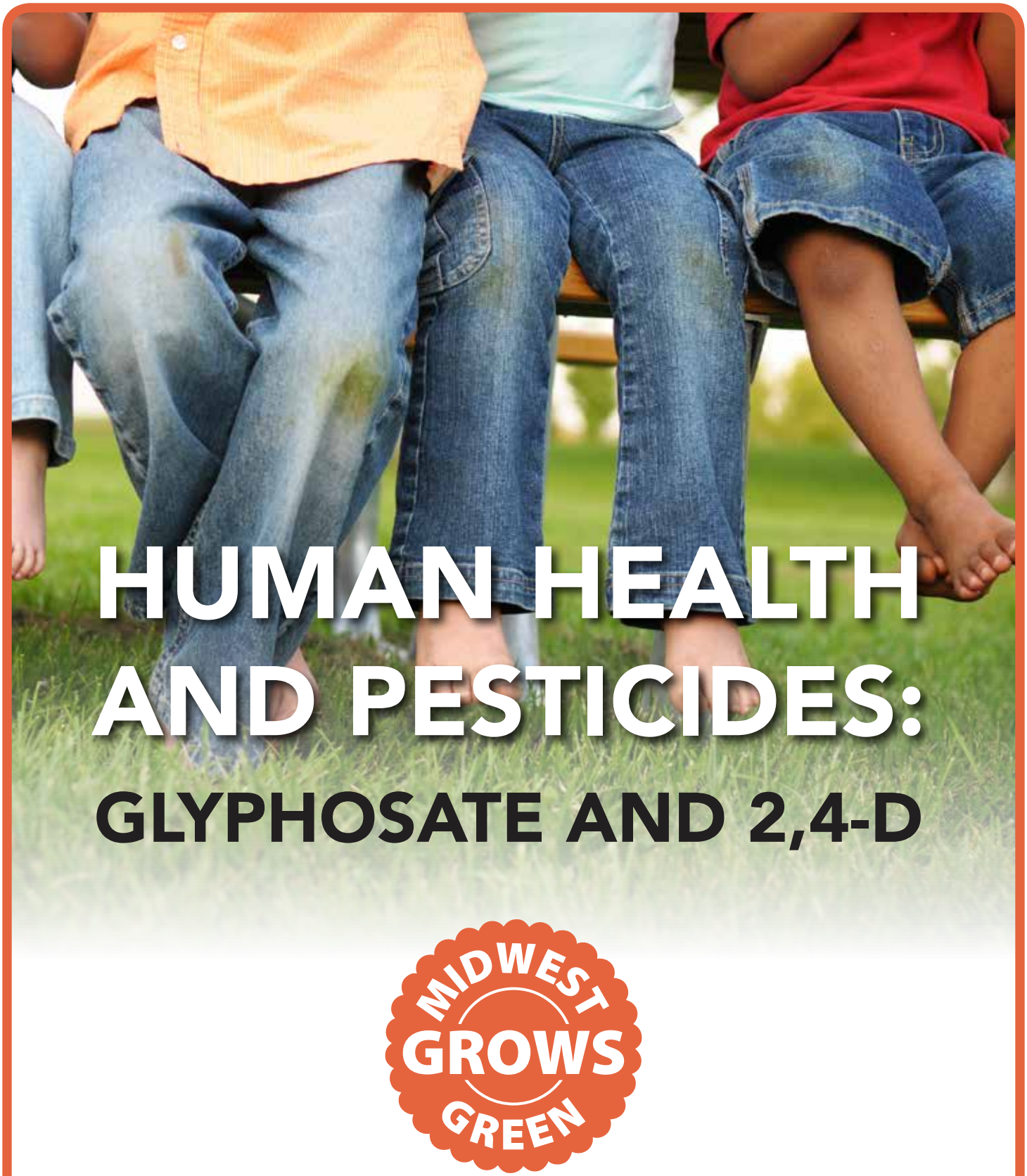

HUMAN HEALTH AND PESTICIDES:

GLYPHOSATE AND 2,4-D

Midwest Grows Green
2019

This document was adapted from the original authored by Midwest Pesticide Action Center.

Contents

Introduction

Pesticides are a wide array of chemicals that are used to prevent unwanted pests, including insects, plants, molds, and animals. The term pesticide is an umbrella term that includes insecticides, herbicides, fungicides, and rodenticides. Most pesticides contain chemicals that can be harmful to humans,[1] and exposure to these chemicals can cause illnesses (ranging from mild irritation to severe poisoning, seizures, and death[2]). Pesticides are a class of biocides, designed to interfere with the biological processes of living beings. An unintended consequence of their ability to kill pests, pesticides have been found to injure the human body as well, affecting critical bodily functions such as the nervous system and hormone regulation.[3]

This report will provide an overview of the health effects associated with the use of 2,4-D and glyphosate, two pesticides commonly found in Weed and Feed products. Weed and Feed products (combination herbicide-fertilizers) merit attention due to the high volume of their use in the U.S., Weed and Feed products are commonly used on gardens, lawns, parks, recreational fields, and playgrounds, and the potential human health risks of exposure. In the most recent year of U.S. Environmental Protection Agency (EPA) data, approximately 89 million pounds of Weed and Feed-type products were used in the non-agricultural sector, comprised of the home and garden, industrial, government, and commercial markets.[4] 2,4-D and glyphosate are toxins that have been linked to a variety of cancers, as well as reproductive, neurological, and respiratory health issues, and are especially harmful to children.2

Pesticide use and exposure can have serious short and long-term effects on human health, with increased risks for continued contact. In addition to exposure to Weed and Feed products, humans face pesticide exposure indoors in homes, schools, places of work, and from agriculture, as well as from pesticide spray drift, the airborne movement of pesticide applications to contaminate other areas. Those at the highest risk are workers who are exposed to pesticides on a regular basis, as well as children, pregnant women, those living in agricultural areas, the elderly, asthmatics, and those with chronic illnesses.[5] Studies have shown, however, that pesticide exposure is a serious health risk not only for those with daily occupational contact – typically farmworkers and professional landscapers – but also for those who encounter pesticides at chronic low levels through residential or municipal exposure. Associated chronic health risks include cancer, and neurodegenerative, neurobehavioral, and reproductive effects. A report led by the National Cancer Institute (NCI), a branch of the National Institutes of Health, states that "evidence clearly suggests that at current exposures pesticides adversely affect human health."[6]

