



## No. 44: Findings from the Agricultural Health Study

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### AGRICULTURAL HEALTH STUDY OVERVIEW

Current research suggests that although U.S. agricultural workers are, overall, healthier than the general population, they do have higher rates of certain types of cancer, asthma, and neurological disorders. The Agricultural Health Study (AHS) is a long-term prospective cohort study of almost 90,000 subjects in Iowa and North Carolina.

The study includes approximately 57,000 private and commercial applicators and 32,000 spouses of private applicators. The central focus of this ongoing project is to identify exposures in the agricultural environment that are responsible for excess cancers and other chronic diseases observed in this cohort and that may affect other agricultural populations throughout the world. This leaflet presents highlights of recently published AHS findings. For more detailed information including a description of the project, authors, and access to full publications, visit <http://www.aghealth.org/>.

Results from the AHS are beginning to have a major influence on the scientific evaluation of pesticide safety. The study directors emphasize their responsibility to minimize the error of falsely identifying a pesticide as a risk factor when it is not, and of failing to identify a pesticide as a risk factor when, in fact, it is. Therefore, the project investigators have incorporated into the study design several safeguards to help avoid either a false positive or false negative association between exposure to a specific pesticide and an outcome.

### Study Safeguards

- Look for consistency across geographical areas. Is there a dose-response relationship in effect in both Iowa and North Carolina?
- Look for consistency across types of applicators. Is there a dose-response effect in both private applicators and commercial applicators?

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- After an initial positive association, look for replicability of the finding. Can the finding be duplicated across a second period of time?
- Validate the questionnaire-based estimates of pesticide exposure by conducting field measurements of both external and internal pesticide exposures among cohort members.
- Evaluate the biological plausibility of epidemiological associations linking specific pesticides with specific adverse effects in well-designed biomarker studies.

## OVERALL HEALTH

Recent findings continue to indicate that study participants are generally healthier than the general population. In both Iowa and North Carolina, AHS participants have lower death rates and fewer cases of cancer than people of the same age, sex, and race in their state. Compared to others in their state, study participants are less likely to die from heart disease, diabetes, lung diseases, and cancer.

In both states, lung cancer rates among study participants are only about half that of the general population, and breast cancer rates are about the same as the rate for the general population. An important factor in the lower rates of deaths and most types of cancer studied may be participants' lower use of tobacco products and higher physical activity level.

## CANCER RISKS

### Risks to Subpopulations

**Private Applicators:** After 7 years of follow-up, private applicators in AHS demonstrated significantly lower risk of

cancers than expected when compared with cancer rates for the general populations in Iowa and North Carolina, adjusted for age, race, and gender. In particular, private applicators had lower rates of buccal cavity, respiratory, digestive system, and urinary system cancers. These applicators also had lower rates of smoking than the general population, which can explain lower rates, at least in part, of some of these cancers.

**Commercial Applicators:** Commercial applicators' overall cancer incidence did not differ significantly from that of the general population's. Commercial applicators in the study tended to be younger than the private applicators, and their use of alcohol and tobacco products was similar to that of the general population.

**Female Applicators and Spouses:** The total number of female applicators was relatively small, but there was a significant increase in their risk of ovarian cancer. Spouses of private applicators did not have an increased risk of ovarian cancer. A separate follow-up study is planned for the female applicators to attempt to better classify this apparent increased risk.

### Risks of Specific Types of Cancer

**Prostate Cancer:** Prostate cancer incidence was found to be significantly higher in private applicators participating in this study. Another recent finding from AHS indicates that diet may explain a portion of the overall increased risk in this or other groups. Participants who ate well and very well done meat had an increased risk for prostate cancer.

**Lip Cancer:** Lip cancer, widely recognized as an increased risk for farmers, was found to be increased in private applicators, their spouses, and commercial applicators, but it was not statistically significant. Studies

underway are looking at the efficacy of preventive measures for lip cancer.

**Melanoma:** Risk of melanoma, an aggressive type of skin cancer, was not increased among applicators (either private or commercial), but was increased significantly among spouses of private applicators. Previous studies have found that spouses of private applicators are often involved in farm practices that increase their exposure to sunlight, which would be expected to raise the risk of melanoma. AHS investigators plan to compare the risk of melanoma in spouses to the risk in female applicators.

## REPRODUCTIVE EFFECTS

In animals, atrazine, carbaryl, carbon tetrachloride, DDT, lindane, mancozeb, and maneb have been shown to affect the reproductive system. Researchers studied a subset of women in the AHS aged 35 - 55 years. They found age at menopause to be increased by 3 months (after controlling for age, smoking, and past use of oral contraceptives) in women who reported using pesticides, and by 5 months in women who reported using hormonally active pesticides. Timing of menopause may affect a woman's risk of developing reproductive hormone-related chronic diseases.

Previous research has shown that organic solvents may contribute to reduced fertility, especially in women. AHS researchers evaluated the fertility of over 5500 male applicators and their female spouses. Twenty-eight percent (28%) of these couples were classified as subfertile (not conceiving a pregnancy after at least 12 months of unprotected intercourse). Overall, about 84% of couples would be expected to have conceived by 12 months, equivalent to a 16% subfertility rate.

