High Pesticide Exposure Events (HPEE): Lessons Learned from the Agricultural Health Study (AHS)

Ruth H. Allen, Ph D, MPH
David T. Mage, Ph D
Anuradha Kodali, MD, MPH

Overview of Ag Health Study

"The Agricultural Health Study is a long-term study to investigate the effects of environmental, occupational, dietary, and genetic factors on the health of the agricultural population. This study will provide information that agricultural workers can use in making decisions about their health and the health of their families."

Source: www.aghealth.org "High Pesticide Exposure Events Among Farmers" Fact Sheets

High Pesticide Exposure Events

- In the AHS a High Pesticide Exposure Event (HPEE) is defined as:

  "An incident or experience while using any pesticide which caused an unusually high exposure."

  This is a self-reported diagnosis and is not verified by a medical evaluation that a high pesticide exposure did indeed occur.

The Acute HPEE

- We restrict our analysis to an HPEE that results in acute symptoms (chloracne, syncope, nausea, etc.)

- A high exposure that results in a chronic condition may not be noted at the time that it occurs as the applicator may not realize that the high exposure occurred without acute symptoms.

Factors Influencing HPEE

- INEXPERIENCE: Pesticide application refers to the entire sequence of handling, mixing, loading, applying, clean-up and repair of equipment. Each step is a deceptively simple unit operation.
- There is a technique involved for safe application that can only be learned by experience. Errors while learning may lead to a HPEE.

Inexperience

- Personal Protective Equipment (PPE)
  - Although PPE is formally specified by the Manufacturer's Label Requirement (MLR) on the pesticide container, the **label** may not be followed, for various reasons.
  - For example, long-sleeve shirt and long-pants may be required but in hot humid **weather** short-sleeves and short-pants are often substituted.
  - Chemically resistant **gloves** may be missing, torn or contaminated from a prior application of the same or a different chemical.

Inexperience (cont.)

- During the learning phase, avoidable accidents (*blunders*) may occur.
  - For example, **spilling** while loading and **splashing** while mixing can occur when these activities are hurried and care is not taken.
- When combined with improper use of full **personal protective equipment (PPE)** required, a HPEE can result.

Unavoidable Accidents

- An unavoidable accident can occur when something unanticipated occurs during the HMLA sequence, such as a hose springing a **leak** and spraying the applicator, or a sudden gust of **wind** blowing a spray back onto the applicator.
- If the applicator wears the MLR PPE he or she may be protected from the acute effects of that incident.

Model for HPEE

Mage et al. (*Environ Res* 2000;83:67-71)

- We model the probability $p(n)$ of an HPEE decreasing with experience (n) as:

$$p(n) = a + b / n \qquad (1)$$

Where a = accident probability,

b / n = blunder probability,

n = number of lifetime applications

Probability Model for HPEE

- Probability of not having an HPEE after N applications $P(N)$ decreases with N:

$$P(N) = \prod_{n=1}^{n=N} [1 - (a + b / n)]$$

Probability of at least 1 HPEE increases with N

Comparison of Model to Data

Relative Probability of at Least 1 HPEE

Applications N	Data (OR)	**Model**: a = 0.0153; b = 0.0468
25 - 55 days	1.00 (ref)	1.00 (reference)
56 - 107	1.34	1.31
108 -149	1.62	1.58
150 - 209	1.86	1.83
210 – 366	2.20	2.25
367 – 449	2.53	2.63
450 – 524	3.06	2.84
525 – 999	3.48	3.62
1000 - 4500	4.32	4.27

Take Home Message for Farmworker Audience

- Accidents happen with or without PPE use.
- PPE (especially chemically resistant gloves) reduces exposure, according to follow-up studies using urinary biomarkers.
- Inexperience is likely to be in yrs of application, not age *per se*, so newly hired inexperienced workers may need extra training.
- Proper initial training to apply pesticides is key to prevention of exposure from sloppy procedures.

Other AHS HPEE Highlights?

- Lessons from Selected Disease Findings
  - Eye disease excesses in applicators and spouses suggests overall farm **hygiene** may be important.
  - Excess prostate cancer, in users of certain but not all pesticides, decreased risk with cessation of use, and increased risk for those with a family history of prostate cancer, all suggest the complexity of the interplay of chemical factors, application methods and personal **risk taking** behavior.
- Lessons from Selected Exposure Findings
  - Amount applied, e.g., minor applications of 0.01 lb vs. 100 lbs sprayed, application methods and engineering controls may alter the chances of HPEE.

