Opportunities to Reduce Children's Exposures to Pesticides: A Truly Grand Challenge

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Symposium Overview
AAAS 2006 Annual Meeting
St. Louis, Missouri

February 19, 2006

I. Purpose and Goals

This symposium will provide an overview of public and private sector efforts to reduce children's exposures to pesticides. We describe new science that reinforces the need for the nation to move forward more systematically with efforts to reduce children's exposures to pesticides. We highlight areas of innovation and activity that are delivering tangible benefits, as well as efforts that have yet to produce evidence of significant pesticide risk reduction.

Data are presented establishing benchmarks for children's exposures to pesticides, and to the extent possible, trends in exposure over the last decade are described. A major focus throughout this symposium will be on risks associated with organophosphate (OP) insecticides. This class of insecticides is the most widely used in food production, poses the most significant and worrisome developmental risks stemming from pesticide use, and has been targeted for risk assessment/risk management by the U.S. Environmental Protection Agency (EPA) for more than a decade.

We will describe and contrast the effectiveness of four major approaches to reducing pesticide risks –

- Discovery and use of reduced-risk and biologically-based pesticides;
- Adoption of biointensive pest management systems, including organic production methods;
- Marketplace incentives and ecolabels; and
- Regulation.

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Two milestones in the 1990s solidified scientific and political consensus in the United States around the need for systematic efforts to reduce pesticide exposures and risks during pregnancy, infancy, and childhood.

In 1993, the National Academy of Sciences released the report *Pesticides in the Diets of Infants and Children* (National Research Council 1993). Dr. Phil Landrigan, our fourth speaker, chaired the National Academy of Sciences/National Research Council (NAS/NRC) Committee that wrote this landmark report; our third speaker, Dr. Charles Benbrook, was the Executive Director of the NRC board that issued the report.

Passage of the Food Quality Protection Act (FQPA) in 1996 was the second milestone in the 1990s (USEPA 1997). The goal of the FQPA was to assure by 2006 a "reasonable certainty of no harm" as a result of pesticide exposures for all U.S. population groups. The FQPA –

- Established a stricter, health-based standard for pesticide regulation, with special emphasis on risks facing infants and children;
- Gave the EPA ten years to develop new risk assessment tools and review and update some 9,600 tolerances covering pesticide residues in food; and
- Provided EPA important new regulatory tools, and a mandate, to reduce pesticide risks to vulnerable population groups, especially pregnant women, infants, and children.

As a result of these two milestone events in the 1990s, significant progress has been made in refining the accuracy of pesticide risk assessments (Consumers Union 2001). Bigger and better pesticide exposure databases are now available, and government-sponsored research on the developmental impacts of pesticides has deepened understanding of both the nature of risks stemming from pesticide exposures, and the levels and distribution of those risks across exposure pathways, foods, and types of pesticides.

II. Contemporary Indicators of Pesticide Exposure

In the early 1990s relatively little was known about the frequency or levels of pesticides in food as actually eaten, a shortcoming highlighted by the NAS/NRC committee in *Pesticides in the Diets of Infants and Children*. Then-existing government data on pesticide residues had been collected as part of tolerance enforcement programs and represented residues at the farm gate, prior to washing, shipping, storage, marketing, and food preparation. Relatively insensitive analytical methods were employed.

To improve the accuracy of pesticide dietary risk assessments, Congress funded the U. S. Department of Agriculture's (USDA) "Pesticide Data Program" (PDP). As recommended by the NAS/NRC, this program focuses on the foods consumed most heavily by children and food is tested, to the extent possible, "as eaten" (Agricultural Marketing Service, 2002). Banana and orange samples are tested without the peel; processed foods are tested as they come out of a can, jar or freezer bag.

Over the last 10 years the PDP has tested over 150,000 samples of the 20-odd foods consumed most frequently by children. The most commonly consumed foods like milk, apples, apple juice, grapes, oranges, bananas, peas, tomatoes, and strawberries have been in and out of the program two or more times. Less common foods like nectarines and spinach have also been included. In general, the more residues found in one round of PDP testing for a given food, the more likely that food will be added again to the program. About one-quarter of the samples in a given year are processed foods and juices.

