectious, immune-mediated, cardiovascular, cancer, orphan).

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

1) This research has far reaching implications that span the mission of NIEHS and other federal agencies, universities, advocacy groups and global health organizations and provides opportunities to support efforts to improve human health.

2) Through its intramural (NTP, DIR) and extramural programs, NIEHS possesses a deep knowledge of how the environment impacts human health and diseases.

3) NIEHS has established epidemiologic expertise in the implementation of large cohort studies.

4) The NIEHS has an internationally recognized and highly respected testing program within the NTP that examines the effects of environmental chemicals on the developing and adult immune system. Highly cited publications from these efforts have positively impacted regulatory guidance on a global scale.

5) NIEHS and its interdisciplinary network of scientists has an opportunity to take a leadership role in understanding the etiology of diseases of enormous public health importance by providing knowledge and expertise on environmental exposures, a crucial, yet underappreciated contributor to human health and well being.

6) This area of research will enhance partnerships to bridge research from the bench to clinical—translational to public health by cultivating multi-institutional interactions within and outside of the NIEHS.

7) NIEHS has expertise in multidisciplinary research and the integration of cross-cutting information that directly impacts human health.

8) NIEHS has an exciting opportunity to create a network of collaborating institutions and lead research efforts to understand how the environment impacts immune system development, function and disease

Priority Topic 7: Exposure

Convener: Sacoby Wilson

Participants: Balshaw, Breysse, Brody, Dellinger, Drew, Hubal, LeMasters, Miller, Serabjit-Singh, S Wilson

Subtopic numbers:

5 Environment/geospatial informatics

14 Wireless technologies to assess environmental exposures

19 Does/response application to environmental health

21 Human variability: sources and contribution to differential susceptibility to exposures to environmental agents

27 Environmental justice and health disparities strategy and grant program

30 Traffic related air pollution and human disease

31 Healthy buildings and communities

32 Indoor Air Quality

33 Novel modeling techniques in environment and health science

47 Exposure science

58 Develop novel technologies and methodologies to detect and analyze (real-time) multiple exposures and their human health effects

71 Environmental pressures over space and time—taking advantage of novel technologies

79 Exposure science and the exposome

82 Environmental light: is NIEHS research focused enough on environmental light and its interaction with chemicals, compounds and organisms in the environment?

84 Workplace exposure to particulate agents

88 Next steps for exposure biology

93 Remotely-sensed and GIS data

Recommended Strategic Goal:

Characterize exposures to improve health and prevent disease

- Address totality of exposures: physical, chemical, biological agents, psychosocial stress, lifestyle factors, etc.
- Use State of the art approaches
- Take a multi-level systems approach: Focus on multiple levels of organization: Systems science approach.
    - Need to understand what the determinants of exposures across individuals, organizations, biological systems, etc.
- Exposure assessment is more than biological monitoring – not a panacea
- Having these tools can change the way we do environmental epidemiology to promote health better
- Promoting health = facilitating prevention, intervention and treatment
- Need to collect relevant exposure data to make decisions

Three major sub themes were identified:

1. Developing new Tools: 5, 33, 93, 58, 14, 72, 71
    a. Challenge = antiquated tools currently used. Develop state of the art exposure assessment tools and technologies
    b. Ability to quantitate personal environment, space and time, and the provision of exposure technology to environmental epidemiology and the community
    c. Integrated complex exposures to multiple agents and stressors over the lifecourse
2. Exposure science: 79, 47, 88, 19, 21, 87, 27
    a. Understanding environmental components of disease
3. Specific environments and populations (Air pollution): 31, 32, 30, 84, 82
    a. Safe living and working environments

Why now:

Having exposure data will allow us to better focus limited resources to have the greatest health improvements

Exposure information is a fundamental input for decision making

POTENTIAL BENEFICIARIES OF THIS STRATEGIC GOAL:

Populations that benefit the most: Disproportionately burdened, disproportionately exposed, differential risks, differential health outcomes, differentially burdened, everybody benefits because it is a fundamental input; Various life stages (children, pregnant women, elderly); SES status; researchers advancing knowledge;

User groups/Partners: Policy makers, health researchers, vulnerable groups, decision makers, advocacy groups, planners, community developers, health departments, clinicians working on env medicine, risk assessors

NIEHS CAPABILITIES AND PARTNERS NEEDED

Partners

Technology partners include: Government Agencies: CDC/NHANES, NIOSH, DOE, USGS and Census, OSHA, DOL, DOD NASA other NIH ICs, NSF, NOAA, HUD,

We need multidisciplinary training and research funding initiatives for academics. Various disciplines to be included are: Engineering, Epi, Statisticians, Medicine, Planning, Electrical, Chemical engineers, geographers, informaticians; behavioral and social scientists.

