Reproductive Health Effects of Pesticide Exposure

Issues for Farmworker Health Service Providers

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# Table of Contents

Introduction and background .................................................................................................................. 5
Pesticides used in agriculture .................................................................................................................. 5
Exposure pathways ..................................................................................................................................... 7
Effects of exposure during the reproductive cycle .................................................................................. 7
  - Preconception exposure ..................................................................................................................... 8
  - Prenatal (in utero) exposure .............................................................................................................. 9
  - Neonatal and long term effects ........................................................................................................ 10
Clinical recommendations ...................................................................................................................... 11
Patient Education Materials .................................................................................................................... 12
Acknowledgements .................................................................................................................................. 13
APPENDIX: Acronyms ............................................................................................................................ 14
Reference List .......................................................................................................................................... 15
Reproductive Health Effects of Pesticide Exposure: Issues for Farmworker Health Service Providers

**Introduction and background**

Exposure to pesticides at any point in the life cycle has the potential for causing a range of short-term or long-term health problems. Documented health effects include a wide variety of illnesses and diseases, from eye irritation, skin rashes and respiratory problems to neurological damage, birth defects, cancer and death. The risk for and severity of adverse health effects from pesticide exposure varies significantly depending on many factors, including individual characteristics such as age and health status, the specific pesticide, and exposure circumstances. Exposure to pesticides at certain developmental stages of life can result in irreversible damage to organ structure and function. Of particular concern is the effect of exposure at during the reproductive cycle, from preconception to breast feeding, because of the possibility of poor birth outcomes, congenital anomalies, developmental deficits, and possibly childhood cancer [1].

Farmworker families often live near or on the farms on which they work, and thus spend much of their time in close proximity to areas where pesticides are applied on a regular basis. Twenty-one percent of farmworkers are women [2], who may be directed to or inadvertently enter recently treated fields while pregnant. Women in farmworker households who do not work in the fields may still be exposed to pesticide residues brought home by farmworker household members on their shoes, clothes and skin; from nearby applications that drift or are directly sprayed on outdoor play areas; and from chemicals used to control pests in and around the home, especially in poor quality housing.

This paper reviews the state of the research on the reproductive health effects of pesticide exposure with an emphasis on the needs and concerns of women in farmworker households. © Farmworker Justice 2008

2 Some of the studies included in this overview investigated exposure in the context of residential pesticides, urban populations, or handler tasks rather than focusing exclusively on hired farmworkers. They are included here because: 1) many pesticides have both agricultural and residential uses; 2) the biological mechanisms of action by which pesticides affect the human body do not depend on product use; 3) some handlers and workers perform similar tasks and therefore face similar exposures; and 4) residential pesticides are regularly applied in poor quality farmworker housing.

**Pesticides used in agriculture**

The chemicals used to control pests (any unwanted flora or fauna, e.g., weeds, insects, fungi, rodents) in agriculture vary widely in their target organism and mode of action. They include insecticides, rodenticides, herbicides, fungicides, and more. As their biological mechanisms are different, so too are
the resulting effects on human health and the environment. Insecticides of the class known as organochlorines (OC; see Appendix for list of acronyms), which were widely used in the United States until the 1970s, are central nervous system stimulators. They cause a variety of neurological symptoms that may lead to convulsions, stupor and coma, as well as damage to organs and the endocrine and immune systems. Perhaps the best-known example of an OC is dichlorodiphenyl trichloroethane (DDT), an organochlorine that caused well-documented damage to the environment and human health before it was banned in the United States in 1972. A study of women who grew up while DDT was in wide use found a five-fold increase in breast cancer among women who were exposed before the age of 14 as compared with women who were not exposed prior to that age [3]. DDT is still used in many developing countries for malaria control [4;5], and a few other organochlorines, such as endosulfan and lindane, remain legal in the US. Lindane is used to treat scabies and lice even though effective alternatives exist and its use is discouraged, especially for infants, young children and pregnant women [6].