The PDP database provides a basis for calculations of the level of pesticide risks, and distribution of relative risks across foods and pesticides, and by food-pesticide combinations. Estimates of how the FQPA and other initiatives have impacted pesticide dietary risks can be made utilizing the PDP dataset, coupled with EPA estimates of each pesticide "Reference Dose" (RfD) or "Population Adjusted Dose" (PAD).[1] All measures of pesticide dietary risk levels combine in some fashion –

- Estimates of how much food, and which foods are eaten in a day;
- How frequently a food is eaten;
- The percentage of the samples of a given food that contain a residue;
- Average residue levels; and
- The pesticide's toxicity, as measured by its dietary RfD or PAD.

While the PDP dataset is extensive, sensitive, and of high quality, it does not test all foods, nor are the analytical methods used able to detect all pesticides. Still, we believe that the PDP dataset encompasses most of the significant sources of dietary exposures to high-risk pesticides in the U.S. diet.

The frequency of infant and childhood exposures to pesticides is poorly understood by the general public, and indeed by most scientists. According to USDA food consumption surveys, the average American consumes about 3.6 servings of fresh and processed fruits and vegetables per day, of which about two are fresh fruits and vegetables. There are about 75 million Americans under the age of 20. About 70 percent of the samples of fresh fruits and vegetables consumed in America contain one or more pesticide residues (Agricultural Market Service 2002; Baker et al., 2002).

Assuming the average young person in America consumes two servings of fresh fruits and vegetables daily, they consume pesticides through their diet about 105 million times each day. Given that this estimate captures just a portion

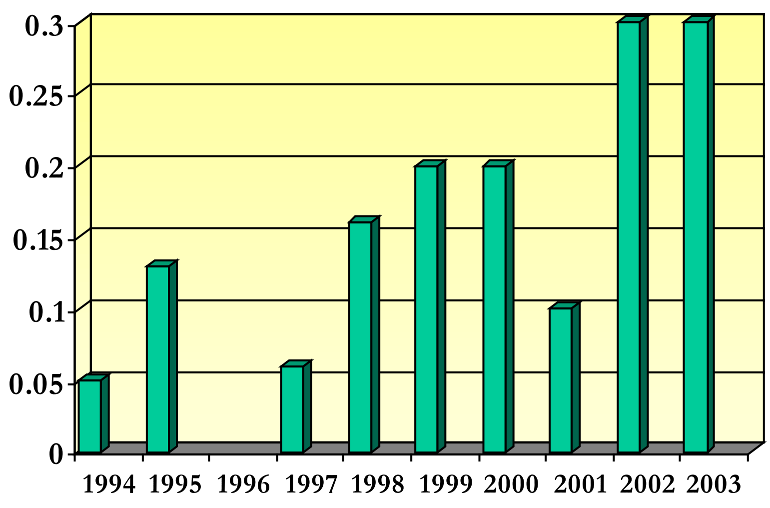
1 EPA typically calculates a pesticide active ingredient's "Reference Dose" by dividing a "No Observable Adverse Effect Level" from an animal study by a safety factor of 100. A "Population Adjusted Dose" is the RfD divided by any applicable, additional FQPA safety factor.

of fresh foods and ignores exposures via processed foods and juices, the actual number of exposures through fruits and vegetables is probably at least 200 million exposure episodes daily.

In addition to exposures in food, drinking water also contributes significantly to daily pesticide exposures for millions of Americans. In recent years the PDP has also tested drinking water as it comes out of the tap; the results that follow are from the program year 2003 report, Appendix M. About 54 percent of drinking water samples tested positive for one or more pesticides and pesticide metabolites. Individuals under 20 years of age in the U.S. therefore consume about 250 million servings of water daily that contain one or more pesticide or pesticide metabolite (average 6.1 servings of water per capita). There are nearly 70 million servings of drinking water consumed by young people daily with four or more pesticides and/or metabolites.

Accordingly, the average young American is exposed to more than five servings of food and water daily that contains pesticide residues at or above the levels of detection included in the PDP. Fortunately, for a significant share of these residues, the levels are very low and pose modest if any risks to healthy young people.

FIGURE 1. Percent of PDP samples found to have residues exceeding the established EPA tolerances, 1994-2003



Unfortunately, some of the residues are in the range where the weight of the evidence points to potential biological impacts, particularly when exposures occur at vulnerable periods of development, or during an illness. Moreover, in the last ten years the frequency of over-tolerance residues in food has increased five-fold, from about 0.05 percent to 0.25 percent, as shown in Figure 1. While a seemingly low percentage, one-quarter of one percent of 200 million exposure episodes each day is 500,000 over-tolerance exposures. There are no doubt an equal number of exposure episodes involving drinking water where levels exceed applicable "Maximum Concentration Limits," or other comparable safety benchmarks. Regulators, the pesticide industry, the food industry, and parents should be concerned about a million or so pesticide exposures each day at levels above what EPA regards as safe.