Community engagement at all levels of research and public health messaging to nurture and support partnerships

Capabilities and innovations needed

Intramural exposure science program in this area is needed

Prioritize resources to fund exposure research that expand focus on mechanistic toxicology driven research program (both intramural and extramural)

Expand exposure assessment expertise to NIEHS Staff and Council

Add focal point in the office of the director to coordinate exposure science across agencies

Add requirements for exposure science cores in center and training grants

Advocate for an exposure science study section

Support discovery science

Ensure exposure science people are included in the October distillation of the strategic plan

Priority Topic 8: EHS Information Strategy

Convener: Ken Fasman

Discussion Participants:

Heather Henry, Stephanie Holmgren, Carolyn Mattingly, Philip Wexler, Deborah Winn, Ken Fasman

Subtopic Report Numbers from Days One and Two:

7 Create a global focal point for online environmental health databases, and seek means of linking and integrating their contents

38 Investing in publicly available resources and computational tools for integrating and analyzing environmental health data

42 Develop an integrated, searchable knowledge base on the impact of environment on health

67 Informatics partnerships, services and infrastructure for intramural and extramural EHS

Recommended Strategic Goal:

NIEHS to lead the creation and implementation of a strategy to integrate environmental health science data to maximize its sharing and utilization for advancing scientific discovery.

This encompasses diverse data sets (GIS, genomics, epidemiology, exposure, etc.), analytical tools, visualization tools, training materials, etc.

Potential Beneficiaries of this Strategic Goal:

- Global EHS researchers, NIEHS, other NIH institutes and grantees, peer organizations such as EPA, CDC, FDA, NOAA, etc., and other users.

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

- Partner with other national and international agencies / organizations that have successfully created and implemented information strategies (e.g. NCBI, …), information sharing standards/approaches
- Inventory of existing systems / coordinating with developers/maintainers of existing resources
- Interacting broadly with the community of users to identify significant unmet needs
- Proactively establish standards and approaches for new data resources as they are being planned and funded
- Database of databases – registry of information resources for EHS research
- Enhancing EHS informatics capacity/capability – for training, strategic planning, consulting/service
- NIEHS to take a strong position around importance of data sharing

Priority Topic 9: Learning from Mechanisms of Resistance, Resilience and Recovery to Develop Therapeutic Treatments for Environmental Disease

Convener: Ed Levin

Discussion Participants: Palmer Taylor and Ed Levin

Subtopic Report Numbers from Days One and Two:

26 Developing interventions for environmental disease

56 Mechanisms of resistance, resilience, and recovery: learning from success in dealing with environmental stressors

Recommended Strategic Goal:

Develop therapeutic treatments for impairments and injuries caused or aggravated by environmental exposure. Good approaches for this effort can be gained by learning about the mechanisms of resistance, resilience and recovery that normally occur in individuals that do not show adverse effects in the face of environmental exposure.

Potential Beneficiaries of this Strategic Goal: Those people who suffer from the adverse effects of environmental exposure. It is an excellent outcome to discover the threshold for adverse effects of toxicants to prevent future exposure but we should no abandon those already exposed.

NIEHS Capabilities and Partnerships Needed to Achieve this Goal: Ally with therapeutics development underway by other NIH institutes, pharmaceutical companies and academic labs to develop effective treatments for environmentally induced disease. Attend to the physiological processes of adaptation and resilience and recovery that provide protection against toxic effects in those not showing adverse effects of toxicant exposures

Priority Topic 10: A systems model & approach for environmental health science

Convener: Karen Adelman

Discussion Participants:

Subtopic Report Numbers from Days One and Two:

Recommended Strategic Goal:

Develop a conceptual framework and tools for enabling a systems model and approach for environmental health science

Potential Beneficiaries of this Strategic Goal:

Environmental health scientists broadly from biologists and social scientists to clinicians to risk assessment to public health advocates and practitioners.