Organochlorines are classified as persistent organic pollutants (POP), because instead of breaking down rapidly over time, they build up in the environment (e.g., soil) and in the fatty tissues of wild and domesticated animals. The half-life in soil for these chemicals can range from months to decades [7]. Over time, OCs accumulate in the food chain as smaller prey are eaten by larger animals and livestock eat feed grown in contaminated soil, ultimately settling in humans at the end of the food chain. Because of their tendency to bioaccumulate and the damage they do to the environment, most POPs were banned through an international treaty in 2001 [8].

With the banning of most OC pesticides, other types of compounds came into widespread use. The largest group of insecticides currently used worldwide includes the organophosphates (OPs), which have both agricultural and residential uses [6]. Unlike OCs, OPs are nonpersistent pesticides (NPP), that is, they break down relatively quickly in the sun, rain and dew found in the environment, and do not accumulate in the body over a long period of time. OPs are nonetheless highly toxic to humans and are responsible for tens of thousands of poisonings in developing countries [9] and thousands of poisonings in the US each year [10]. Many OPs are limited in the extent to which their effects discriminate between target and non-target organisms, including humans [11]. The NPP class also includes the carbamates and pyrethroids, both of which are neurotoxins and have similar effects on human health as the OPs. Pyrethroids, which are chemicals synthesized to mimic a naturally occurring plant pesticide, are also neurotoxins, but are generally considered less harmful than OPs, OCs, or carbamates.

Herbicides, which are designed to control unwanted plant growth, are also widely used in agriculture. Herbicides have a different mechanism of action from insecticides just described. The most common health effect of herbicides is irritation to the skin and respiratory tract, however, acute exposure to certain highly corrosive herbicides can cause multi-system injury and pulmonary failure [6]. Exposure to more than one class of pesticide at a time may amplify the negative health effects [12], while exposure to multiple pesticides that share a common mechanism can increase their specific toxicity [13].

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1 Alternatives to lindane for controlling head lice include Lice B Gone (Safe Effective Alternatives, www.licebgone.com) and Lice Away Enzyme Shampoo (Nature’s Best, www.naturesbestenzyme.com).
Exposure pathways

Pesticides are used in 85% of homes in the US [14], but they or their residues can be found even on surfaces that have never been directly or peripherally treated. POPs introduced into the environment years ago are still around today, transported by human activity and through the food chain. Despite being banned in the US (and many other countries) some 30 years ago, traces of these insecticides are still found in the homes and bodies of individuals in the US who were not even alive when these products were used [6;15]. Chlorpyrifos (a nonpersistent OP) has also been found to accumulate on newly-introduced surfaces, such as pillows, carpet and soft toys, when brought into a treated area up to two weeks after application, even if applied according to manufacturer’s instructions [16].

In agricultural settings, work-to-home exposure, or a “take-home pathway,” has been identified as a key source of pesticide residues (primarily to OPs) in children’s environment [17- 21]. Workers who are exposed on the job on a daily basis, whether as applicators or re-entry workers, are likely to carry home pesticides on their shoes, clothes, skin, and vehicles. Most workers are not provided with adequate washing or changing facilities to remove residues and put on clean clothes before leaving the worksite. If these workers do not take basic precautions (e.g., removing work shoes outside the dwelling, showering before picking up a child), they may transfer residues to the indoor environment or directly to other household members.

The primary routes by which pesticides enter the body are ingestion in food, soil, or water; inhalation, through the skin, and through the eyes [22]. OCs are absorbed through the lungs, stomach and skin, and excreted only slowly, sometimes over a period of years (e.g., DDT) [7]. Dietary ingestion is a significant source of exposure, especially for infants and children [23;24]. The residue monitoring program conducted by the FDA in 2003 found measurable levels of pesticides in baby foods, including DDT (6% of samples), captan + THPI (a possible carcinogen) (9%), carbaryl (carbamate) (6%), endosulfan (9%), dimethoate (4%), malathion (3%), and chlorpyrifos (all OPs) (2%) [25].