High Pesticide Exposure Events (HPEE) in 22,884 Pesticide Applicators

- Cohort Characteristics:
  - •Approximately 11% are commercial applicators (*n*=2467, all from Iowa) and
  - •89% private (primarily farmers) applicators (*n*=20,417; 12,495 from Iowa and 7,922 from North Carolina).
  - •Males represent 97% of this cohort (*n*=22,212), while Females are 3% of the cohort (*n*=672);
  - •98.6% of the cohort is white and the 1.4% nonwhites are predominately African-American farmers living in North Carolina.

Source: Alavanja, M. C., Sandler, D. P., McDonnell, C. J., Mage, D. T., Kross, B. C., Rowland, A. S., Blair, A. (1999). Characteristics of persons who self-reported a high pesticide exposure event in the Agricultural Health Study. *Environ Res*, 80(2 Pt 1), 180-186.

High Pesticide Exposure Events (HPEE): 22,884 Pesticide Applicators (cont.)

- AHS Covers a Large Number of Applications
  - Approximately 7.2 million pesticide applications were made by subjects in this analysis,
    - About 3.3 million by Iowa private applicators, over 1.1 million by Iowa commercial applicators, and
    - Over 2.7 million by North Carolina private applicators.
- During their working lifetime, **14% of the cohort (*n*=3231) had at least one HPEE**, as defined in the methods.
  - HPEE by License Type
    - IA Private (15%), IA Commercial (22%)
    - NC Private (10%)

Source: Alavanja, M. C., Sandler, D. P., McDonnell, C. J., Mage, D. T., Kross, B. C., Rowland, A. S., Blair, A. (1999). Characteristics of persons who self-reported a high pesticide exposure event in the Agricultural Health Study. *Environ Res*, 80(2 Pt 1), 180-186.

AHS HPEE Results: 2006

- Increased risk of HPEE among private pesticide applicators with:
  - increasing pesticide application days,
  - history of HPEE at enrollment,
  - decreasing age,
  - Storing pesticides in the home,
  - living in Iowa, and
  - not removing work boots when entering the home.

Source: Bell EM, Sandler DP, and Alavanja MC. (2006) High pesticide exposure events among farmers and spouses enrolled in the Agricultural Health Study. *Journal of Agricultural Safety and Health*, 12(2): 101-116.

Symptom Reporting Patterns

- For those with an HPEE in the 12 months prior to the interview,
  - 50% of applicators and
  - 55% of spouses reported symptoms related to the HPEE.
  - Skin and eye irritation were the most commonly reported symptoms , followed by headache or dizziness, and nausea.
- Under-reporting:
  - Only 13% of the applicators with symptoms and 22% of the spouses with symptoms sought care (and would come to the attention of medical personnel responsible for reporting pesticide exposure events).

Source: Bell EM, Sandler DP, and Alavanja MC. (2006) High pesticide exposure events among farmers and spouses enrolled in the Agricultural Health Study. *Journal of Agricultural Safety and Health*, 12(2): 101-116

Surveillance Improvements: Track and Foster Prevention

- Self reported HPEE vary in frequency for AHS from ~8-13% (check and add source)
- Poison Control Centers (PCC) collect data on clinically confirmed acute pesticide poisonings.
  - PCC data are available from a national network of comparable populations, and expanded use of these existing systems by farmworkers is under discussion.

Surveillance Improvements: How to Track and Foster Prevention?

- Selected States have surveillance programs and 12 report to NIOSH SENSOR
  - State data are valuable for prompt remedial action and to track long term trends and results of focused interventions on recurring problems.
- Required industry reports about self reported incidents (events equivalent to HPEE) is under US EPA's 6 (a) (2).
  - These and other data are routinely examined as part of the periodic registration review and earlier reregistration efforts under various laws regulating use of pesticides.

Agricultural Health Study: Prospective Design

- Collaborative effort involving:
  - National Cancer Institute (NCI).
  - National Institute of Environmental Health Sciences (NIEHS).
  - National Institute for Occupational Safety and Health (NIOSH).
  - U.S. Environmental Protection Agency (EPA).
  - Iowa and North Carolina State Agriculture Departments, State Cancer Registries, Universities, others.
- The study has four major components:
  - The main prospective cohort study - cancer and non-cancer outcomes.
  - Linkage with cancer registries, vital statistics, United States Renal Data System (USRDS).
  - Ongoing data collection (i.e., Telephone interview, food frequency questionnaire).
  - Biological sample collection, e.g., cheek cell collection.