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

NIEHS could leverage infrastructure and knowledge at other NIH institutes for some components of this, but should invest strategically to expand systems approaches to environmental health sciences.

Involves use and sharing of databases, policies and public availability.

This initiative would involve all parts of NIEHS (DIR, DERT, NTP), working collaboratively to achieve the goal.

Generation of broad, flexible framework for synthesis and integration of systems level data. This framework could be populated by a spectrum of data types from genetic variability to epidemiology to epigenomics, deposited in a standardized format to facilitate integration. Concrete steps would include creating an 'omics strategy for environmental health science, and to encourage development of new techniques for monitoring exposures.

Infrastructure investment will be required to provide a repository for data (and perhaps samples)

To maximize utility, significant investment is required in the tools and approaches to connect various data types, permit mining of data, analysis, statistical evaluation, and curation.

Priority Topic 11: Global Environmental Health

Convener: Joshua Rosenthal

Discussion Participants: John Balbus, Trisha Castranio, Luz Claudio, Julia Gohlke, Richard Kwok, Joshua Rosenthal, Jane Schroeder, Bono Sen, Kimberley Thigpen-Tart, Wendy Thomas, Mary Wolfe, Harold Zenick

Subtopic Report Numbers from Days One and Two:

13 Global environmental change and human health

15 Should NIEHS be a global diplomat?

22 Research translation/communication

39 Global environmental health and the changing burden of disease in the developing world

41 Partnering with communities

51 One health

59 The National Prevention Strategy: integrating environmental health research to focus on disease prevention and health promotion

75 Environmental health economics

83 Health impacts from disasters with emphasis on vulnerable populations

Recommended Strategic Goal:

Provide international leadership on global environmental health imperatives

Potential Beneficiaries of this Strategic Goal: US scientific and public health communities, Global Populace, US foreign policy interests including national security.

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

- Senior level expertise to lead internal programs and provide external leadership and communications
- Expanded staffing and resources for program development including research and training.
- Participation of extramural, intramural components of the NIEHS including the NTP
- Analytical skills in large geospatial datasets and epidemiological statistics
- Extensive partnerships within the NIH, other agencies, domestic and international academic institutions, ngos, foundations, international government agencies.
- Communications and education/training plan

Priority Topic 12: Early life exposure (Preconceptual through adolescence) leading to later life impacts (fetal to old age) - Prevention and Intervention

Convener: Goldman & Bearer

Discussion Participants:

Subtopic Report Numbers from Days One and Two:

Primary:

65 Early life exposures in childhood and adult disease: role of susceptibility factors

21 Human variability: sources and contribution to differential susceptibility to exposures to environmental agents

12 Early life exposures (periconceptual through adolescence) leading to later life impacts (child to old age)—prevention and intervention

+/-2

Research areas:

2 Identification of pre-, peri-, and post-natal environmental factors that contribute to variation in neurodevelopmental outcomes

10 Define translational research and its role in EHS

17 Regenerative approaches to correcting complex structural birth defects

18 Acquired DNA modification (both DNA sequence and epigenetic modifications) may provide an integrated dosimeter of environmental exposure and be a useful predictor of disease

24 Nutritional modulation of environmental insults (or interplay of nutrients with toxicants to modulate health and disease)

61 Basic research on mutagenic mechanisms using model systems

94 Toxicants as potential metabolic disruptors

Specific environments:

30 Traffic related air pollution and human disease

32 Indoor air quality

57 Healthy buildings and communities

76 Healthy environments for children: IEQ

Methodologies:

41 Partnering with communities

49 Children's environmental health research: networks and more bang for the buck

64 Protecting our investments by providing infrastructure and support to biorepositories, cohorts, and datasets to expand our ability to study new and emerging hypotheses

Overarching NIEHS goals:

22 Research translation/communication

66 Science based risk assessment

80 Preventing prenatal exposures to toxicants

91 The role of public health prevention in environmental health research

Recommended Strategic Goal:

Understanding how early life environmental exposures impact development and health across the lifespan.

