

Toward Better Teamwork

Recommendations for Improved Integration of Epidemiology and Risk Assessment

A four-person team of epidemiologists and risk assessors has taken a somewhat unusual step for their fields: working closely together. Concerned that their colleagues don't collaborate much, despite the interdependence of their work and their mutually shared goal of improving public health, the team developed recommendations designed to alleviate this problem [*EHP* 119(12):1671–1675; Fann et al.]. The recommendations focus on air pollution but could be adjusted to work for many other topics, such as water pollution, food contamination, or exposure biomarkers.

The primary focus of their recommendations is the need for epidemiologists to report specific data elements that would help risk assessors avoid misinterpreting epidemiologic findings, more accurately quantify risks, and better advise policy makers. These additional data could also help epidemiologists who conduct meta-analyses. The team says adding this information requires only modest adjustments in typical practices.

One straightforward suggestion is to report detailed data on all confounders considered—in the case of air pollution studies, this might include other pollutant exposures, use of air conditioning, and

demographic variables such as age, sex, race, income, and education. Researchers should also specify diagnostic codes used, list the data source, and provide as much detail as possible about nuances of the data, such as whether the code was considered the primary or secondary health end point, whether an emergency room visit led to hospital admission, and whether rates were age-adjusted.

To better characterize the pollutants being evaluated, the authors recommend including all time variables assessed (e.g., 8-hour, daily, annual), speciation of particulate matter, location of monitors, measurement method of the monitor instrument, and data on missing values and exceptional events. For statistical analyses, the recommendations include listing all uncertainty factors (e.g., *t*-statistics, *p*-value, 95% confidence interval, standard error of central estimate) and reporting null or statistically insignificant findings.

The authors say these commonsense ideas haven't been adopted by epidemiologists for a variety of reasons, such as lack of awareness about their importance to risk assessors, unavailability of the information in the base data, or lack of space due to journal restrictions (although some journals now publish supplemental data at no additional cost). They suggest that workshops involving both epidemiologists and risk assessors would help get these recommendations out to their colleagues.

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Full of Beans?

Early Soy Exposure Associated with Less Feminine Play in Girls

Animal studies have shown that sexually dimorphic behavior can be influenced by soy isoflavones—compounds with a structural and functional similarity to estrogen—but there is a lack of information regarding the effects of soy isoflavone exposure on postnatal child development. A new study reports an association between early soy feeding and less female-typical play behavior in young girls [*EHP* 119(12):1811–1816; Adgent et al.].

The authors analyzed gender role-play behaviors among 3,664 boys and 3,412 girls enrolled in the United Kingdom Avon Longitudinal Study of Parents and Children. They used feeding data from questionnaires completed by mothers at 1, 6, 15, and 24 months postpartum to divide children into four categories: “primarily breast” (breastfed for at least 6 months), “early formula” (introduced to nonsoy milk or infant formula at or before 4 months old, with sustained use at 6 months of age), “early soy” (introduced to soy milk or soy formula at or before 4 months old, with sustained use at 6 months of age), and “late soy” (introduced to soy milk or soy formula anytime between 5 and 15 months of age). The Preschool Activities Inventory (PSAI), which measures how often a child plays with certain toys, engages in certain activities, and displays certain characteristics over a month's time based on “masculine” or “feminine” classification, was used to assess gender-role play behavior at 30, 42, and 57 months of age.



Early exposure to soy infant formula was associated with less female-typical play in girls at age 42 months.

Focusing on outcomes at age 42 months to correspond with other, similar studies, the investigators found higher PSAI scores (indicating less typically feminine play) among “early soy” girls compared with “early formula” girls, but scores remained in the normal range for female play behavior. They saw no significant difference in girls' behavior when breastfeeding and early formula feeding were compared. They also observed marginally higher PSAI scores among “early soy” boys compared with other boys, and noted the lowest PSAI scores among boys who were primarily breastfed. However, no significant difference was observed between “early soy” and “early formula” boys. In both sexes, PSAI scores were higher if an older brother were present in the home and lower if an older sister were present. Maternal prenatal smoking also was associated with higher PSAI scores in both sexes, and higher maternal education was associated with lower scores in boys and higher scores in girls.