Further, the researchers found that exposure to solvents was associated with subfertility in both male and female members of the spousal pairs. These researchers also found body mass index (BMI) was an independent risk factor for subfertility in males in the study population. BMI is well-known to affect fertility in women, but had not been studied for this effect in men.

## RETINAL DEGENERATION

Retinal degeneration / macular degeneration is the leading cause of impaired vision with aging, but little is known about its cause. In the AHS, those who reported retinal degeneration were more likely to have orchards and to have used certain pesticides. The disease was more common in:

- applicators who used fungicides, particularly maneb, mancozeb, or ziram
- and
- applicators who had used organochlorine insecticides including aldrin and DDT.

## PARKINSON'S DISEASE

Pesticide exposure may increase the risk of developing Parkinson's disease, a progressive neurodegenerative disease characterized by tremor, slow movements, poor balance, and other symptoms. Data from the AHS showed:

- Both male applicators who used pesticides for more than 400 days in their lifetime, and their female spouses had an increased risk of Parkinson's disease.
- Parkinson's disease was also related to high pesticide exposure events such as spills.

- Using personal protective equipment (PPE) reduced the risk of developing Parkinson's disease in the study group.
- Individuals who had used paraquat, cyanazine, trifluralin, or 2,4,5-T had an increased risk of Parkinson's disease.

These findings support existing evidence that exposure to some pesticides may increase the risk of Parkinson's disease. AHS is continuing to investigate this finding in another sub-study.

### **FARMER'S LUNG DISEASE**

Among AHS participants, Farmer's Lung disease occurred more often in farmers and spouses who had applied pesticides for more years than in farmers and spouses who applied pesticides for fewer years. Farmer's Lung disease is a rare lung disease generally associated with dairy farming and the handling of moldy hay and grain. Other findings related to Farmer's Lung Disease included the following:

- This disease was still rare among study participants. Only 2% of applicators and 0.2% of spouses in the AHS reported having Farmer's Lung disease.
- Dairy and poultry farmers had a higher risk of Farmer's Lung disease than other farmers.
- Most cases were in Iowa. Differences in climate and/or farming practices between the two states may be the reason for this difference.
- Individuals who used DDT, lindane, or aldicarb were more likely to report having Farmer's Lung disease.
- Farmers who had applied pesticides for

more than 30 years were 50% more likely to have reported having Farmer's Lung disease than other participants. Results for spouses were similar.

### **RESPIRATORY EFFECTS**

#### Wheeze

Incidence of wheeze is commonly used to predict potential respiratory hazards in occupational studies. Wheeze incidence in the AHS was increased with certain general farm elements, including use of tractors and exposure to farm animals.

AHS researchers also found wheeze to be associated with 11 of 40 different pesticides used during the year previous to the investigation. Pesticides associated with increased risk of wheeze included the organophosphate insecticides chlorpyrifos, dichlorvos, fonofos, malathion, and parathion, phorate, and terbufos, and the herbicides alachlor, atrazine, chlorimuron-ethyl, and paraquat. Results from animal studies have recently led to a proposed mechanism linking organophosphate pesticides and airway hyperreactivity at doses below those causing cholinesterase inhibition.

#### Chronic Bronchitis

Farmers are known to have increased risk for chronic bronchitis. One recent AHS investigation indicates that pesticide use may increase chronic bronchitis prevalence. However, this evidence is considered only preliminary, since there is not enough supporting evidence from any other studies.

A second AHS study found that, in non-smoking farm women, pesticides as well as grain and dust exposures were associated with chronic bronchitis. Further targeted

investigations will be needed to predict with confidence whether there is truly an association between pesticide exposure and chronic bronchitis.

## **HIGH PESTICIDE EXPOSURE EVENTS**

Six AHS papers have now been published concerning High Pesticide Exposure Events (HPEE). Incidents involving single (or occasionally repeated) high exposures are of concern because they may lead to a different type of outcome than chronic low-dose exposures. To date, there is no single, accepted definition of HPEE. Study authors identified a subset of applicators with HPEE by asking the question, “Have you ever had an incident or experience while using any type of pesticide which caused you unusually high personal exposure?” Fourteen percent (14%) of the 22,884 applicators completing both baseline questionnaires at the time of recruitment into the study reported such an outcome.

Through analysis of this subset, the researchers identified several factors associated with HPEE:

- HPEE risk increased with the number of days spent applying pesticides.
- Men were more likely than women to have experienced a HPEE.
- Iowa applicators were more likely than North Carolina applicators to have a

HPEE.

- Applicators with at least some college were more likely than those with a high school level of education to have experienced a HPEE.
- Younger applicators were more likely than older applicators to have a HPEE.
- Storing pesticides in the home increased the likelihood of a HPEE.
- Applicators who failed to remove work boots before entering the home were more likely to have had a HPEE.
- Those who washed work clothes with the family laundry were more likely to have a HPEE.

It is unlikely that washing work clothes with family laundry and entering the home with work boots still on were directly responsible for HPEE. Rather, these are likely indicators of applicators or spouses who are less careful overall, and who may be more careless in directly handling pesticides.

Of those applicators who reported a HPEE within 12 months prior to the questionnaire, about 50% of both applicators and spouses experienced symptoms from the exposure event. However, only 22% of spouses and just 13% of applicators with symptoms sought care from a health professional, clinic, or other source.

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