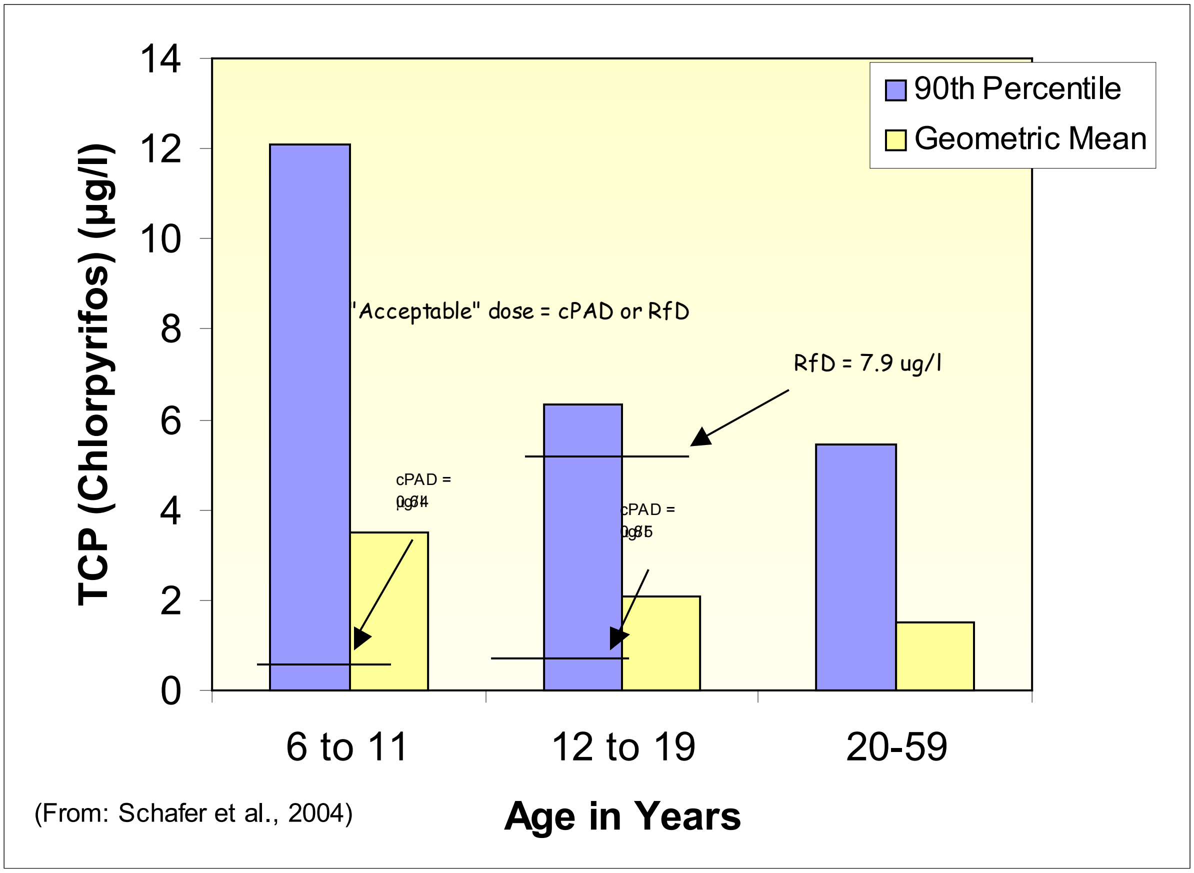
While we lack the knowledge needed to accurately calculate the health outcomes triggered by these over-tolerance and all other pesticide exposures, we can say with confidence that reducing their prevalence will lower the incidence of a range of reproductive problems, will reduce the frequency of childhood developmental abnormalities, and will enhance life long well-being for thousands of people.

