

Exposome workshop uncovers the devil in the details

By Eddy Ball

For many environmental health scientists, it is self-evident that the totality of internal and external exposures, the exposome, is more significant than any single exposure in the overall health of an organism. But, as the NIEHS Exposome Workshop Jan. 14-15 made abundantly clear, the process of putting the emerging exposome approach to work in scientific research is hardly straightforward.

The 2 days of breakout workgroups and animated discussions highlighted the philosophical, practical, technical, and financial challenges that lie ahead. David Balshaw, Ph.D., chief of the NIEHS Exposure, Response, and Technology Branch, emphasized that holistic approaches to exposure biology require global involvement.

“Although NIEHS has a significant role in implementing the exposome,” Balshaw told attendees, “it’s going to have to be an international EHS [environmental health science] community program.”

NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., pointed to the importance of crafting creative solutions, adopting new approaches in training, and reaching across the social, financial, and intellectual spectra. “We need partners,” she said. “I think one of the important things about the exposome is that it requires integrated methods.”

Listen as Gary Miller, Ph.D., of Emory University, and others describe how understanding the exposome can help protect people at a societal level. (6:31)

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[Transcript](#) (25KB)

One chemical – one set of outcomes no longer suffices

In planning their meeting, Balshaw and his colleagues across NIEHS underscored the role of work in the term workshop. Participants spent 5 months preparing for the workshop, hashing out the troublesome details behind the self-evident truth of the exposome. They discussed promotion strategies, including the development of exposome case studies, or use cases, as proof of principle. They also worked toward papers to submit to peer-reviewed journals.

A number of developments in [21st century environmental health science](#) (<http://www.nap.edu/catalog/13507/exposure-science-in-the-21st-century-a-vision-and-a>)

parallel themes and goals in the NIEHS 2012-2017 [strategic plan](#). Attendees engaged in virtual workgroups before meeting face-to-face at NIEHS to frame the following developments within the exposome concept:

A messy, but necessary process

The Exposome Workshop was necessarily short on data and long on discourse and analysis. Balshaw and his colleagues collected an impressive group of scientists from the U.S., Europe, and Asia, in fields ranging from clinical medicine, epidemiology, and toxicology, to exposure biology, pharmacology, and bioinformatics to review the state of the science in the emerging field of exposomics.

Although attendees were still divided on several issues — including some basic definitions — as the workshop came to an end, most were energized and ready to move forward with a clearer understanding of what needs to be done.

“We can’t let uncertainty prevent us from moving forward,” said [Susan Teitelbaum, Ph.D.](#) (<http://www.mountsinai.org/profiles/susan-teitelbaum>), of Mount Sinai School of Medicine. Several attendees, such as Vermeulen, called for adapting the tools they have now to evaluate additional data, as scientists work toward the new tools and methodologies a global approach will require.

- **Appreciating variation in host susceptibility and response** — Individuals experience a complex mixture of chemical, natural, and social exposures. A range of external and internal factors shapes how an organism responds as it struggles to maintain metabolic balance, or homeostasis.

Gary Miller, Ph.D.

(http://hip.emory.edu/resources/faculty/miller_gary.html)

, of Emory University and chair of the Biological Response Workgroup, introduced the concept of allostatic load as a way to discuss this variation. The term refers to the cumulative cost of correcting perturbations to homeostasis, and a way to frame resilience against further stress.

- **Understanding critical windows of development** — In a dynamic matrix, time is a key determinant in host response to internal and external exposures. Exposures vary in effect depending on when they occur during the lifetime. Exposures may also trigger changes in gene expression linked to the onset of disease later in an individual's life.

"We have to have life course information," said Epidemiology Workgroup member Roel Vermeulen, Ph.D.

(<http://www.uu.nl/staff/RCHVermeulen>)

, of Utrecht University, Utrecht, The Netherlands.

- **Making fundamental changes in scientific method and promoting interdisciplinary approaches** — "The exposome is really about changing the way we do science, moving from a reductionist approach to an integrated complex exposure approach," argued the chair of a breakout group on refining recommendations, Dean Jones, Ph.D.

(http://med.emory.edu/facultyprofiles/profile_bio.cfm?id=128)

, of Emory University.

Several researchers argued for the need to directly challenge disciplinary silos and reengineer training — and retraining — for the scientific workforce across the physical, medical, chemical, biological, and social sciences.

- **Exploiting big data to survey the exposome** — Immediate goals include data mining and integration of existing epidemiological cohorts. Data Workgroup chair Chirag Patel, Ph.D. (<https://connects.catalyst.harvard.edu/profiles/display/Person/122979>), of Harvard University, floated the idea of establishing databases of databases and pursuing partnerships with private-sector information companies.

Exposome theorist Martyn Smith, Ph.D.

(<http://coeh.berkeley.edu/people/faculty/smithmartyn.htm>)

, of the University of California, Berkeley, proposed a global database of exposure, GHANES, modeled on the U.S. National Health and Nutrition Examination Survey (NHANES). Smith was a member of the response work group and chaired a breakout group on use cases.

These represent only a few of the many ideas attendees discussed during the workshop, but they are important components of what may one day become a cohesive theory of exposure biology.



Balshaw encouraged attendees to repurpose what they already have, as they wait for new resources. "As you go home," he said, "think about what you can do [right away]." (Photo courtesy of Steve McCaw)



Teitelbaum, left, addressed questions about her report on epidemiology and the exposome from Petros Koutrakis, Ph.D. (<http://www.hsph.harvard.edu/petros-koutrakis/>), of Harvard University. (Photo courtesy of Steve McCaw)



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[Shoji Nakayama, M.D., Ph.D.](http://www.environmentalhealthconference.com/bio-shoji-nakayama.html)

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, left, shared insights from his work with the Japan Environment and Children's Study, a longitudinal birth cohort study involving 100,000 mothers and children. [Carolyn Mattingly, Ph.D.](http://mattinglylab.com/carolyn-mattingly/)

(<http://mattinglylab.com/carolyn-mattingly/>)

, of North Carolina State University, is lead researcher for the Comparative Toxicogenomics Database. (Photo courtesy of Steve McCaw)



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When the discussion turned to the relative value of measuring internal and external exposures, NIEHS Division of Extramural Research and Training (DERT) Director Gwen Collman, Ph.D., called for integrated measurement. "My point is, it's not one or the other," she said. (Photo courtesy of Steve McCaw)



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Like many attendees, Miller emphasized the biology of outliers, people who are especially resilient or especially susceptible to environmental exposures. (Photo courtesy of Steve McCaw)



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Stephanie London, M.D., Dr.P.H., was one of several lead researchers in the NIEHS Epidemiology Branch at the workshop. (Photo courtesy of Steve McCaw)



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Former NIEHS epidemiologist [Jane Hoppin, Sc.D.](http://workthatmatters.ncsu.edu/newhires/hoppin.php)

(<http://workthatmatters.ncsu.edu/newhires/hoppin.php>)

, of North Carolina State University, called for revisiting cohorts, data, and samples from earlier studies. "I'm really interested in how we can leverage what we already have in the freezer," she said. (Photo courtesy of Steve McCaw)



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Among attendees representing the three NIEHS research divisions were, from left, NTP toxicologist Cynthia Rider, Ph.D.; DERT health scientist administrator Danielle Carlin, Ph.D.; and Division of Intramural Research clinical researcher Shepherd Schurman, M.D. (Photo courtesy of Steve McCaw)

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