Much of the research exploring the health effects of pesticides has been conducted in agricultural regions, due to those regions having both higher rates of pesticide application and more reliable data measuring pesticide use. These studies are still helpful in understanding the effects of pesticide use on the general public health. Though applied in a different manner and at different concentrations, the same active ingredients used in most home and garden pest control products can be found in

large-scale agricultural operations. Furthermore, it is not certain that those living in agricultural areas face the highest level of ambient pesticide exposure – inexpert pesticide users tend to face far higher levels of exposure than intended by safety regulations.[7] Misuse and overuse of pesticides in domestic situations is common. A study by the Australian Environment Protection Authority found private residents applying herbicides at five times the recommended rate.[7] This study also found that homeowners tend to apply pesticides at higher than recommended rates, using more pesticides per hectare than farmers, likely due to a lack of expertise and training. Pesticides are easily tracked indoors via adherence to shoes and clothing, which can result in increased and continued exposure in the home.[8] Urban environments also pose unique health hazards, since pesticides take far longer to biodegrade indoors and exposure is concentrated.[9]

I. 2,4-Dichlorophenoxyacetic acid (2,4-D)

2,4-D is one of the most commonly used active ingredients in herbicides, and is the most used active ingredient in the entire U.S. non-agricultural sector; ranking first in the home and garden market, as well as the industrial, commercial, and government sectors.4 2,4-D is a synthetic plant hormone which kills plant life by changing the way plant cells grow, causing the plant cells to divide and grow uncontrollably until tissue damage and plant death occurs.[10] It was first developed by scientists for its potential in chemical warfare, and was one of the active ingredients in Agent Orange used in the Vietnam War. The EPA estimates annual domestic usage of 2,4-D is approximately 46 million pounds per year, used for weed control.[11] Annually, 30 million pounds are used in agriculture and 16 million pounds are used in non-agricultural settings. Approximately 8,740,000 pounds (19% of total annual 2,4-D use in the U.S.) of 2,4-D are applied by homeowners and landscapers every year.[11]

Acute & Chronic Exposure

According to the EPA chemical toxicity report on 2,4-D, acute exposure to high concentrations of this chemical can cause stupor, coma, coughing, burning sensations in lungs, loss of muscular coordination, nausea, vomiting, and dizziness.[12] Acute exposure to 2,4-D can result in skin and eye irritation. Fatal outcomes from 2,4-D exposure have resulted from renal failure, electrolyte imbalance, and multiple organ failures.[13] 2,4-D is highly toxic and has been linked to increased incidence of cancer and damage to reproductive systems. The human health effects of chronic 2,4-D exposure reported for adults include blood, liver, and kidney toxicity; a reduction in hemoglobin and red blood cell numbers, decreased liver enzyme activity, and increased kidney weight.[12]

II. Glyphosate

Glyphosate is the most used active ingredient in pesticides used within the U.S. agricultural sector, and has been for the most recent six years of EPA data. Over 180 million pounds were applied to agricultural lands in the most recent year of recorded data.[4] Glyphosate is the second-most used active ingredient in the U.S. non-agricultural sector – 13-15 million

pounds are used annually by the industrial and government sectors, and 5-8 million pounds are used in the home and garden market alone. Glyphosate is more commonly known by its most popular brand name, Roundup, though it is contained in many other products. Glyphosate is a popular active ingredient in Weed and Feed products, present in over 750 products in the U.S. alone.[14] The EPA has stated that, based on its current level of use in the U.S., both occupational and residential exposure to glyphosate can be expected for the general population.[15]

Glyphosate is a broad spectrum herbicide, which kills most types of plants by preventing plant cells from producing proteins critical for growth and stripping micronutrients necessary for the plant immune system function.

Acute & Chronic Exposure

Glyphosate has been ranked as a chemical of relatively low toxicity by the EPA since its primary mechanism of action is upon plant cells; its high toxicity is often due to the inactive ingredients which accompany it in a product.[16] Pesticide products are a combination of an active ingredient, the primary chemical responsible for killing or repelling pests, and an undisclosed amount of other "inert" ingredients. Current regulations require neither the inert ingredients nor the complete pesticide product to be tested for their effects on human health. The inert ingredients are not chemically or toxicologically inert; rather, they are protected as "trade secrets," and remain unnamed to the public. In Roundup, one such accompanying toxin has been identified as the surfactant TN-20, which greatly enhances the cytotoxic (destructive to cells) effect of glyphosate.[17] There is debate over whether glyphosate itself is acutely toxic to humans; while agricultural companies point to the EPA finding that glyphosate is low-toxicity, both glyphosate in isolation and Roundup have been clinically proven to trigger placental and embryonic cell death in humans,[18] and have been connected to many other health hazards. According to the EPA, acute exposure to glyphosate can cause eye irritation, skin irritation, congestion of the lungs, and increased breathing rate.[19] Chronic exposure to glyphosate is known to cause kidney damage, neurological impairment, and negative reproductive health effects. In the most recent EPA re-registration of glyphosate, the agency did not include information regarding acute inhalation toxicity or a study of occupational and residential exposure to glyphosate, though both are usually required for chemical re-registration.[20]