OP Metabolites

Since passage of the FQPA in 1996, the EPA has focused on reducing exposures to the organophosphate (OP) class of insecticides. The Centers for Disease Control and National Institutes of Health have periodically monitored levels of OP metabolites in urine and blood across the population. In CDC and private surveys of OP metabolites in urine and blood, 90 percent or more of children test positive for usually several of these insecticide metabolites (Adgate et al., 2001; Centers for Disease Control and Prevention 2001). As Landrigan will point out, drawing on these data, there have only been modest reductions in OP metabolites in the urine across our population, despite 10-years of focus on reducing OP exposures and risk.

A report entitled "Chemical Trespass" was issued in May 2004 by the Pesticide Action Network (Schafer et al., 2006). It contained detailed analysis of 2001-2001 NHANES OP urinary metabolite data, and used published methods to estimate exposure levels to parent compounds from creatinine corrected urinary metabolite levels. They focused on chlorpyrifos and its metabolite 3,4,6-Trichloro-2-pyridinol, or TCP, and found that chlorpyrifos exposures for children ages 6-11 and 12-19 exceeded EPA's chronic Population Adjusted Dose (cPAD) by surprisingly wide margins. Geometric mean TCP levels were three to 4.6 times higher than the EPA-estimated "safe" dose, as shown in Figure 2. The more heavily exposed children received daily doses more than 10-times the "safe" level

FIGURE 2. Chlorpyrifos exposure above "acceptable" levels in many children (2001-2002 NHANES data)



III. The Need to Further Reduce Exposures

During fetal development and the first years of life, infants are much less able to detoxify most pesticides and are uniquely vulnerable to developmental toxins, especially neurotoxins. Heightened vulnerability arises from the ability of pesticides to pass through the blood-brain barrier, and the long period of time during which the brain and nervous system continue to develop (Cooper et al., 1999; Eskenazi et al., 1999; National Research Council 1993; Shaw et al., 1999; Whyatt et al., 2003; Zahm et al., 1998).

In June 2005, *Science* published the first study to show that developmental changes triggered by pesticides can last multiple generations (Anway et al., 2005). Fungicides were shown to cause decreased sperm counts and mobility – not just to animals exposed in utero, but for three subsequent generations. In other words, assuming the same biological impacts occur in humans, what each of us was exposed to in our mother's womb might affect the health of our great-grandchildren – for better or worse.

A study involving more than 44,000 children measured pesticide residues in stored frozen blood samples from pregnancies in the early 1960s (Longnecker et al., 2001). Children were divided into five groups based on levels of maternal pesticide exposure. Odds ratios were calculated for preterm birth and small-for-gestational-age babies across the five groups, and increased in a dose-response manner as shown in Table 1. Those in the group with the smallest exposure had a 50 percent increased chance of being born prematurely, compared to those with none. Those at the highest level had greater than a 200 percent increased chance of premature birth. The authors estimate that pesticide exposure was responsible for 15 percent of all infant deaths during the years of the study, the only such estimate we are aware of.

Table 1. Maternal serum DDE concentration in relation to odds of preterm or small-for-gestational-age birth

	Serum DDE (µg/L)				
	<15	15-29	30-44	45-59	≥ 60
Preterm birth					
Number of cases	34	153	80	50	44
Number of controls	375	944	404	176	120
Adjusted odd ratio (95%CI)	1	1·5	1·6	2·5	3·1
Small-for-Gestational-Age					
Number of cases	20	106	47	22	26
Number of controls	389	991	436	204	138
Adjusted odd ratio (95%CI)	1	1·9	1·7	1·6	2·6

Source: Longnecker et. Al., Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. Lancet, 2001 Nov 17;358(9294:1732).

A similar study was conducted jointly by investigators at the Center for Research on Women's and Children's Health, the Mount Sinai School of Medicine, the University of North Carolina, Chapel Hill, the Kaiser Permanente Division of Research, and the University of California San Francisco School of Medicine (Cohn et al., 2003). They measured pesticide metabolites in preserved postpartum maternal serum samples from 1960 to 1963. They also recorded time to pregnancy in their eldest daughters 28-31 years later. The daughters' probability of pregnancy fell by 32 percent for each 10 mcg/L detected, three decades after the exposure.

A team of researchers at the University of California-Berkeley School of Public Health found that exposures to pesticides during pregnancy significantly heightened risk of children developing leukemia, and that the more frequent the exposures and the earlier in life, the greater the increase in risk (Ma et al., 2002). A team in the Department of Preventive Medicine, University of Southern California, found that exposure to pesticides in the home during fetal development and the early years of life increased the risk of non-Hodgkin's lymphoma, with odds ratios as high as 9.6 for Burkitt lymphoma (Buckley et al., 2000).

