

Neurobehavioral Effects of Pesticide Exposure in Children

Diane S. Rohlman, Center for Research on Occupational and Environmental Toxicology, Oregon Health & Science University

There is increasing concern that the use of pesticides in agriculture may be adversely affecting farmworker communities, including children. And this concern is well-founded. Detectable levels of agricultural pesticides have been documented in home dust, primarily in agricultural areas, where farmworkers transfer pesticides from their clothing and hands into the home.¹ Moreover, biological markers of pesticides have been documented in adults and children in agricultural communities, and levels of exposure are higher in residents of agricultural communities than non-agricultural communities.² Furthermore, many farmworker families do not recognize the seriousness of pesticide exposures, have limited resources to pay for preventive health care and do not trust health care or government systems.³

Organophosphate pesticides are of great concern due to their well-characterized neurotoxic effects and persistence once in the home. While the neurotoxic effects of acute organophosphate pesticide exposure are well established, chronic low-level exposure is poorly characterized in adults, and even more so in children. It is presumed that children of farmworkers are exposed to pesticides throughout development, which may produce subtle health effects that would not be detected by clinical examinations nor recognized by parents.

An ongoing research project conducted through the Pacific Northwest Agricultural Safety and Health Center is examining the health effects from chronic exposure to organophosphate pesticides in children to determine if they are associated with current home pesticide exposure and lifetime exposure measures. Methods to assess neurobehavioral functioning in school-age children and a measure of lifetime exposure to pesticides have been developed. Children's exposure to pesticides from the parent's work or residence in an agricultural community will be measured through dust samples collected from the home. Children will complete the neurobehavioral test battery a second time one year later to obtain longitudinal data that will be used to characterize developmental progress and relate that progress to exposure estimates.

Children More Vulnerable

Children can have greater exposure to toxicants than adults due to behaviors, such as crawling on the floor and increased hand-to-mouth contact, as well as to their greater surface area relative to body weight. Significant changes occurring in the brain during early development through adolescence make children especially vulnerable. Evidence from animal studies clearly demonstrates adverse effects of pesticides on neurodevelopment.^{4,5,6}

Evaluating Risk from Exposure

To assess risk to children it is necessary to associate measures of exposure with adverse outcomes, establishing a dose-response relationship. Studies examining pesticide exposure in children have used a variety of methods to classify exposure, including: environmental monitoring of indoor air, dust samples, and surface wipes; maternal and child exposure measures, such as urinary metabolites and acetyl cholinesterase level; and pesticide source information, including pesticide use, home inventory, proximity to agricultural fields, and parental occupation.

Pesticide Effects in Children

A variety of methodologies have been developed to evaluate the health effects of pesticides in populations ranging in age from prenatal to adolescent, and with varying exposures to pesticides, including acute poisoning incidents and chronic lifetime exposure.⁷

The majority of studies have focused on the effects of chronic pesticide exposure, either from parental occupation or living in an agricultural community. These studies were conducted in several countries and used a variety of methods, but all demonstrated deficits in performance, including increased behavioral problems as reported by parents, slower response speeds, visual motor and visual spatial deficits, and deficits in memory and learning.

Because of the rapid growth and development of children, there is a need for longitudinal studies to assess functional changes over time. Moreover, functional effects of early exposure may not become apparent until later in life. Three longitudinal birth cohort studies examining early exposure to pesticides are currently underway: the Mt. Sinai Children's Environmental Health Study, the Mothers and Newborns Cohort Study at the Columbia Center for Children's Environmental Health,⁸ and the University of California Berkeley Center for the Health and Assessment of Mothers and Children of Salinas.⁹ Both the Mt. Sinai and the Columbia Centers are focused on residential pesticide exposures in cohorts in New York City. The CHAMACOS study follows Latino mothers and children living in agricultural communities in California, where 75% of the homes have at least one household member working in agriculture. Although there are inconsistencies between the three studies when associations between exposure and outcomes are examined, more recent evidence demonstrates a convergence of findings across studies. Two studies have reported an association between prenatal exposure and pervasive developmental disorder assessed by the Child Behavior Checklist.^{10,11}

Conclusions

The methods used to measure pesticide exposure and assess development and performance in children varies across studies. Although there are methodological inconsistencies, the evidence suggests that pesticide exposures are associated with performance deficits and an increased reporting of developmental and behavioral problems in children. The current study will help to identify health effects associated with pesticide exposure in children living in agricultural communities. ■