III. Childhood-Specific Risks

Pesticides are often used in school and childcare facilities, as well as on parks and playing fields, though they pose a heightened health risk to children. Because they eat and drink more than adults in proportion to their body weight, children receive higher doses of toxic chemicals when exposed to pesticides in their surrounding environment, or through food and water. As another result of their body size, children are closer to the floor and ground, and this lower breathing zone increases their exposure if pesticides are present. Children have a more rapid respiratory rate, taking in a greater volume of air per body weight

compared to adults, leaving them more vulnerable to the respiratory illnesses associated with pesticide exposure.[21] Prenatal and early childhood exposure is especially hazardous, as internal organs are still developing, are less able to detoxify chemicals, and are therefore more vulnerable toxic exposures.[22] Childhood activity patterns, including a high level of hand-to-mouth activity, likely contribute to an increased oral ingestion of the pesticides in their environment.[23]

Children exposed to pesticides indoors face heightened health risks. According to the U.S. Centers for Disease Control and Prevention (CDC), humans spend approximately 90% of their time indoors, and the air indoors can often be more polluted than outdoor air, even in industrial city centers. The CDC asserts that for many people, especially children, risks to health from indoor air pollution are greater than from outdoor air pollution.[24] Children exposed to pesticides indoors suffer from higher concentrations of the toxins to which they are especially sensitive. Pesticide application is unlikely to remain isolated to the area to which it is applied – in a two-year long study conducted on Midwestern homes, levels of 2,4-D inside the home were found to be ten times higher after an application of 2,4-D to the lawn.[25] The lack of exposure to external elements like sunlight, which promote chemical degradation, leads to pesticides persisting longer indoors. As a result, indoor exposure for young children in the home by non-dietary means of ingestion – from contact with floors, table tops, and contaminated dust in the air – was ten times higher after a lawn application. Children whose parents used garden insecticides were found to have significantly higher levels of pesticide metabolites in their urine, for months after the last application.[26] Researchers concluded that garden pesticides and pesticide ingestion via diet were the sources of elevated pesticide levels in children, and recommended that pesticide use be avoided in areas where children play.

In a 2012 report, the American Academy of Pediatrics (AAP) recognized that the association between pesticide exposure and childhood "cancer, abnormal neurodevelopment, asthma, perturbation of gestational growth, and endocrine-mimicking effects" is greatly concerning.[27] Pesticides that affect the endocrine system like glyphosate are particularly dangerous for children, as they disrupt the glands and hormones that facilitate regular growth and development.[28] The AAP noted specifically that "the most comprehensive reviews of the existing literature implicate an association of pesticides with leukemia and brain tumors." The AAP as a whole, comprised of 60,000 primary care pediatricians and pediatric specialists, issued a recommendation in 2012 that a serious effort be made to reduce childhood contact with pesticide.[29] As it stands, almost all children have contact with pesticides – in a study of pre-school aged children in Seattle, pesticide metabolites (detectible pesticide residues found in urine samples) were found in 99% of children tested, with at least two different pesticides present in approximately 75% of children tested.[26]

Childhood-Specific Risks: Neurodevelopmental Impairments

The brain and nervous system of a fetus, infant, or child, are particularly susceptible to the effects of neurotoxic substances during vulnerable periods of development. During

the period of neurological development – in utero through adolescent years – exposure to neurotoxins can result in developmental neurotoxicity. This can manifest as changes in functionality of the nervous system, including changes in cognition and behavior.[30] Many pesticides are neurotoxins – the entire class of organophosphate pesticides, which includes most insecticides, is neurotoxic. Even a very low level of exposure to neurotoxic pesticides, during critical periods of fetal development, has been shown to fundamentally alter brain architecture.[31] Children with little or no pesticide exposure have a lower probability of neurologic health risks.[32]

A 2010 study by the AAP found that children exposed to organophosphate pesticides are more likely to meet the diagnostic criteria for ADHD.[33] American Academy of Pediatrics researchers examined over 1,100 children aged 8 to 15 as a representative sample of children across the U.S., and found that children with higher than median levels of pesticide in their urine were twice as likely to have ADHD. This study concluded that pesticide exposure, "at levels common among U.S. schoolchildren," may contribute to the prevalence of ADHD. In 2008 the International Journal of Occupational Medicine and Environmental Health published a study which found an association between childhood pesticide exposure and neurodevelopmental and behavioral impairments.[34] This study found that children exposed to organophosphate pesticides, both prenatally and during childhood, may have difficulties performing tasks that involve short-term memory, and may show increased reaction time, impaired mental development or pervasive developmental problems. In newborns, the effects of pesticide exposure were found to manifest as an increased number of abnormal reflexes and increased reaction time; in adolescents, as mental and emotional problems.

Childhood-Specific Risks: Cancer

Childhood cancer risk is significantly increased by pesticide exposure at home and at school facilities. A 2005 publication from the CDC National Institute for Occupational Safety and Health found that pesticide exposure at schools produces acute illnesses among students, and recommended that schools reduce child pesticide exposure and pesticide-related illnesses by creating pesticide spray buffer zones around schools.[35] A 2009 study led by Georgetown University researchers found exposure to household pesticides to be associated with a two-fold increase in risk for acute lymphoblastic leukemia (ALL), the most common childhood cancer. Parents of children with ALL were twice as likely to be using pesticides in the home.[36] Children newly diagnosed with ALL were found to have elevated levels of pesticide toxins in their urine. In a systematic review of all studies concerning residential pesticide exposure and childhood leukemia from 1950-2009, prenatal and childhood exposures to residential pesticides, insecticides, and herbicides were positively associated with childhood leukemia.[37] For children under ten, garden pesticide use has been associated with an almost seven-fold increase in risk of leukemia.[38]

Childhood-Specific Risks: Asthma

Asthma is the most common chronic disease for children, whose lungs and airways are still developing and are thus more vulnerable to respiratory illnesses.[39] From 1980 to 1996,

childhood asthma prevalence in the U.S. doubled, and rates continue to rise.[40] As of 2005, nine percent of U.S. children have asthma. Many studies correlate pesticide exposure with the development of childhood asthma, and may prove insightful in understanding why asthma has become so widespread. Typically, the earlier in life that pesticide exposure occurs, the more likely a child is of becoming asthmatic. In 2004, researchers from the University of Southern California's Keck School of Medicine found that children exposed to herbicides in their first year of life were four and a half times more likely to be diagnosed with asthma by the age of five.[41] Children exposed to any pesticides in the first year of life were approximately two and a half times more likely to be diagnosed with asthma by the age of five. Researchers emphasized that infancy and early childhood is time when children are most vulnerable to developing asthma.