A study in Ontario, Canada showed that exposures to pesticides three months prior to conception and during pregnancy increased the risk of spontaneous abortions (Arbuckle et al., 2001).

IV. Four Major Ways to Reduce the Impacts of Pesticides on Children's Health

Presenters will describe the four major efforts underway in the U.S. to reduce children's pesticide exposures and risk. Three fall largely within the private sector and will be addressed by Benbrook and Lu, and Landrigan will cover the fourth – the impacts of regulation and the FQPA.

New Chemistry

Several important classes of new pesticides have been developed and adopted over the last decade that are less toxic and persistent, and less likely to find their way into food, drinking water, and the environment. To the extent that these new chemistries have displaced higher-risk pesticides, risk reduction has been achieved.

Shift to Biointensive Pest Management

From the 1960s through the 1990s, farmers have relied largely upon pesticides to keep pest populations below economic thresholds. The focus of most pest management specialists was chemical control of populations that threatened farm yields, crop quality, and profits.

In the 1960s and 1970s, concern over the impacts of DDT on wildlife populations and early experiences with the emergence of pesticide-resistant pest populations raised questions about the sustainability of pest management systems largely reliant on chemical control. These questions led to early research on Integrated Pest Management (IPM) and biological control.

Alternatives to pesticide-based systems shift the focus of farmers and pest managers to prevention through the management of biological systems, in the hope of lessening reliance on pesticides, especially those chemicals known to pose risks to non-target species (Benbrook et al., 1996). While a significant share of American farmers utilize one to a few core elements of IPM, pesticides remain by far the dominant pest management tool in American agriculture.

Integrated Pest Management systems exist along a continuum from largely pesticide-based to fully reliant on prevention and biological interventions. A growing segment of farmers are combining modern, reduced-risk pesticides with proven methods to reduce pest populations through disruption of pest feeding, physiological development, or reproduction. A small but growing percentage of farmers is using organic production systems that prohibit the use of toxic synthetic pesticides and place heavy emphasis on cultural, mechanical and biological control tactics.

The impacts of both IPM and organic production systems on pesticide exposure and risks will be reviewed.

Food Marketplace Incentives and Ecolabels

Food companies and grower groups have promoted adoption of IPM and reduced-risk pest management systems through a variety of marketplace initiatives. Most programs include some sort of ecolabel that certifies that food was grown in ways reducing the environmental impacts of farming systems. The expense of administering ecolabel programs, and the costs imposed on farmers adhering to their provisions, is hopefully covered by premium prices and/or preferential market access.

Ecolabels making pesticide-related claims typically are based on –

- Presence of “No Detectable [Pesticide] Residues,” or NDR (“pesticide free”);
- Use of Integrated Pest Management (IPM grown); and/or
- Produced in accord with the principles of organic farming (certified organic).

Evidence of the impacts of programs making these three sorts of claims will be presented and contrasted with the impacts of regulation and discovery of new chemistry.

Regulation

Through the 1970s and until the late 1990s, EPA based its pesticide risk assessments on exposures to healthy adults. The Food Quality Protection Act (FQPA) directed the EPA to conduct a reassessment of all food uses of pesticides, taking into account the heightened susceptibility of infants and children, the elderly, and other vulnerable population groups.

Infants consume more food per kilogram of bodyweight than adults and a much less varied diet. As a result, exposure to a pesticide from consumption of a given food is greater per kilogram of infant/child body weight.

We offer our best estimates of the degree to which the FQPA has reduced dietary risks, and offer our best collective judgment regarding whether the FQPA has achieved its stated purpose. Our findings highlight some emerging challenges that the EPA and the food industry must contend with.

VI. Endnote

While progress has been made in the past decade in better understanding pesticide dietary exposures and risks, relatively little has been done that has produced tangible exposure and risk reduction. The findings presented during this symposium provide a sound basis to identify promising and cost-effective options to achieve significant reduction in children's pesticide dietary risks, if farmers, the food industry, and government choose to make a concerted effort to do so.

This panel believes that the scientific case supporting the need to systematically reduce prenatal and childhood exposures to pesticides has greatly strengthened over the last decade. We also believe that there are proven options and actions that will dramatically reduce high-risk exposures, as well as evidence that such reductions will quickly translate into improved public health.

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