References

1. Quandt SA, Hernández-Valero MA, Grzywacz JG, Hovey JD, Gonzales M, et al. 2006 Workplace, Household, and Personal Predictors of Pesticide Exposure for Farmworkers. *Environmental Health Perspectives* 114(6): 943-952.
2. Lambert WE, Lasarev M, Muniz J, Scherer J, Rothlein J, Santana J, McCauley L. (2005). Variation in Organophosphate Pesticide Metabolites in Urine of Children Living in Agricultural Communities. *Environmental Health Perspectives* 2005: 113:504-508.
3. Mott L. The disproportionate impact of environmental health threats on children of color. *Environmental Health Perspectives* 1995;103:33-35.
4. Levin ED, Addy N, Baruah A, Elias A, Christopher NC, Seidler FJ, Slotkin TA. Prenatal chlorpyrifos exposure in rats causes persistent behavioral alterations. *Neurotoxicology and Teratology* 2002;24:733-741.
5. Moser VC, Padilla S. Age- and gender-related differences in the time course of behavioral and biochemical effects produced by oral chlorpyrifos in rats. *Toxicol Appl Pharmacol* 1998;149:107-119.
6. Dam K, Seidler FJ, Slotkin TA. Chlorpyrifos exposure during a critical neonatal period elicits gender-selective deficits in the development of coordination skills and locomotor activity. *Developmental Brain Research* 2000;121:179-187.
7. Rohlman DS, Lucchini R, Anger WK, Bellinger DC, van Thriel C. Neurobehavioral testing in human risk assessment. *Neurotoxicology* 2008: 556-567.
8. Perera FP, Rauh V, Whyatt RM, Tang D, Tsai WY, Bernert JT, Tu YH, Andrews H, Barr DB, Camann DE, Diaz D, J. D, Reyes A, Kinney PL. A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and Pesticide exposures. *Neurotoxicology* 2004.
9. Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of in Utero Organophosphate Pesticide Exposure and fetal Growth and Length of Gestation in an Agricultural Population. *Environmental Health Perspectives* 2004;112:1116-1124.
10. Eskenazi B, Marks AR, Bradman A, Harley K, Barr DB, Johnson C, Morga N, Jewell NP. Organophosphate Pesticide Exposure and neurodevelopment in young Mexican-American Children. *Environmental Health Perspectives* 2007;115:792-798.
11. Rauh VA, Garfinkle R, Perera FP, Andrews HF, Hoepner L, Barr DB, Whitehead R, Tang D, Whyatt RW. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. *Pediatrics* 2006;119:e1845-e1859.

streamline

The Migrant Health News Source



The Migrant Clinicians Network's (MCN) TBNet project has been selected as the 2010 Border Models of Excellence in Tuberculosis Surveillance and Control recipient by the U.S.-Mexico Border Health Commission (USMBHC). At left, Deliana Garcia receives the award from Bertha Almendariz. TBNet is a transborder patient navigation project that has transferred more than 4,000 individuals under treatment for TB from the US to 60 different countries across the globe.

"TBNet is to be recognized as a vital and integral part of tuberculosis work along the U.S.-Mexico border," said Dan Reyna, M.S.S., M.P.A., General Manager, U.S. Section, USMBHC. "This recognition demonstrates your organization's exceptional leadership, innovation and determination," Reyna continued.

"This recognition celebrates the 15 years that MCN and our dedicated colleagues have devoted to ensuring that health care justice is a reality for the mobile poor," said Ed Zuroweste, MD, Chief Medical Officer of MCN.

To IRB or Not to IRB— Can There Be Any Question?

James O'Barr

To assure that the highest quality health care is provided to migrant and seasonal farmworkers and their families, both the practice of evidence-based medicine and the utilization of practice-based research are essential. When humans are the subject of study, Institutional Review Boards (IRBs) are charged with the responsibility for reviewing, approving, and monitoring the research to assure their protection and ethical treatment. However, research with mobile, marginalized populations requires particular vigilance to ensure that appropriate safeguards are in place to protect their rights, safety, and welfare, and to see that such elements as cultural differences, language barriers, and literacy levels are taken into account in research design. Conventional IRBs, whether linked to academic or community institutions, are rarely conversant with what is needed to work effectively with migrant, low-literate populations, and with the unconventional methods that must often be employed to ensure informed consent. Fortunately, the Migrant Clinicians Network, long committed to serving farmworkers and other mobile poor with just such methods, stepped into the breach, creating its own IRB in 1999.

When MCN took that step, Institutional Review Boards were still a recent innovation,

and it is worth considering the sordid history that preceded their introduction. Since antiquity, and across different cultures, healers have been revered as persons with special knowledge of the mysteries of life and death, and the relationship between patient and physician has held deep moral and religious significance. Over time, the concept of medicine as a profession has taken hold, and science replaced religion as the basis of medical practice. Nevertheless, even as that practice has evolved, the moral and ethical aspects of medicine have remained central to the understanding of what it means to be a member of a health profession. In the twentieth century, however, the explosive growth of scientific knowledge, the increasing involvement of government support for research, and the callous disregard for human life in scientific research that culminated most notoriously in the Nazi concentration camp medical experiments, lent urgency to the need for outside regulation and informed consent when human beings are the subjects of research. In 1964, the World Medical Association made recommendations, later codified and periodically revised as the Declaration of Helsinki, that would govern international research ethics and define rules for research combined with clinical care, as well as for non-therapeutic

research. Two years later, Dr. Henry Beecher, a Harvard Medical School anesthesiologist, authored an article in the *New England Journal of Medicine* examining 50 studies published in the U.S. since 1945 that were what he called "examples of unethical or questionably ethical studies." One study that Dr. Beecher did not include, because it was a closely guarded secret, was the infamous Tuskegee Study of Untreated Syphilis in the Negro Male, which was conducted by the U.S. Public Health Service from 1942 to 1972. Terminated only as a result of a leak to the press, the Tuskegee Study led to the Belmont Report in 1979, and the establishment of the Office for Human Research Protections in the Department of Health and Human Services. It also led to federal regulations requiring Institutional Review Boards for protection of human subjects in studies funded by DHHS.

For Americans, with our famously short attention spans, the Tuskegee Study may seem like ancient history. Certainly the words of the national director of the study, attempting to justify the refusal to provide treatment once penicillin was discovered in the 1940's, are from another era, if not another ethical universe: "The men's status did not warrant ethi-

continued on page 2