Agriculture and Cancer

A NEED FOR ACTION

Agriculture and Cancer

What Do We Know?

Well designed and resilient agricultural systems are essential for producing the food and fiber necessary for secure, prosperous and healthy communities. Yet farming is one of the most dangerous industries in the United States, according to the Bureau of Labor Statistics.[1] Illnesses, acute injuries and even fatalities are high among agricultural workers compared to other industries due to the use of machinery and equipment, repetitive physical work, close interactions with animals, and exposure to chemical toxicants.[2,3]

Overall cancer incidence and mortality rates are low among farmers relative to the general population.[4] However, studies of farming populations routinely reveal elevated risk for several specific types of cancer, including leukemia, non-Hodgkin's lymphomas, multiple myeloma, soft-tissue sarcoma, and cancers of the skin, brain, prostate, stomach and lip.[4] Researchers continue to explore whether there are a set of common exposures that may explain these higher incidence rates using epidemiologic studies. This work documents that a variety of substances either created by or used in agricultural practices may increase cancer risk, [see evidence side-bars] including: pesticides, nitrates in fertilizers, dusts, solvents, fuels, engine exhaust, paints and welding fumes.[4] Although agricultural populations are exposed to a broad array of substances that have been linked to cancer, the bulk of the research to date has focused on pesticides.

In 2001, an estimated 5 billion pounds of pesticides were used in the United States.[5] Of that, 1.2 billion pounds were used primarily in the agricultural and home and garden sectors.[5] Approximately 165 currently registered pesticidal chemicals (including active and inert ingredients in pesticides) have been classified by the Environmental Protection Agency (EPA) or the International Agency for Research on Cancer (IARC) as known, probable or possible human carcinogens.[6] Yet only a small number of these chemicals have been severely restricted.[6]

Agricultural Exposures

Not Just Workers

Agriculture is one of the largest industrial sectors in the United States, with nearly 2 million full-time workers employed in agricultural production as of 2007.[7] As noted above, these workers face many occupational exposures to pesticides and other industrial agents that may contribute to cancer risk. However, full-time adult agricultural workers are not the only people potentially exposed to these substances. Agriculture is one of the few industries in the U.S. in which families often share the work. Based on 2006 statistics, 50% of farm-based children under age 20

perform farm work and an additional 307,000 children and adolescents are hired to work.[7] Among pesticide applicator families in the National Cancer Institute's Agricultural Health Study, 21% of homes are within 50 yards of pesticide mixing areas; 27% of applicators store pesticides in their home; and 94% of clothing worn for pesticide work is washed in the same machine as other laundry.[8] Data from this study also reveal that 51% of male pesticide applicators' wives worked on the farm during the last growing season; a significant number of wives (40%) reported mixing or applying pesticides themselves; and just under half (46%) have done so for more than 10 years.[8]

Pesticide levels in carpet dust are typically 10- to 200-fold higher than levels in air inside the home.

Indirect environmental exposure is also a significant problem for people living near farms. For example, a recent study found that pregnant women living in an agricultural area had 2.5 times higher levels of organophosphate insecticide metabolites in their urine compared to the general US population.[9] Twenty years ago, the US Department of Agriculture estimated that 50 million people in the US obtain their drinking water from groundwater that is contaminated with pesticides and other agricultural chemicals such as nitrates from fertilizers.[10] Although such a survey needs updating, these data are informative for exploring existing patterns of cancer incidence. Studies also confirm that pesticides used in agricultural areas contaminate the air miles from where they are applied, and also show up in dust samples from inside people's homes.[11,12] Pesticide levels in carpet dust are typically 10- to 200-fold higher than levels in air inside the home.[13] Pesticides are also found in the soil surrounding homes, although usually at lower levels than indoors because sun, water and soil microbes can degrade pesticides in soil over time.[13] Indoor pesticide exposure can be especially problematic for children and pets, since they spend more time on the floor and they explore the world by putting objects in their mouths.