Agricultural Health Study: Methods

- Cross-sectional studies begun in 1993 -- including questionnaire data, functional measures, biomarkers, and GIS
- Nested case-control studies in Phase 2 data collection begun in 1998
- Exposure assessment, biomonitoring, and field validation studies recently completed
- Molecular epidemiology and genetics studies are included in current 4 year, Phase 3 data collection begun in 2005

AHS Cohort and Data Collection Table 8

	Phase I (Complete)	Phase II (In Progress) [2]		
	Contacts Completed	**Main Qx Admin (CATI)***	**Buccal Cell Collection**	**Dietary Health Qx Admin**
Private Applicators	52,395	33,450	18,340	17,804
Spouses	32,347	23,778	14,279	15,372
Commercial Applicator	4,916	0	0	0
Total	**89,658**	**57,228**	**32,619**	**33,176**

[1]Phase II data collection on Commercial Applicators not yet begun.
[2] Progress through September 2003, *Computer Assisted Telephone Interview
Source: <www.aghealth.org>

AHS Post-enrollment (Incident Only) Table 9

	Post-enrollment Cases Only			
Cancer Site	**Total with Cancer**	**Completed Phase II**	**Returned Buccal Sample**	**Returned DHQ**
Breast	433	342	238	249
Prostate	908	605	407	384
Colon	298	172	101	102
Lung	302	101	52	60
NHL	135	69	48	48
Other [4]	1,300	670	426	438
Total	**3,376**	**1,959**	**1,272**	**1,281**

Malignant Cancer Cases by Site and Phase II Data Collection progress, <www.aghealth.org>

Agricultural Health Study

- Prospective cohort characteristics
  - 89,658 private pesticide applicators, spouses of private applicators, and commercial pesticide applicators recruited within Iowa and North Carolina (Table 8).
- Phase I, initial cohort recruitment, began in 1993 and concluded in 1997.
  - Phase I observation
    - Administration of a questionnaire to obtain information on pesticide use, other agricultural exposures,
    - Work practices that modify exposures, and other activities that may affect either exposure or disease risks (e.g., Diet, exercise, alcohol consumption, medical conditions, family history of cancer, other occupations, and smoking history).

Agricultural Health Study: Phase II

- Phase II follow-up began in 1999 and concluded in 2003
  - Phase II interviews are designed to record updated information on:
    - Pesticide use since enrollment,
    - Current farming and work practices, and
    - Changes in health status.
  - In addition, the dietary health questionnaire in Phase II makes a detailed evaluation of subjects' cooking practices and dietary intake.
  - The buccal cell collection of Phase II was implemented to assess the impact of genetic risk factors on epidemiologic outcomes.

AHS Case Example

- Prostate Cancer- 50 chemicals tested
- Statistical significant interaction with family history and predicted exposure intensity
  - Chlorpyrifos OR 1.65, CI 1.02-2.66, p=0.04
  - Fonofos OR 2.04, CI 1.21-3.44, p=0.008
  - Permethrin OR 2.31, CI 1.17-4.56, p=0.02
  - Phorate OR 1.64, CI 1.02-2.63, p=0.04
  - Methyl bromide at highest exposure*

    OR 3.47, CI 1.37-8.76, p= 0.004

*Not confirmed in second analysis, Me Br use was down

Source: Alavanja MCR, Samanic C, Dosimeci M, Lubin J, Tarone R, Lynch CF, Knott C, Thomas K, Hoppin JA, Barker J, Coble J, Sandler DP, Blair A. (2003). Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. *American Journal of Epidemiology*, 157(9), 800-814.

Summary

- Findings on HPEE events in the AHS
  - provide an important source of new information to identify where farmers are at lower risk, e.g., they smoke less and have a lower rate of lung cancer compared to the general population
  - Highlight factors to guide current and future farmer and farmworker educational, as well as applicator certification and training efforts (see especially updates, HPEE Fact Sheet and other Fact Sheets at http://www.aghealth.org)

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- Disclaimer: The views expressed are those of the authors and do not necessarily reflect the policies of EPA, NCI or any other AHS partner agencies.