Potential Beneficiaries of this Strategic Goal: Women of childbearing age, children, fathers

Broadly, economic benefits: for education, health care across the life span, taxpayers, the US economy

NIEHS Capabilities and Partnerships Needed to Achieve this Goal:

To achieve this strategic goal requires focus on understanding vulnerability, susceptibility, variation and implications for prevention and intervention.

Partnerships: Especially, people who have resources, research related to children: NICHD (NCS and other research networks), NHLBI, NCI, EPA, CDC, WHO, Other international networks, NGO's, industry. Potentially: many institutes of NIH (NIAAA, NIDDK, NIDA) and many other organizations.

Capabilities:

- Development and core facilities to measure Genetics, epigenetics, metabolomics, proteomics, exposome
- Develop tools and methods for basic mechanistic studies, exposure assessment, biorepositories, models of molecular/cellular/animal/virtual development,
- Develop core facilities which are open to the scientific community: for novel emerging technology, for data, biorepository, access to models, exposure assessment
- Develop interventions at multiple levels
- Tools for communication and intervention across disciplines
- Community based research and research networks

Priority Topic 13: Exposure - Yay!

Convener: Sacoby Wilson

Participants: Balshaw, Breysse, Brody, Drew, Hubal, LeMasters, Miller, Serabjit-Singh,

Subtopic numbers:

5 Environmental/geospatial informatics

14 Wireless technologies to assess environmental exposures

19 Does/response application to environmental health

21 Human variability: sources and contribution to differential susceptibility to exposures to environmental agents

27 Environmental justice and health disparities strategy and grant program

30 Traffic related air pollution and human disease

31 Healthy buildings and communities

32 Indoor air quality

33 Novel modeling techniques in environment and health science

47 Exposure science

58 Develop novel technologies and methodologies to detect and analyze (real-time) multiple exposures and their human health effects

71 Environmental pressure over space and time—taking advantage of novel technologies

79 Exposure science and the exposome

82 Environmental light: is NIEHS research focused enough on environmental light and its interaction with chemicals, compounds, and organisms in the environment?

84 Workplace exposure to particulate agents

88 Next steps for exposure biology

93 Remotely-sensed and GIS data

Recommended Strategic Goal:

Lead the advancement of the state-of-the-art for characterizing exposures to promote health and prevent disease

- Address totality of exposures: physical, chemical, biological agents, psychosocial stressors, neighborhood stressors, lifestyle factors, etc.
- Use State of the art approaches
- Take a multi-level systems approach: Focus on multiple levels of organization: Systems science approach.
    - Need to understand what the determinants of exposures across individuals, organizations, biological systems, etc.
    - Focus on built environment and social environment
- Understand historical exposures
- Focus on exposures across the life course
- More work on vulnerability and susceptibility including environmental health disparities
- Assess differential burden, exposure, risks, effects, and health outcomes
- Exposure assessment is more than biological monitoring – not a panacea
- Integration of human and ecological exposure assessment
- Having these tools can change the way we do environmental epidemiology to promote health better
- Promoting health = facilitating prevention, intervention and treatment
- Need to collect relevant exposure data to make decisions

Three major categories emerged:

4. Developing new Tools: 5, 33, 93, 58, 14, 72, 71
    a. Challenge = antiquated tools currently used. Develop state of the art exposure assessment tools and technologies
    b. Ability to quantitate personal environment, space and time, and the provision of exposure technology to environmental epidemiology and the community
    c. Integrated complex exposures to multiple agents and stressors over the lifecourse
5. Exposure science: 79, 47, 88, 19, 21, 87, 27
    a. Understanding environmental components of disease
    b. Understand cumulative exposures and risks
    c. Exposure to multiple agents and stressors including social stressors
    d. Assess differential burden, exposure, risks, and health outcomes
    e. More work on mechanisms
    f. Include systems science
    g. Include lifestyle exposures
    h. Focus on positive exposures
6. Specific environments and populations (Air pollution): 31, 32, 30, 84, 82
    a. Safe living and working environments
    b. Health disparity populations
    c. Susceptible groups including children, pregnant women, elderly, populations with co-morbidities
    d. Maximally exposed populations

e. Urban, suburban, and rural
f. Heavily industrialized areas
g. Agricultural regions
h. Indoor Environment
i. Coastal environments
j. Tribal/Indigenous Communities and Populations
k. Military populations and veterans