Cancer

A Disease Resulting from the Combined Effect of Multiple Risk Factors

Many studies document increased risk of cancer among children and adults associated with exposure to an array of pesticides.[14-16] Yet regulatory actions to ban or severely restrict pesticide use based on evidence of carcinogenicity in humans are rare. One of the main reasons that regulatory bodies such as EPA and OSHA do not act on the current evidence base is the difficulty of quantifying human exposure

to specific pesticides and assessing associated health risks. Workers and the public are often exposed to several types of pesticides, as well as other carcinogenic substances such as tobacco smoke and diesel particulates. Thus, it is difficult to establish strong epidemiological evidence that exposure to a single, specific pesticide causes cancer or other health effects. In the absence of strong evidence that a pesticide causes harm, it remains in use.

example, in the Agricultural Health Study, pesticide applicators exposed to the organophosphate pesticides phorate and fonofos had an elevated risk of prostate cancer, but only among those with a family history of the disease.[18,19] Higher nitrate levels in public water supplies were linked to nearly a two-fold excess risk of kidney cancer, but only in combination with consuming above the median amounts of red meat or below the median amounts of vitamin C.[20]

Cancer is not caused by a single factor. Rather, it results from a complex, multi-factorial, multi-stage process.

Yet cancer is not caused by a single factor. Rather, it results from a complex, multi-factorial, multi-stage process. Researchers have identified at least six essential cellular alterations that must occur in order for cancer to develop.[17] Animal studies show that pesticides may increase the risk of cancer through a variety of mechanisms, including genotoxicity, tumor promotion, hormonal action and immunotoxicity.[14] Cancer risk is also influenced by a variety of factors, including diet, genetic inheritance, reproductive factors, other lifestyle factors, and exposure to a variety of agents at work and in the general environment.

Studies examining the links between pesticides and risk of prostate cancer have shown that genetics and pesticide exposure together influence risk. For

Scientific evidence reveals that it is not only what a person is exposed to, but also the timing of the exposure that influences cancer risk. Exposure to toxicants during periods of rapid growth and cell differentiation—from fetal life through puberty—can be an important contributor to cancer risk later in life. Risks of childhood cancers are linked with parental exposures to pesticides prior to conception, *in utero* exposures and direct exposures during childhood.[16] Some evidence indicates that children are at greatest risk if exposed to pesticides *in utero*.[21] A recent study demonstrates that girls exposed to elevated levels of DDT before puberty—when mammary cells are more susceptible to the carcinogenic effects of hormones, chemicals and radiation—are *five times*

Strength of the evidence linking specific cancers with human exposure to agents in the agricultural environment[14-16,20,27,45–47]

Bladder ■ SUSPECTED: PAHs

Breast ■ SUSPECTED: 2,4-D, chlordane, DDT/DDE, dieldrin, hexachlorobenzene, malathion, organic solvents, PAHs, triazine herbicides, farm wives living/presence near pesticide-applied crops

Brain and other central nervous system ■ SUSPECTED: N-nitroso compounds (fertilizers), parental occupation/occupation associated with pesticide exposure

Colorectal ■ SUSPECTED: alachlor, aldicarb, aldrin, chlorpyrifos, chlordane, dicamba, dieldrin, occupation associated with pesticide exposure

Hodgkin's Disease ■ SUSPECTED: chlorophenols, DDT/DDE, dioxin-contaminated phenoxy herbicides, occupation associated with pesticide exposure, solvents

Kidney ■ SUSPECTED: N-nitroso compounds (fertilizers), parental occupation/occupation associated with pesticide exposure, solvents

Leukemia ■ SUSPECTED: aldrin, carbon disulfide, chlordane, DDT/DDE, dieldrin, ethylene dibromide, heptachlor, lindane, mancozeb, methyl bromide, parental occupation/occupation associated with pesticide exposure, phosphine, simazine, toxaphene

Lung ■ STRONG: air pollution, arsenic and arsenic compounds, diesel exhaust, wood dust ■ SUSPECTED: carbofuran, chlorpyrifos, DDT/DDE, diazinon, dicamba, dieldrin, metolachlor, occupation associated with pesticide exposure, pendimethalin, phenoxyherbicides and/or dioxin contaminants

more likely to develop breast cancer when they reach middle age.[22]

Risks of childhood cancers are linked with parental exposures to pesticides prior to conception, in utero exposures and direct exposures during childhood.

Single cancer risk factors always act within multidimensional causal webs reflecting the cumulative interaction among risks across the life course. Moreover these risk factors interact at various levels of organization (biological, social, and ecological) and scales (individual, family, community, society and ecosystem). Preventing cancer will depend on addressing the broader set of conditions that influence risk in both our research and cancer prevention and control programs.