IV. Reproductive Health/Pregnancy

Reproductive health encompasses the diseases and disorders that affect the reproductive system during all stages of life. Such disorders include reduced fertility, birth defects, developmental disorders, preterm birth, and impotence. Pesticide exposure has been linked to damage to reproductive health and the endocrine system. The herbicide atrazine, for example, has been linked to abnormal sperm, menstrual disorders, and low birth weight.[42] According to the National Institutes of Health, exposure to environmental pollutants and endocrine disruptors may pose the greatest threat to reproductive health.[43] The weight of scientific evidence shows pesticide-related damage to human reproductive health, with particularly high risks for pregnant women and fetuses.

Reproductive Health: Endocrine Disruption

The endocrine system is the collection of glands in the human body responsible for regulating hormone levels. Many pesticides are endocrine disruptors, affecting critical processes of hormone production that the body needs in order to maintain homeostasis, the state of stable internal bodily functions.[44] The EPA has found that disruption of the endocrine system can result in "reproductive disorders, birth defects, immune suppression, and other harmful effects."[45]

Glyphosate and 2,4-D Endocrine Disruption

Both 2,4-D and glyphosate have been linked to disruption of the endocrine system. The EPA has stated that based on current data regarding effects to the thyroid and gonads, there is concern regarding the potential of 2,4-D to disrupt the human endocrine system.[46] In 2009, the glyphosate herbicide Roundup was confirmed as both genotoxic (damaging to cellular DNA) and an endocrine disruptor.[47] At doses lower than what is commonly applied in agriculture, Roundup caused endocrine disruption and cell death in human liver cells, within 24 hours of introduction. Scientists observed endocrine system disruption which had the potential to alter metabolism, development, and reproduction, as well as cause hormone-dependent diseases like prostate and breast cancer. An additional university study found Roundup disruptive to steroidogenesis (the production of steroids) in testicular cells

which produce testosterone, which plays a "crucial role in male reproductive function."[48] Exposure to Roundup disrupted StAR protein expression and reduced sex hormone production in human testicular cells by 94 percent. The StAR protein, susceptible to environmental pollutants, is responsible for the process by which all steroid hormones are synthesized.

A 2005 study observed Roundup's endocrine disrupting and toxic effects in the disruption of human estrogen synthesis and messenger DNA.[49] Exposure to Roundup, at sub-agricultural doses, was found toxic to human placental cells within 18 hours of exposure. This study is an excellent example of the role inert ingredients play in pesticide toxicity, as the commercial product Roundup (which is a combination of glyphosate and unspecified inert ingredients) was found to be more toxic to placental cells than glyphosate alone. In a follow-up study conducted in 2007, it was determined that although Roundup is more toxic to embryonic and placental cells than glyphosate alone, glyphosate does act directly as a partial inactivator of aromatase, the estrogen-producing enzyme. It was concluded that Roundup exposure may affect human reproduction and fetal development, and that "chemical mixtures in formulations appear to be underestimated regarding their toxic or hormonal impact."[50]

Reproductive Health: Importance of Prenatal Development

A mother's environmental and dietary pesticide exposures may translate directly to increased toxic exposure for her fetus or newborn, in a process known as placental transfer. Certain pesticide metabolites easily cross the placenta to reach the fetus. In 2011, researchers found that when pregnant women consumed potatoes, corn, and soybeans that had been genetically modified to be pesticide-tolerant, metabolites of one of the herbicides showed up in the cord blood of 100 percent of their babies.[51] Pregnant women exposed to pesticides have been linked to a variety of adverse birth outcomes, including miscarriage, fetal death, birth malformations, lowered birth weight, and embryonic cell death.

While the long-term health consequences of maternal pesticide exposure during pregnancy are not fully known, research suggests that prenatal (in utero) and neonatal (in infancy) exposure can manifest itself in a myriad of grave health consequences. Low-dose exposure to neurotoxic pesticides in infancy may create modified responses to environmental contaminants as adults. When exposed to toxic substances later in life, it can result in hastened age-related degenerative changes, accelerating dysfunctional processes such as impairment of learning and memory.[52]

In 2012, a group of children's health experts published a study that measured the effects of exposure to pesticides at low levels – typical of ingestion through food or residential exposure – on pregnant women. The study found that the amount of pesticide exposure of a pregnant woman was inversely proportional to length of gestational period and her baby's birth weight. The pregnant women with the highest exposure to pesticides delivered their babies on average half a week earlier, with a starting birth weight on average one third of a pound lighter.[53] A team of scientists from Columbia University's School of Public Health

have also found that mother-newborn pairs with higher levels of insecticide detected in their umbilical cord plasma at delivery had a birth weight on average 0.4 pounds lighter.[54] These researchers found that the level of pesticide in umbilical cord plasma was inversely associated with birth length, with birth length decreasing by 0.24 cm for additional every log unit of insecticide present in the plasma. This study concluded that insecticide exposure impaired fetal growth, and emphasized the importance of phasing out residential use of insecticide. Lowered birth weights are known to be associated with increased rates of heart disease, stroke, hypertension, and diabetes.[55] Scientists believe these negative health associations are the result of "fetal programming," whereby deficiency or damage at critical stages of development has permanent effects on the body's physiology and metabolism. Exposure to toxins such as pesticides may be one type of damage that produces fetal programming.