Why now: Having exposure data will allow us to better focus limited resources to have the greatest health improvements

Exposure information is a fundamental input for decision making

Need NIEHS to take the lead to do better community engagement and partnerships with community-based organizations for exposure science research including bench and applied research to promote health, prevent disease, and translate into interventions and policies

POTENTIAL BENEFICIARIES OF THIS STRATEGIC GOAL:

Populations that benefit the most: Disproportionately burdened, disproportionately exposed, differential risks, differential health outcomes, maximally and highly burdened, vulnerable populations, everybody benefits because it is a fundamental input; Various life stages (children, pregnant women, elderly); SES status; researchers advancing knowledge;

User groups/Partners: Policy makers, health researchers, vulnerable groups, decision makers, advocacy groups, planners, epidemiologist, toxicologists, community developers, health departments, clinicians working on env medicine, risk assessors, engineers

NIEHS CAPABILITIES AND PARTNERS NEEDED

Partners

Expand partnership with EPA for funding initiatives and other programs

Technology partners include: Government Agencies: CDC/NHANES, NIOSH, DOE, USGS and Census, OSHA, DOL, DOD NASA, other NIH ICs, NSF, NOAA, HUD,

We need multidisciplinary training and research funding initiatives for academics. Various disciplines to be included are: Engineering, Epi, Statisticians, Medicine, Planning, Electrical, Chemical engineers, community development, health and environmental policy, geographers, informaticians; behavioral and social scientists.

Community engagement at all levels of research and public health messaging to nurture and support partnerships

Capabilities and innovations needed

Exposure Science Training Grants and Programs at ASPH schools and other institutions

Intramural exposure science program in this area is needed

Prioritize resources to fund exposure research that expand focus on mechanistic toxicology driven research program (both intramural and extramural)

Revamp and expand the Exposure Biology Program

Expand exposure assessment expertise to NIEHS Staff and Council

Add focal point in the office of the director to coordinate exposure science across agencies

Add requirements for exposure science cores in center and training grants

Fund exposure science centers

Advocate for an exposure science study section

Partner with colleges and universities to start departments of exposure science using infrastructure and seed grants

Support discovery science

Ensure exposure science people are included in the October distillation of the strategic plan

Recommended Strategic Goals

Of the 13 Priority Topics, 12 recommended strategic goals were posted for voting and participants were given another 5 sticky dots to vote on them. (Two of the recommended strategic goals were related to exposure. Only one of them was posted for voting so as not to split the vote, although there is a report for both included here). The results of the vote are as follows:

Topic	**Vote**
Understanding how early life environmental exposures impact development and health across life span (See priority topic 12)	83
Lead the advancement for state-of-the art for characterizing Exposure to promote health and prevent disease (See priority topics 7 and 13)	71
Attract, train, and retain the next generation of environmental health scientists and professionals (See priority topic 1)	65
Connecting environmental influences to disease through the study of epigenomics and epigenetic mechanism as an opportunity and important long-term goal for NIEHS (See priority topic 2)	62
Identify NIEHS as the Prevention Institute within NIH, through research, training, and education that leads to exposure reduction and disease prevention (See priority topic 5)	60
Provide leadership and resources in translating and communicating scientific knowledge on the role of the environment on human health (See priority topic 4)	60
Develop a conceptual framework and tools for enabling systems model and approach to environmental health sciences (See priority topic 10)	53
Increase understanding of how environmental factors impact health disparities in minority and low income populations (See priority topic 3)	45
To make investigation of the interactions between the environment and the immune system and its relationship to human development, health and disease a major research priority for NIEHS (See priority topic 6)	38
Provide international leadership on global environmental health imperatives (See priority topic 11)	36
NIEHS to lead the creation and implementation of a strategy to integrate environmental health science data to maximize its sharing and utilization for advancing scientific discovery (See priority topic 8)	32
Develop therapeutic treatments for impairments and injuries caused or aggravated by environmental exposure. Good approaches for this effort can be gained by learning about the mechanisms of resistance, resilience and recovery that normally occur in individuals that do not show adverse effects in the face of environmental exposure. (See priority topic 9)	13

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