Under-Studied and Overexposed

Migrant Workers Face Higher Risks

It is estimated that 2.5 to five million individuals and their families work as migrant and seasonal agricultural workers.[23] These workers provide crucial labor for much of crop production and processing in the US.[23] Due to working and housing conditions, farm workers often encounter disproportionate exposure to pesticides. Children of migrant workers often accompany their parents into the field due to lack of child care.[4]

The study of cancer among farm workers is an under-researched area given the difficulty of conducting long-term studies of a highly mobile population. Indeed, published studies may not be generalizable to the broader farm worker population, as successful studies depend on factors such as permanent or semi-permanent residence and the presence of community-based research programs.[24] Nevertheless, existing studies can be instructive. Several studies conducted among members of the United Farm Workers of America (UFW) in California reveal increased risk of leukemia[25] as well as cancers of the stomach, liver and gallbladder, biliary passages and uterine cervix.[26] Risk of breast cancer was also found to be elevated in a registry-based study of female farm labor union members in California.[27] In this study, there was a six-fold elevation of breast cancer among those who worked with mushrooms. In addition, a number of pesticides were associated with elevated breast cancer risk, including chlordane, malathion, and 2,4-D. The association between pesticide exposure and breast cancer risk was stronger among younger women and those with early-onset breast cancer. A more recent case control study of UFW members that examined

the risk of gastric (stomach) cancers found a near 3-fold elevation in risk among workers in the citrus industry.[28] In this study, risk of stomach cancer was also elevated among those using 2,4-D, chlordane, propargite and trifluralin.

Addressing the multidimensional causal web by which cancer develops in migrant and seasonal agricultural workers will require additional research on the multiple risk factors experienced by these workers. Intervention to prevent future cancers will also require a greater understanding of the broader social context that influences cancer risk.

Don't We Have Regulations to Protect Agricultural Workers?

Both EPA and the Occupational Safety and Health Administration (OSHA) have regulations designed to safeguard agricultural workers. But these regulations are often ignored in the field and many are inadequate to protect migrant and seasonal agricultural workers from cancer risks related to pesticide exposures.

OSHA regulates farm worker health and safety issues but not as they relate to pesticides. However, other provisions within the Occupational Safety and Health Act influence cancer risk reduction measures, including the obligation to provide training and communications about hazards and to provide safe drinking water and field sanitation. Yet OSHA's limited resources mean that it has a minimal capacity to inspect facilities subject to OSHA standards to ensure compliance.

Within OSHA's field sanitation provisions, regulations exempt agricultural operations with ten or fewer employees from providing drinking water, handwashing facilities and toilets for their employees, regardless of the conditions or hours required for their work in the fields. Even among farms required to comply with OSHA farm worker standards—farms with 10 or more workers—compliance is poor. A recent North Carolina survey found that only 4 percent of farmworkers surveyed had access to drinking water, hand washing facilities, and toilets.[23] Lack of protective equipment and prompt access to showers and laundry facilities may exacerbate exposure to hazards like pesticides by prolonging contact with the skin.[4]

A serious cancer prevention agenda must ensure that policies and programs are in place to guarantee the safe and equitable working conditions necessary to prevent cancer and other diseases in workers.

In 1992, EPA revised the Worker Protection Standard (WPS) for agricultural pesticides. This regulation is designed to protect farm workers and requires pesticide safety training, notification of pesticide applications, use of personal protective equipment,

Multiple myeloma ■ SUSPECTED: DDT/DDE, dioxin-contaminated phenoxyherbicides/chlorophenols, glyphosate, occupation associated with pesticide exposure, solvents

Non-Hodgkin's Lymphoma ■ STRONG: dioxin-contaminated phenoxyherbicides/chlorophenols ■ SUSPECTED: 2,4-D, carbamate, carbaryl, chlorophenols, dicamba, ethylene dibromide, glyphosate, hexachlorocyclohexane/lindane, MCPA, mecoprop, methyl bromide, organochlorine pesticides, occupation associated with pesticide exposure, phosphine, solvents

Pancreatic ■ SUSPECTED: DDT/DDE, occupation associated with pesticide exposure

Prostate ■ SUSPECTED: butylate, chlordane, chlorpyrifos, coumaphos, cyanazine, DDT/DDE, dioxin-contaminated phenoxyherbicides, fonofos, hexachlorobenzene, methyl bromide, occupation associated with pesticide exposure, permethrin, phorate

Ovarian ■ SUSPECTED: atrazine, occupation associated with pesticide exposure

Soft-tissue sarcoma ■ SUSPECTED: chlorophenols, DDT/DDE, dioxin-contaminated phenoxyherbicides, occupation associated with pesticide exposure