2,4-D and Prenatal Development

In 2005, California's Office of Environmental Health Hazard Assessment formally identified 2,4-D and its associated compounds to be reproductive toxicants, and lists 2,4-D as a substance "known to the State to cause reproductive toxicity."[56] Maternal exposure to 2,4-D has been linked to birth malformations in a major EPA study. In an examination of the wheat-producing regions of the Midwest, this study found that infants conceived from April to June – the time of peak herbicide application – had an increased chance of circulatory and respiratory malformations.[57] In regions with higher rates of herbicide application, infant musculoskeletal anomalies increased, and male infant death resulting from birth defects significantly increased. 2,4-D, at both agricultural and residential levels of exposure, has been shown to produce developmental injury to embryos, by increasing the incidence of embryonic cell death and reducing early gestation cell development in the period corresponding to the first five to seven days of conception.[58] Even at concentrations assumed to be without adverse health consequences by regulatory agencies, reflecting typical human exposure in the Midwest, exposure was damaging to reproduction and early fetal development.

Glyphosate and Prenatal Development

Studies point to the hazard glyphosate poses to pregnant women and their fetal development. A 2001 study by the Canadian Public Health department examined the effect of increased pesticide exposure on embryonic and fetal death by tracking miscarriage in women who reside on farms where pesticides are used. The study found that pre-conception maternal exposure to glyphosate, along with other pesticides, increased risk of miscarriage.[59] The same study found an elevated risk of early-stage miscarriage (less than 12 weeks after conception) associated with exposure to a family of herbicides that include 2,4-D. An elevated risk of late-stage miscarriage (12-19 weeks after conception), or fetal death, was associated with preconception exposure to glyphosate. The science suggests that exposure to multiple pesticides leads to heightened risk, as the combination of certain chemicals may be far more toxic than either in isolation. The human body now encounters this exposure even before birth – a 2005 study found an average of 200 industrial chemicals and pollutants

in the umbilical cord blood of newborns in the U.S, including waste products, flame retardants, and pesticides.[60] The general population faces exposure to pesticides and other toxins from both indoor and outdoor environments throughout a lifetime, many of which bio-accumulate in the body long after exposure.[61] Regarding miscarriage, exposure to more than one type of pesticide among women over 35 led to a drastically increased risk. These varied toxic inputs are health hazards, as many chemicals have the potential to amplify the negative health effects of other chemicals. Specifically, those exposed to carbaryl and 2,4-D together had 27 times the risk of miscarriage compared to similar women exposed only to carbaryl.[62]

Reproductive Health: Autism

Autism, which the CDC reveals has increased 289.5% between 1997 and 2008,[63] has been extensively linked to both prenatal and neonatal pesticide exposure. A team of public health experts recently identified a list of ten contaminants most likely to be linked to the development of autism – organophosphate pesticides, organochlorine pesticides, and endocrine disruptors were all included on the list.[64] Maternal residence during pregnancy near pesticide applications has been linked to the development of autism spectrum disorders in children. Mothers whose proximity to agricultural areas exposed them to pesticide drift during early gestation (the first one to eight weeks of pregnancy) were found to be six times more likely to have children with Autism Spectrum Disorders.[65] Risk for autism spectrum disorders in children increased with the number of pounds of pesticide applied, and decreased with maternal distance from crop sites.

Reproductive Health: Neurodevelopmental Impairments from Prenatal Exposure

Scientific studies suggest a troubling connection between prenatal pesticide exposure and neurodevelopmental damage. In a 2006 study published by the AAP, children exposed prenatally to higher levels of an insecticide were found to be significantly more likely to experience delays in psychomotor (wherein children learn the relationship between cognitive function and physical movement) and mental development, attention problems, attention deficit/hyperactivity disorders, and pervasive developmental disorders by the age of three.[66] Children exposed to higher levels of the insecticide studied were five times more likely to experience delays on the Psychomotor Development Index. This study focused on children living in inner-city areas, where insecticides are more common than herbicides, and is a helpful illustration of the fact that although the population faces different types of pesticide exposure across the U.S., the human health impact is similarly destructive.

Glyphosate and Neurodevelopmental Impairments

Glyphosate and Roundup have been linked to negative neurodevelopmental health effects, particularly for prenatal exposure. In a detailed examination of the effects of pesticide exposure on reproductive outcomes in an agricultural region of Minnesota, scientists found that conceptions in spring, at the height of pesticide application, resulted in significantly more children with birth defects than found in any other season (7.6% vs. 3.7%). Forty-

two percent of children from families with recurrent birth defects were conceived in spring, a significantly higher rate than that for any other season.[67] Specifically, adverse neurobehavioral developmental effects were almost four times as likely for children with parental glyphosate exposure. Roundup was found to be "uniquely associated with specific adverse birth or developmental outcomes" – 43% of children with ADD/ADHD had parents who reported using Roundup.

Reproductive Health: Male Fertility

Male fertility has consistently been shown to suffer when confronted with pesticide exposure. A 2013 systematic review of 17 studies on the effect of pesticides on sperm found that there are significant associations between exposure to pesticide and semen quality indicators.[68] The most common finding, among all pesticide classes investigated, was a decrease in sperm concentration. Decreased sperm motility and an overall decrease in sperm health was also associated with exposure to all pesticides investigated.

2,4-D and Male Fertility

The EPA has listed a variety of negative effects that 2,4-D has on male sex organs, including atrophy of the testes, degeneration of sperm-producing tissues, and decreased number of sperm in the testes.[69] Though it is well known that exposure to pesticides at occupational levels can adversely affect semen quality, chronic low-level environmental exposure to 2,4-D has also been linked decreased male fertility.[70] Men from agrarian areas in the U.S., merely by living in regions with higher ambient levels of pesticides, were found to have higher levels of 2,4-D present in their body than men from urban centers, which corresponded with poor semen quality and lower sperm concentration.