Post-natally, infants can be exposed to pesticides via breast feeding. The POPs, despite having mostly been banned, are still found in breast milk because they are stored in body fat [6;13]. Postpartum weight loss increases the likelihood of the release of OCs into the breast milk [13]. There is some evidence that the maternal body burden is actually transferred to her children via breast feeding, as the pesticide concentrations decrease with the more times a mother has breastfed [26]. Fortunately, the benefits of breast feeding still far outweigh the possibility of harm from pesticide transfer in breast milk, and should be encouraged for all mothers regardless of exposure history [26;27]

Effects of exposure during the reproductive cycle

Assessing the effects of pesticide exposure on human health in general, and reproductive health in particular, is an enormous challenge. Research in this area draws heavily on animal tests since direct human testing would be unethical, but it is tricky to translate between animal and human health
effects. While a variety of techniques are used to assess exposure, most can only estimate the amount actually absorbed by the body, e.g., surveys of occupational exposure, ambient air and environmental monitoring, skin surface measurements. Some can measure only fairly recent exposure, as is the case with urinary analysis for NPPs, while assessing exposure to fat-soluble pesticides such as OCs requires invasive tissue samples. Also, identifying populations that have not already been multiply-exposed to pesticides over the years is exceedingly difficult, rendering the possibility of finding a “clean” (non-exposed) control group for comparison close to nil [13;23]. Furthermore, the timing of exposure plays an important role in the characterization of the risks to reproduction from pesticides [28].

Exposure during periods of rapid development, especially in utero, is when pesticides cause the most damage in humans [13;24]. However, assessing exposure during this time is tricky. Amniotic fluid collected during amniocentesis, a process that carries its own risks, is the only medium available to characterize direct fetal exposures early in pregnancy (up to around 18 weeks of gestation) [29]. The placenta may be used to assess exposure during gestation, but it can obviously only be tested after birth [30]. But even with these limitations, enough data have been collected to indicate that exposure to pesticides at any point in the reproductive cycle can have serious and potentially devastating effects on both mother and child.

**Preconception exposure**

Even before the fetal periods of increased sensitivity, studies have found that preconception exposure of either the mother or father may have an effect on reproductive outcomes. These increased risks include spontaneous abortion, neural tube and other birth defects, and even deviation from the expected ratio of male-to-female births (fewer males born than normal). Maternal occupational exposure during a critical risk period, from three months before to one month after the last menstrual period, has been associated with higher risk for anencephaly, an extreme form of neural tube defect. Furthermore, children of men who applied pesticides even prior to that critical period were at higher risk as well [31]. Preconception exposure to common phenoxy acetic acid herbicides such as 2,4-D is associated with increased risk of early spontaneous abortion. Preconception exposure to glyphosate (RoundUp®) is associated with late spontaneous abortion [28]. One study found that mothers with occupational exposure to pesticides as long as 2 years prior to conception were at an increased risk of having a child with childhood kidney cancer [32].

Evidence has been accumulating since the 1970s that exposure to certain pesticides reduces sperm counts and reduces sperm quality [23], first noticed with a nematocide, dichlorobromopropane [33], and more recently with OPs [34]. A large number of international studies suggest that occupational exposure to pesticides negatively affects male fertility [13]. A study being conducted in Minnesota with a group of male pesticide applicators since 1989 has identified increased risk for birth anomalies and miscarriages, and a lower-than-expected maleto- female birth ratio, especially among applicators exposed to a combination of herbicides, insecticides and fungicides. Lifetime use of fungicides by male

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applicators was associated with lowered testosterone levels, which may contribute to the change in sex ratio at birth [35-38]. Males who have been exposed may experience a decline in fertility due to interference with thyroid function [33;38].

Within this same population of male applicators, the researchers found that the rates for overall birth defects, as well as for specific categories of defects, such as circulatory, urogenital, musculoskeletal, and dermatological, were significantly increased. Interestingly, rates varied by crop region and by season of conception, with the highest rates occurring in children conceived in the spring. They also varied by the infant’s sex, with males being at considerably more risk. Preconception exposure of male applicators to the fumigant phosphine and to the herbicide glyphosate, the active ingredient in RoundUp®, was also associated with elevated risk for later neurodevelopment problems. (Another study conducted with RoundUp® suggests that the commercial product, which contains additional chemicals, is in fact more toxic than glyphosate alone [39]). Overall, reproductive toxicity was primarily through the males, which implies that the damaging exposure took place preconception [36]. Similar results have been found in other farming areas, notably in several wheat-producing states where chlorophenoxy herbicides are used extensively (Minnesota, Montana, South Dakota and North Dakota) [40].