Skin ■ STRONG: arsenic and arsenic compounds, PAHs ■ SUSPECTED: DDT/DDE, occupation associated with pesticide exposure

Stomach ■ SUSPECTED: atrazine, agricultural work in the citrus industry, chlordane, occupation associated with pesticide exposure, propargite, and trifluralin

Testicular ■ SUSPECTED: occupation associated with pesticide exposure

restricted entry intervals following pesticide application, decontamination supplies and emergency medical assistance.[29] Yet despite improvements in farm worker protection that have resulted from the WPS, there are major documented compliance failings. According to a recent study of migrant farm worker families residing along the Texas-Mexico border, only 46.1% of mothers participating in migrant farm work reported having received training in the safe use of pesticides within the previous five years as required by WPS.[30] Similar findings regarding the low penetration of pesticide safety training among farmer workers have been reported in other regions of the country as well.[31]

This evidence makes clear the need for continued efforts to eliminate exposure disparities among seasonal farm workers and their families. A serious cancer prevention agenda must ensure that policies and programs are in place to guarantee the safe and equitable working conditions necessary to prevent cancer and other diseases in these workers.

If Some Pesticides Contribute to Cancer or Other Serious Health Conditions, Why Aren't They Banned?

The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) gives EPA the authority to assess and manage the risks of pesticides. Under FIFRA, industry is required to submit toxicity and environmental data to demonstrate evidence of safety when registering a pesticide. However, pesticide regulation is not based on a public health or safety standard. Rather, it is based on a risk-benefit standard. EPA registers a pesticide for use if it does not pose "unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide."[32]

Although EPA has banned or restricted dozens of pesticides, approval of a pesticide for registration by EPA is no assurance that it is safe, as demonstrated by the following examples.

- Under FIFRA, new pesticides coming on the market (an average of 18 new pesticides a year)[33] can be used based on a "conditional registration" allowance, which allows use of the pesticide before complete health and safety testing are supplied to EPA.[34] A survey by the Northwest Coalition for Alternatives to Pesticides (NCAP) found that of the 41 new conventional pesticides registered for use between 1991 and 2001, over half were conditionally registered.[33]
- The active ingredient of the pesticide may not be the only source of exposure to cancer-causing agents. Yet toxicity testing for chronic diseases such as cancer is only required for the active ingredient of the pesticide, and only active

ingredients are required to be listed on the product label.[35] "Inert" ingredients may also be toxic, but they are not often listed on the label because the formulation is protected as trade secret. For example, xylene is used as the inert ingredient in almost 900 pesticides.[32] Some evidence supports an increased risk of leukemia, brain and rectal cancers as well as a range of more acute effects such as neurological conditions and eye, throat and nose irritation associated with exposure to xylene.[33,36,37]

- As of this writing, data regarding the ability of pesticides to disrupt endocrine systems and contribute to a variety of disease outcomes have not been required for pesticides. Yet dozens of published studies report on the ability of a variety of pesticides to disrupt hormone signaling at extremely low levels of exposure and these disruptions may contribute to cancer development or progression. Although EPA has convened scientific panels to assist the Agency in determining testing procedures for endocrine disruption, and has proposed an initial list of pesticide active and inert ingredients to be considered for screening[38], no pesticides registered to date have been reviewed in the context of the emerging literature regarding endocrine disrupting effects.
- EPA relies heavily on data from pesticide manufacturers to assess and manage the risks of pesticides—in fact FIFRA requires that pesticide manufacturers provide data for registration. Yet an analysis of research conducted and/or funded by pesticide manufacturers versus government funded or academic research found important differences in research conclusions.[39] Studies funded by pesticide manufacturers are far more likely to report null findings regarding deleterious health outcomes associated with exposure to pesticides compared to studies funded by other sources—findings which keep specific pesticides on the market.
- Both newly registered and re-reregistered pesticides can show evidence of cancer and still be used. For example, the fungicide vinclozolin is widely used on vineyards and was registered for use in 2000, despite laboratory tests indicating that it causes testicular cancer and disrupts normal androgen activity in laboratory animals.[40] Recent animal studies demonstrate epigenetic effects such that rats exposed to high levels of vinclozolin while in utero developed tumors at a much higher frequency than non-exposed rats; the pattern held true for their offspring and their offspring's offspring.[41] In fact, the subsequent generations with no direct exposure to the fungicide had a *higher* frequency of tumor development and a range of other diseases compared to those only exposed while in utero. Additional multi-

generational studies at levels routinely experienced by agricultural workers are needed. At the same time, these findings are sufficient to raise serous concerns about impacts to human health and warrant precautionary action related to use of such pesticides.