V. Epigenetics: Inheritance of Pesticide Damage

The scientific study of the effects of pesticides on epigenetics is an important emerging field that helps us understand the long-term, multi-generational consequences of pesticide exposure. Epigenetics is the process of changing gene expression, while maintaining the same DNA sequence, which occurs throughout everyone's lifetime. This separate cellular process regulates if and when certain genes are expressed, and is driven by the interaction between genes and the environment. Epigenetic changes can include inactivation of normally active genes, or the expression of genes that are typically silent – such changes in gene behavior can be responsible for the development of a wide variety of health issues, from fetal growth restriction to diabetes and cancer. "Persistent Organic Pollutants," or POPs, are long-lasting chemicals like DDT that persist for decades in the environment.[71] For their longevity, POPs are considered a potential source of environmental modification of epigenetic responses in humans.

It is theorized that pesticide exposure is one environmental influence that can influence transgenerational epigenetics – when environmental cues result in heritable alterations to genetic expression. In 2012, biologists researching inheritance of epigenetic responses

found that pesticide exposure in mice altered the way certain genes were activated, and that change was passed down along generations, resulting in mental disorders and obesity.[72] Exposure to a pesticide as far as three generations back caused adverse health effects. Studies demonstrate the same effect on human health. Parental exposure to pesticide has already been linked to childhood cancer risk. Being the child of a licensed pesticide applicator has been shown to increase risk of all childhood cancers. The risk of all lymphomas increased two-fold and the risk of Hodgkin's lymphoma specifically increased as well for children of pesticide applicators.[73] Parental failure to use chemically resistant gloves in the course of pesticide application was associated with a further increased risk of childhood cancer. Understanding epigenetics is especially important when considering the effects of pesticides on reproductive health, as the most vital time for genetic development is in the womb.

2,4-D and Genetics

2,4-D exposure has been associated with genetic damage. In 2004, medical researchers discovered that a 2,4-D herbicide had genotoxic (damaging to cellular DNA) effects, causing chromosome breakage in human blood cells.[74]In 2005, researchers found that human exposure to 2,4-D, at "environmentally realistic levels," can elicit gene expression changes in genes that affect stress response, cell cycle control, immunology and DNA repair.[75] University of Minnesota researchers studying U.S. pesticide applicators found that the men with the highest level of 2,4-D metabolites in their urine had elevated hormone levels and altered genomic stability. Frequency of chromosome aberrations correlated to the volume of pesticide to which they were exposed.[76] A study produced by Egyptian geneticists found that 2,4-D caused chromosome breakage in bone marrow cells of mice.[77] Though is not known how damaging the cumulative effect of such genetic alterations may be, genetic damage has the potential to cause irreversible adverse effects, which is why many health experts advise that all efforts be made to limit pesticide exposure.

Glyphosate and Genetics

Recent science has associated glyphosate, isolated from any accompanying inert ingredients, with dangerous consequences for human genetics. A 2013 study found that ingesting glyphosate residues through diet is biologically disruptive, damaging gut bacteria necessary for detoxification, and inducing disease.[78] Researchers at MIT found that glyphosate's damage to the immune system and the gastrointestinal tract facilitates the development of most diseases associated with the Western diet, including obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease. Researchers characterized glyphosate's negative impact as "insidious," causing slow and steady damage to cellular systems by blocking enzymes the body relies on for detoxification. The study concluded that glyphosate is the "textbook example" of a disruption of homeostasis by an environmental toxin.

VI. Health Effects on the General Population

Studies have shown that the negative health effects of pesticide exposure reach not only higher-risk groups such as children and pregnant women, but the general population as well, particularly in the form of cancers and neurological effects. Significantly, many studies have founds links to these serious diseases in otherwise healthy groups of people who face elevated pesticide exposure by means of occupational contact, and even those who encounter only ambient (non-occupational) levels of pesticide.

General: Neurological and Parkinson's

There is extensive scientific literature showing strong associations between pesticide exposure and serious neurological damage, particularly Parkinson's disease. Individuals exposed to pesticides have been found to be 70% more likely to contract Parkinson's than those not exposed.[79] According to an NCI review of scientific literature concerning the health effects of chronic pesticide exposure, there is very strong support for the link between pesticide exposure and Parkinson's disease. [80]

Parkinson's disease is a degenerative central nervous system disorder, which progresses from motor function decline to cognitive decline and dementia, with a high associated mortality risk. In a 2013 meta-analysis of over 100 studies, researchers found that exposure to pesticides and solvents is associated with an elevated risk of Parkinson's disease.[81] Rural living in general, for its increased environmental exposure to pesticides, also increases risk of Parkinson's. In another meta-analysis, public health experts concluded that in a majority of peer-reviewed studies, environmental factors such as rural living and farming elevate risk of Parkinson's. Pesticide exposure elevated risk an average of two-fold across all studies examined.[82] Still another meta-analysis found that 17 out of 19 studies examined, exposure to pesticide was linked to an increased risk of Parkinson's, with risk increasing with increased duration of exposure.[83]

A 2011 study led by researchers at the University of California Los Angeles's School of Public Health found that ambient residential (home or garden) and workplace pesticide exposure can greatly increase risk of Parkinson's.[84] In this study, those with ambient workplace exposure to certain pesticides had a three-times higher risk of Parkinson's. Younger onset Parkinson's was associated with those who faced both ambient workplace exposure and ambient residential exposure. Those exposed to certain combinations of pesticides experienced the greatest increase in Parkinson's risk, which led the authors of this study to suggest that pesticides affecting different mechanisms that contribute to neuron death "may act together to increase the risk of Parkinson's disease considerably."

With regards to neurobehavioral performance and neurological disease, NCI researchers found that studies indicate chronic pesticide exposure is associated with deficits in cognitive function and psychomotor function, as well as Alzheimer's disease and dementia.[85]

In another study, chronic exposure to pesticides has been associated with impaired performance on neuropsychological tests; scores for memory, attention, verbal fluency and abstract thinking were all lowered with increased pesticide exposure. Low performance on neuropsychological tests was found to be more than twice as likely for those who had chronic pesticide exposure. Information selection and information processing were the most affected.[86] The authors concluded that these results may be indicative of long-term progressive neurological degenerative changes brought on by pesticide exposure.