It is worthwhile noting that certain types of birth anomalies observed in the Minnesota study were more strongly associated with the application of the fumigant phosphine and the herbicide glyphosate (active ingredient in RoundUp®) [35;36], rather than products targeting insects or animals. Studies of perceptions of pesticide held by both farmworkers and growers have found that herbicides are not considered as dangerous as the other chemicals and that pesticides in general are believed to only affect the target organism [41-43]. This points up the importance of emphasizing in pesticide safety education settings that all agricultural chemicals are potentially harmful and exposure to them should be avoided to the maximum extent possible.

Prenatal (in utero) exposure
Extensive research worldwide has identified potential associations between in utero exposure and a number of adverse birth outcomes, such as miscarriage, low birth weight, and small head circumference. Exposure during gestation has also been associated with developmental and neurobehavioral problems in infants and young children, as well as with potentially increased risk for childhood cancers. Pesticide exposure experienced by the mother during pregnancy also results in exposure for her developing child, generally by means of the placenta [7;26;30;44-46]. Post-conception exposures have been associated with a number of negative birth outcomes, including late spontaneous abortions [28]. One study found that occupational exposure during the first and second trimesters was associated with increase in stillbirths due to all causes, while exposure in first two months of gestation contributed to an even higher risk of stillbirth due to congenital anomalies [47].

Exposure to DDE and chlorpyrifos in the third trimester was associated with lower birth weight, smaller head circumference and shorter birth length, especially when coupled with certain maternal genetic features (low PON1 activity, an enzyme needed to detoxify OPs) [15;48]. One study found that exposure to OCs, as measured in breast milk, was associated with increased risk for undescended testicles in male newborns [49]. Pesticides can interfere with endocrine function of both men and women. Dioxins,
organochlorines, and other POPs at even low environmental levels during pregnancy can disrupt maternal thyroid function, which is an important determinant of infant brain development [6;50].

While the relationship of birth anomalies to pesticide exposure is difficult to assess with certainty because of limited access to the population, reporting issues, and the overall small number of cases [23], several recent, very serious birth defects in infants born to farmworker women underscores the importance of making the effort both to continue the investigation, and to protect farmworkers from exposure as much as possible. Three women who worked for the same employer, Ag-Mart Farms, at the same time in Florida and North Carolina worked during a critical stage in their pregnancies in fields that had been treated with six pesticides that have been associated with birth defects in animal studies. All three gave birth within an 8-week span to children with major deformities. All the mothers had worked in treated fields, sometimes in violation of post-application re-entry intervals; each had few or no other risk factors for birth defects; and two had already given birth to normal children [51]. Because of the large number of variables that contribute to birth outcomes, it is difficult to definitively connect the three cases to pesticide exposure. However, an investigation by the North Carolina Department of Health & Human Services concluded that it is “plausible” that occupational pesticide exposure caused one of the children to be born with no arms or legs [52]. The fact that the exposures occurred at nearly the same time and in the same setting is cause for major concern. Farmworker women who may become pregnant should insist that all possible measures be taken to reduce the likelihood of their occupational exposure to teratogenic pesticides.

**Neonatal and long term effects**

Beyond the adverse effects of *in utero* exposure, neonates and infants are at a high risk for, and especially vulnerable to, pesticide exposure from numerous sources. Certain protective biological features do not develop in infants for several months (e.g., enzymes) increasing the risk of pesticide accumulation in the brain. Furthermore, the blood-brain barrier is not fully developed in infants, making it easier for pesticides to cross into the brain [13].