- As in the case of the re-registration of phosmet, EPA regularly approves continued pesticide use despite known harm to farmworkers based on predictions about the effectiveness of new mitigation measures.[42] However, EPA has limited resources to confirm that the mitigation measures work as expected to reduce risks.

We can no longer depend on a system of enumerating costs and benefits that repeatedly fails to prevent cancer and other diseases associated with pesticide exposure.

We need to revamp our pesticide registration procedures to protect the public's health. We can no longer depend on a system of enumerating costs and benefits that repeatedly fails to prevent cancer and other diseases associated with pesticide exposure. There is an inherent flaw in a system which requires years of research and review for a single pesticide, when hundreds remain in use and inadequately regulated. Incentives to adopt safer pesticide alternatives are needed, including broader adoption of integrated pest management and organic agriculture practices.

Are Pesticides in Food a Major Source of Exposure to Carcinogens?

Under the Food Quality Protection Act (FQPA) of 1996, EPA began reassessing food tolerances for concentrations of pesticides or their breakdown products that are allowed to remain in or on food, using a new set of standards that are more protective of public health.

EPA sets tolerance levels for food at a level such that a person's combined exposure to a given pesticide from different sources (such as food, drinking water, and home use of pesticides) and applied according to label instructions and harvesting guidelines is 100 to 1,000 times lower than "no observable effect level" (NOEL) or the dose at which no adverse effects were observed in toxicity studies. This includes a safety factor to account for the susceptibility of children. If a pesticide causes cancer in experimental animal studies, then EPA adjusts use guidelines so exposure will be less than the amount calculated to cause one extra case of cancer per million people. [43]

Although FQPA is an important step forward in protecting the health of the public from pesticide residues, it has significant limitations:

- The procedures still do not account for the fact that individuals are exposed to multiple pesticide residues and other chemicals that may influence cancer risk.
- In its food tolerance reassessments, EPA has routinely discarded the tenfold safety factor requirement intended to protect infants and children. The law requires EPA to use this safety factor if the toxicology data indicate that children will be more susceptible to adverse effects than adults, or if there are data gaps. Yet even when data clearly show that young animals are more susceptible to the effects of a pesticide than adult animals, EPA has failed to include the child safety factor. This was the case, for example, in EPA's tolerance reassessment for endosulfan.[44]

FQPA is an important step in safeguarding the public from exposure to pesticides that may present a cancer risk at low levels of exposure and during critical windows of vulnerability. It provides us with key lessons about how science-based regulatory decisions can better prevent cancer and other significant health conditions by addressing the complexities of disease causation. However, vigilance is needed to ensure that the law is implemented as intended. Moreover, there is a need for a new generation of policy approaches that move beyond regulations that simply address the risk of one pesticide at time or one agent at a time. Most of us are exposed to a complex array of agents that may increase cancer risk not only in the food we eat, but also in the air we breathe and the materials we encounter in daily life. If we are serious about preventing cancer, we need a broad, concerted plan.

There is a need for a new generation of policy approaches that move beyond regulations that simply address the risk of one pesticide at a time or one agent at a time.

How Can We Prevent Cancer Linked to Agricultural Exposures?

A comprehensive US cancer prevention agenda that promotes health, prevents cancer and protects the most vulnerable members of society will need to safeguard the people who grow and harvest the nation's food and others exposed to harmful substances used in agriculture. Here are five ways we can prevent cancer linked to agricultural exposures:

- **Support** cancer research that captures the complexities of cancer causation, including multiple exposures, low-dose effects and critical windows of vulnerability.
- **Eliminate** disparities in permitted exposures associated with agricultural work and increased risk of cancer, especially among seasonal and migrant farm workers.
- **Revamp** our pesticide regulatory system to avoid introducing pesticides that increase cancer risk among workers and the general public. Phase out pesticides that show evidence of harm.
- **Require** EPA to consider non-pesticidal alternatives when considering pesticide registration applications.
- **Identify** safer alternatives to harmful pesticides and provide economic incentives for least-toxic agricultural production. Through policy and market-based efforts, stimulate adoption of effective integrated pest management and organic agriculture practices.
- **Acknowledge** that while scientific certainty is seldom possible, from our duty to inquire flows an obligation to take preventive action when sufficient evidence of harm exists.

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