General: Cancer

The weight of scientific evidence suggests that occupational exposure to pesticides is carcinogenic. A carcinogen is a substance or exposure capable of causing cancer in living tissue.[87] The World Health Organization's International Agency for Research on Cancer, responsible for the most widely used carcinogenic classification system, has been one of many expert agencies to have cautioned about the carcinogenic effects of pesticide. The IARC has designated the spraying and application of insecticides a "probable" human carcinogen, its second-highest classification cancer-causing potential.[88] Using its own evaluator model, the EPA has found dozens of pesticides "likely" to be carcinogenic to humans.[89] 2,4-D still has not yet undergone a complete evaluation by the EPA for its carcinogenic potential,[90] though the EPA acknowledges that 2,4-D has demonstrated neurotoxic and developmentally toxic effects.[91] The EPA has set a deadline of 2015 to review the available science on glyphosate and determine whether use of the chemical should be controlled or restricted.[92]

According to a review by the NCI, existing scientific literature supports an association between pesticides and the following types of cancer: non-Hodgkin lymphoma, leukemia (particularly childhood leukemia), multiple myeloma (a malignancy of the plasma cells), soft-tissue sarcoma, prostate cancer, pancreatic cancer, lung cancer, and ovarian cancer.[93] In a 2007 review of 10 years of studies on the relationship between pesticides and various types of cancer, researchers found that pesticide exposure was positively associated with non-Hodgkin lymphoma and leukemia in most studies.[94] The "most consistent" associations for pesticide exposure were brain and prostate cancer, and many studies also showed positive associations between exposure and the development of solid tumors. Though most cancer studies have been conducted on rural populations, pesticide use in other environments carries the same risk. In a sixty year-long study of the mortality of pesticide applicators in urban Rome, university researchers found a significantly increased risk for cancer of the liver, gallbladder, and nervous system.[95]

2,4-D and Cancer

Other health effects of 2,4-D are more universally understood, such as the link to increased cancer risk. In 2007, scientists studying the Cancer Registry of Central California found that working in fields treated with 2,4-D is associated with increased rates of gastric cancer.[96] Agricultural workers who were routinely exposed to 2,4-D were found to be almost twice as likely to develop gastric cancer. A study conducted by the EPA's National

Health and Environmental Effects Research Laboratory found increased cancer mortality in the Midwest wheat-growing region, where chlorophenoxy herbicides, of which 2,4-D is the most prominent, usage is high.[97] 2,4-D is heavily used in wheat production, and high wheat acreage regions are associated with statistically significantly higher rates of cancer and cancer deaths. EPA scientists, assuming widespread ambient exposure of 2,4-D, have indicted an association between 2,4-D exposure and general cancer mortality.

Non-Hodgkin Lymphoma

Exposure to herbicides generally leads to a significantly increased risk of non-Hodgkin lymphoma.[98] Two Swedish case-control studies showed an increased risk of non-Hodgkin lymphoma from exposure to a wide range of pesticides. Herbicides, insecticides, and fungicides were all found to be risk factors for lymphoma.[99] Glyphosate exposure in particular had a strong association, carrying a three-times higher risk for non-Hodgkin lymphoma. The highest incidence of non-Hodgkin lymphoma occurred within 10 years of exposure to the toxins. Like the U.S., Canada has seen a decades-long rise in non-Hodgkin lymphoma. The Canadian Cancer Registries Epidemiology Research Group investigated this matter in 2000, and found an increased risk of non-Hodgkin lymphoma for men exposed to pesticides, with increased risk corresponding with increased duration of exposure to herbicides. Excess risk of non-Hodgkin lymphoma among females was associated with exposure to pesticides.[100] Men and women who were exposed to herbicides for 15 years or longer were 50 percent more likely to develop non-Hodgkin lymphoma. The authors concluded that exposure to pesticides and other toxins plays an important role in the rise of non-Hodgkin lymphoma, and that residential pesticide and herbicide use is of concern.

Glyphosate and Non-Hodgkin Lymphoma

Glyphosate has been extensively linked to non-Hodgkin's lymphoma. A 2008 study published in the International Journal of Cancer found that in a broad population sample of males and females aged 18 to 74, those who had been exposed to glyphosate over the course of their lifetime were over twice as likely to have non-Hodgkin's lymphoma.[101] Glyphosate was found specifically to be associated with a more than two-fold increase in risk of in T-cell lymphomas, and an over three-fold increase in risk of lymphocytic lymphoma. The risk of non-Hodgkin's lymphoma for men exposed to glyphosate for just two or more days per year was twice as high as the risk for men who were unexposed or exposed for less than two days per year.[102] Still another study labeled glyphosate as "potentially carcinogenic" and found the chemical to be significantly associated with an increased risk of non-Hodgkin's lymphoma.[103]

Prostate Cancer

Researchers have concluded that certain pesticides have strong associations with prostate carcinogenesis.[104] In 2003, a major study led by an NCI researcher examined the relationship between 45 common pesticides and incidence of prostate cancer, studying over 55,000 male pesticide applicators in the U.S. with no prior history of prostate cancer. [105] Compared to prostate cancer rates of the general population, the men who regularly handled pesticides

were at a significantly increased risk of developing prostate cancer. Another study found that Californian farm workers, who face higher environmental levels of pesticide exposure despite not being directly involved in pesticide application, have been found to experience an elevated risk of prostate cancer.[106] In 2011 the Keck School of Medicine at the University of Southern California, using a population-based cancer registry, found evidence of an association between ambient pesticide exposures in and around homes in agricultural areas and prostate cancer. Environmental exposure to certain pesticide compounds was found to have a role in prostate carcinogenesis.[107]