Much of the research on the accumulation and subsequent effects of pesticides in breast milk, especially for pesticides that have been banned in the US, e.g., DDT and other POPs, has been conducted in countries outside the US. Some of the effects reported include shorter length at birth, a variety of developmental problems, and increased risk for cancer. Combinations of pesticides, or pesticides with nicotine in smoking mothers, may magnify the toxic effects [7]. Studies in North Carolina and Mexico found that the presence of DDE (the metabolite of DDT) in breast milk was associated with a shorter period of breastfeeding, perhaps the result of interference with the mother’s milk production due to DDE’s estrogenic effects [53;54]. However, the importance of breast feeding in optimal infant development cannot be overemphasized, even for mothers with high exposure levels [27].

The potential long-term effects of fetal pesticide exposure, especially *in utero*, continues to be a subject of considerable research. Establishing definitive links between exposure and a health outcome that may develop years or decades later is a huge challenge. Current research is being conducted on connections possible between prenatal pesticide exposure and allergies and hay fever [55]; neurodegenerative
diseases such as Parkinson’s Disease and Alzheimer’s Disease [56]; neurodevelopment delays [27;57]; neurobehavioral problems [58], hyperglycemia [59]; and obesity, diabetes, and depression [60].

The potential carcinogenic effect of pesticide exposure is a major children’s health concern. While epidemiological investigations cannot directly establish causal links or determine mechanisms of action, a number of studies have nonetheless identified statistically significant associations between prenatal exposure and some childhood cancers [32;61-65]. It should also be noted that, because of small sample sizes common in studies of childhood cancers and the inherent limitations of ecological studies, this research may underestimate the true risk of childhood cancer [62;64]. Nonetheless, the totality of the evidence is sufficiently compelling to warrant the imposition of strong measures to protect children from exposure to pesticides from the moment of conception, if not before.

Clinical recommendations
Health care providers are in an ideal position to identify and assess a patient’s risk for exposure. The first step is to obtain an environmental history that covers residential and employment histories, types of work activities performed currently and in the relevant past, and possible sources of exposure to biological or chemical agents. For each exposure source identified, additional information needs to be collected, such as frequency, duration, and intensity. Women who are pregnant or planning a pregnancy, especially those currently performing farmwork, should be informed of the implications of exposure before, during and after pregnancy, and assisted in making decisions that are appropriate for their individual work and home situations [66]. In addition, providers should encourage mothers to avoid exposure that might contaminate breast milk without unduly alarming them, perhaps by associating it with the importance of not smoking or drinking alcohol during pregnancy and nursing [26]. Of course, breast feeding should continue to be strongly encouraged since all evidence indicates that the known benefits far outweigh the potential risks [27].

Education about pesticide safety is an important measure for preventing exposure. The Migrant Clinicians Network has recently developed a 14-page full-color Spanish language comic book and Wake Forest University School of Medicine has produced patient education handouts and posters in English and Spanish (see box). Women living in farmworker households should be offered additional education on ways they and the farmworkers with which they live can reduce take-home exposure:

- remove work clothes and shoes before entering the home
- shower or bath upon returning home and before touching other people
- store and launder dirty work clothes separately from other clothing [20]

As the evidence continues to accumulate of the overall hazards that pesticides pose to human health, it is important that health care providers consider the possibility and consequences of occupational, dietary and residential exposure to pesticides for their female patients. Occupational exposure is almost certainly the primary source of exposure for farmworkers and their families [66]. Awareness of the ways in which pesticide exposure occurs and the danger it poses are a crucial component of comprehensive preconception and prenatal care for farmworker women.
Patient Education Materials:

- Migrant Clinicians Network. Lo Que Bien Empieza ... Bien Acaba: Consejos para las mujeres para prevenir daños a la salud y a sus bebés causados por pesticidas. Austin, TX: Migrant Clinicians Network, 2007. available for download at: (http://www.migrantclinician.org/resources_search?qry=lo+que+bien+empieza&filter_scope=all).

For more information:

- Additional NEETF pesticide-related links and documents for health care providers available at http://www.neefusa.org/health/Resources/healthcare.htm
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APPENDIX: Acronyms

OP: organophosphate (category of pesticide)
OC: organochlorine (category of pesticide)
NPP: nonpersistent pesticide (includes OPs)
POP: persistent organic pollutant (includes OCs)
DDT: dichlorodiphenyl trichloroethane (an organochlorine)
Reference List