The authors acknowledge that soy users in the study were not exclusively fed soy formula in all instances, nor could they assess a dose–response relationship between soy feeding and PSAI score. These preliminary data suggest a subtle reduction in female-typical play behaviors at age 42 months in girls who were fed soy formula or soy milk early in life—an association that weakened by age 57 months. Replication of these findings in cohorts with more prevalent soy use and improved exposure assessment is needed.

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Artificial Food Color Additives and Child Behavior: Weiss Responds

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The Food and Drug Administration's (FDA) response to my commentary (Weiss 2012) reflects the wide gulf between how the FDA translates "weight of evidence" into regulatory policy for artificial food colors (AFCs) and how it is translated into meaningful action on behalf of public protection.

The FDA essentially took the position that for a study to be considered as evidence of adverse effects, it must be totally free of uncertainties. The study by McCann et al. (2007) played a large role in provoking the FDA review, but for that study, like almost any epidemiological study, it would be difficult to meet that absolute criterion. It is why *Environmental Health Perspectives (EHP)* publishes so many such studies addressing the same question (e.g., air pollution). But isn't it fair to ask whether any of the negative AFC studies meet that criterion?

In their critique, the FDA faults McCann et al. (2007) because they characterized "... a treatment effect as adverse when it may, in fact, fall within the normal range of childhood behavior." This is an issue discussed over and over again in the pages of *EHP*. Take the example in my commentary (Weiss 2012), modeled on numerous publications in the lead literature (e.g., Lanphear et al. 2005): If developmental exposure to low levels of lead reduces a population IQ (intelligence quotient) by 3 points (3%), from, say, 100 to 97, it is taken as evidence of a major adverse effect. Both scores, of course, fall within the normal range. The same criticism is used by the FDA to dismiss the effect size calculations; that is, the altered behavioral activity seen in published data lies "... in the range of normal activity for children."

The FDA finds the study by McCann et al. (2007) lacking because the authors relied mainly on parental observations. A high proportion of child development research, in fact, enlists parents as observers; hundreds of validated inventories and questionnaires are based on parent ratings. They are the observers, of course, who see the most extensive samples of the child's behavior, especially with younger children. This is the reason I chose parental observations for my own food color study of young children (Weiss et al. 1980) and why we relied on parent ratings for our study of how phthalates mold play behavior in preschool children (Swan et al. 2010).

It is difficult to grasp the FDA argument that AFCs do not possess "inherent"

neurotoxic properties but may provoke neurotoxicity in susceptible subpopulations. Neurotoxicity is neurotoxicity.

The FDA does acknowledge that AFCs may be associated with adverse behavioral outcomes in some (unknown proportion of) susceptible children. As I note in my commentary (Weiss 2012), such a conclusion would prompt decisive action by the U.S. Environmental Protection Agency. Why not the FDA?

I was pleased to hear that the FDA noted the need for further research. My question remains: What parent or institutional review board (IRB) would be convinced that such research is without significant risk, given what we already know? If IRBs would hesitate, shouldn't that prompt the FDA to at least require warning labels on foods containing AFCs that are consumed mainly by children?

Finally, the FDA policy reflects a point of view that is endemic in federal regulatory policy toward potentially toxic chemicals. Namely, a chemical is innocent until proven guilty. Many environmental health researchers believe the proposition needs to be reversed. Some advocate adoption of the precautionary principle. Perhaps, if the FDA had required neurotoxicity testing, especially in young children, before allowing AFCs and other additives to be marketed, we would not be having this debate at all. Harvey Wiley, who became the FDA's first commissioner, recruited his legendary "Poison Squad" volunteers for precisely this purpose. That was in 1902.

The author declares he has no actual or potential competing financial interests.

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ERRATUM

The December Science Selections articles "More Lack in the World" [*Environ Health Perspect* 119:A524 (2011); <http://dx.doi.org/10.1289/ehp.119-a524a>] and "Full of Beans?" [*Environ Health Perspect* 119:A525 (2011); <http://dx.doi.org/10.1289/ehp.119-a525b>] mistakenly reversed the page numbers for the associated research articles. The December Forum article "NY DEC Takes on Fracking" [*Environ Health Perspect* 119:A513 (2011); <http://dx.doi.org/10.1289/ehp.119-a513>] incorrectly suggested that the public comment period for the New York Department of Environmental Conservation's Supplemental Generic Environmental Impact Statement had already closed. *EHP* regrets the errors.

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