Pancreatic Cancer

Occupations with high level pesticide exposure have been associated with an increased risk of pancreatic cancer. In a study of occupational hazards in Spain, of all occupations studied, pesticide exposure was one of only a few occupational hazards to be associated with a three-fold increase in risk of pancreatic cancer.[108] Most individuals with highest risk of pancreatic cancer were farmers, workers employed in agricultural industries, or landscapers. Authors concluded that pesticide exposure leads to an increased risk of pancreatic cancer. National Cancer Institute researchers confirmed this finding, in a study that demonstrated occupational exposure to fungicides and herbicides led to "excess risks" for pancreatic cancer. Authors concluded that increased amounts of pesticide exposure were associated with a significantly increased risk of pancreatic cancer, and that the evidence supports a finding of pesticides playing a role in human pancreatic carcinogenesis.[109]

Breast Cancer

Studies examining women in living in U.S. agricultural areas have shown an increased risk of breast cancer. A 2004 study by NIH researchers found an elevated risk of breast cancer for women who lived closest to sites of pesticide application.[110]A case-control study in North Carolina found that women who reported being present in the fields during or shortly after a pesticide application had elevated risk of breast cancer.[111] Analyzing three years of reported data on breast cancer rates, the authors concluded that women with higher pesticide exposure may be more likely to develop breast cancer. Using acres of crops planted as a proxy measure for level of pesticide exposure, one study found evidence for an association between pesticide exposure and risk of breast cancer mortality.[112]

VII. Systematic Concerns

Overall, pesticide use in the U.S. has increased by about 7% since 1996, a change which equates to the additional use of millions of pounds of pesticides per year.[113] The U.S. Geological Survey has found that in the U.S., over 90% of streams and over 50% of all groundwater, both sources of drinking water, in both urban and agricultural areas contain pesticides.[114] Herbicide-resistant crop technology has led to a 527 million pound increase in herbicide use in the U.S. between 1996 and 2011. This increased volume of pesticide application is driven in particular by the spread of glyphosate-resistant weeds, as well as genetically modified crops intended to withstand glyphosate treatment. The pervasiveness

of pesticides means that, increasingly, even those who choose not to use pesticides in their homes will face ambient exposure. In the American Association of Pesticide Control Officials' three most recent years of reported data (2002-2004) from the Pesticide Drift Enforcement Survey given to state pesticide regulatory agencies, 2,4-D and glyphosate were the two active ingredients most commonly involved in state-confirmed occurrences of pesticide drift.[115] Additionally, the total number of reports of pesticide drift received by state pesticide regulatory agencies rose every year.

The EPA is the agency that assesses pesticides and other toxic chemicals for whether their active ingredients pose "unreasonable" risks to humans. The EPA then sets limits on how an approved pesticide may be used, including who may use it, how frequently it may be used, where it may be used, and what protective clothing must be worn when in use. Pesticides are considered for both their short term (acute) and long term (chronic) health consequences. To learn what chemicals are at work in any given pesticide product, one can look to the active ingredients and their concentrations as listed on the product label. The same active ingredient can be found in hundreds of differently named products, while products of similar names or brands can have entirely different active ingredients.

Pesticides are also labeled by the EPA as belonging to one of four Toxicity Categories which are based on immediate risks brought on by exposure.[116] Acute exposure to pesticides of Toxicity Categories I and II is known to be fatal in high doses. Packaging for pesticides in order of the three most severe Toxicity Categories are required to bear the signal words "danger-poison," "warning," or, "caution." Immediate health effects of pesticides can range from mild, like slight skin irritation, to extremely serious, like irreversible damage to ocular and skin tissue. While much is known by the medical community regarding immediate treatment of acute exposure, understanding the long-term health effects and carcinogenity of repetitive low-level exposure to pesticides remains a matter of grave concern for scientists and regulators.

The pesticide toxicity ranking system currently in use in the U.S. is likely not sensitive enough to the human health effects shown to be brought on by even low-dose exposure. Chemical regulations are based on the assumption that higher doses are always more dangerous, as such, any level of exposure below the "safe" dosage is assumed to be without health risks. Yet a 2012 study found that endocrine-disrupting chemicals, including pesticides, function in such a way that moderate doses are the least damaging, while very low and very high doses are most dangerous to the human body.[117] This means that the chronic low-level exposure to pesticide which most Americans face may not be "safe" at all, and that there may be no such thing as a safe dosage of endocrine-disrupting chemicals. Scientists have suggested that another inadequate aspect of the EPA's model of premarket toxicologic testing is its reliance on relatively short-term administration of a single active ingredient to inbred strains of animals. This, scientists argue, does not reflect the reality of human exposure to pesticides, which is far more likely to be "a complex mix of compounds over a lifetime," and may lead to products that negatively affect human health gaining regulatory approval.[118] It is impossible to fully see the human health impact of pesticide

exposure when utilizing an incomplete strategy, testing each chemical's effects in isolation.

Though this report was limited to the effects of pesticides on human health, it is important to note that pesticides have long-lasting damaging effects on the natural environment, by contaminating ground water, lakes, and rivers, and disturbing the ecosystem by killing non-target species.

VIII. Moving Forward

The scientifically demonstrated health effects of pesticide exposure call for a reduction in use of these toxic chemicals. The precautionary principle is a scientific principle which states that in situations where substances have a serious risk of harm but there exists scientific uncertainty regarding the degree of risk, the danger should be assumed, and preventative measures should be taken to protect the public health.[119] The American Academy of Pediatrics, American Public Health Association, World Health Organization, and California EPA all advise limiting toxic chemical exposure under the precautionary principle.[120][121][122] The European Union has codified the precautionary principle as law, specifically applied to preventing pesticide exposure.[123] The Los Angeles Unified School District, the second largest school district in the U.S., has adopted the precautionary principle as a "long-term objective" to reduce risk to students and employees as well as Integrated Pest Management (IPM) as a pest control strategy.[124] Integrated Pest Management is a strategy for pest control which avoids the need for using chemical products by correcting the underlying sources of pest problems, and can be applied to both indoor and outdoor environments. By adopting the preventative mentality of the precautionary principle and IPM, the grave health risks of pesticide exposure can be mitigated.

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