



Pesticides and our Health

A GROWING CONCERN

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Executive Summary

Since 1950 the human population has doubled, yet the area of arable land used to feed these people has increased by only 10%. There are huge pressures to provide food, at low cost, on land that is becoming more and more degraded as nutrients are stripped from the soil. Reliance on external inputs – fertilisers and pesticides – continues to be the short-term solution for large-scale commercially intensive agricultural systems.

Synthetic pesticides have been widely used in industrial agriculture throughout the world since the 1950s. Over time, many of these chemicals have become extremely pervasive in our environment as a result of their widespread repeated use and, in some cases, their environmental persistence. Some take an extremely long time to degrade, such that even those banned decades ago, including DDT and its secondary products, are routinely found in the environment today.

As a consequence of this persistence, and potential hazards to wildlife, effect-related research on the impact of pesticides has increased exponentially over the past 30 years (Köhler and Triebkorn 2013). It is now clear that these effects are wide and varied. Over the same period, scientific understanding of the effects of pesticides on human health and their mechanisms of action has also expanded rapidly, with studies revealing statistical associations between pesticide exposure and enhanced risks of developmental impairments, neurological and immune disorders and some cancers.

Nevertheless, proving definitively that exposure to a particular pesticide causes a disease or other condition in humans presents a considerable challenge. There are no groups in the human population that are completely unexposed to pesticides, and most diseases are multi-causal giving considerable complexity to public health assessments (Meyer-Baron et al. 2015). Furthermore, most people are exposed to complex and ever changing mixtures of chemicals, not just pesticides, in their daily lives, through multiple routes of exposure. Pesticides contribute further to this toxic burden.

Widespread Health Impacts

Health impacts that have been reported for children exposed to elevated levels of pesticides in the womb include delayed cognitive development, behavioural effects and birth defects. There is also a strong correlation between pesticide exposure and incidences of childhood leukemia.

Studies have also related higher pesticide exposures to increased incidence of several types of cancer (prostate, lung and others), and neurodegenerative diseases such as Parkinson's and Alzheimer's disease. There is also evidence that suggests some pesticides can disrupt normal endocrine function and immune systems in the body. Whilst the mechanisms of such impacts are poorly understood, it is clear that, in some cases, enzyme function and important signaling mechanisms at cellular levels can be disrupted. Studies using DNA-based methods also indicate that certain chemicals disrupt gene expression and this may follow on to generations that are not exposed to pesticides through epigenetic inheritance. This means that the negative impacts of pesticide usage can be extremely long term, even after the substance has been outlawed.

This report examines a growing body of research relating to known, and suspected, human health effects of pesticides. While recognising the inevitable uncertainties and unknowns, and including conflicting and developing research, this review collates and analyses the evidence indicating how industrial agriculture, and the use of synthetic pesticides in particular, is currently undermining the health of farmers and their families, as well as the wider population. Among the many active ingredients that are potentially dangerous to health are the currently approved organophosphates, chlorpyrifos and malathion. Chlorpyrifos is routinely found in food, and in human breast milk, and public health studies indicate strong evidence that it is linked to numerous cancers, impaired development in children, impaired neurological function, Parkinson's disease and hypersensitivity.

Particularly Exposed or Vulnerable Populations

The general population is exposed to a cocktail of pesticides through the food we consume every day. In agricultural areas in which pesticides are used, these substances drift in the air, pollute the soil and waterways, and are sometimes systemically absorbed by non-target plant species. In cities, spraying of recreational areas also exposes people nearby to a mixture of chemicals. Everyday use of various household pest control substances can also contaminate homes and gardens.

Particularly highly exposed or vulnerable population groups include:

- Farmers and pesticide applicators, especially greenhouse workers, exposed to high levels of chemicals in their work. This has been clearly shown though levels found in the blood and hair of these workers.
- The unborn and young children. When women are exposed to pesticides during pregnancy, some of these chemicals pass directly to the developing child in the womb. During development, the fetus is particularly vulnerable to the toxic impacts of pesticides. Young children, in general, are more susceptible than adults due to their increased exposure rates, in that toddlers and crawling babies are more likely to touch surfaces in the home and put their hands in their mouths. Children also have much smaller body sizes than adults and are less able to metabolize toxic substances within their systems.

The Solution – Ecological Farming

The only sure approach to reducing our exposure to toxic pesticides is through a move towards a more long-term and sustainable approach to producing food. This will require legally-binding agreements to immediately phase-out all pesticides that are toxic to non-target organisms implemented at both national and international level. Fundamentally changing our approach to farming involves a paradigm shift from industrial agriculture, which relies heavily on chemical additives, towards the full implementation of ecological farming as the only means of feeding the population and protecting the ecosystems we live in. Ecological farming is a modern and effective approach to farming that does not rely on toxic chemicals, and delivers healthy and safe food.



Ecological broad beans, local protein plants in Greece.
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1. Introduction



A worker without protective clothing only wearing a paper breathing protection sprays pesticides on vegetables in a greenhouse / Spain.
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1.1 Pesticides in Agriculture

The use of synthetic chemical pesticides in agriculture around the world began in the 1950s, though the types and diversity of chemicals used have changed over time. Organochlorine, organophosphate, carbamate and pyrethroid pesticides were introduced onto the world market at that time, marking the beginning of industrial agriculture or the ‘Green Revolution’. In the decades since then, other types of pesticides (e.g. neonicotinoids) have been introduced onto the world market and industrial agriculture has come to rely more and more on the use of synthetic chemical pesticides to protect crops from pests and diseases and to secure or boost yields.

An introduction into some of the pesticides used in current industrial agriculture is given in Text Box 1.

Some of the main classes of pesticides are listed below.

What Are Pesticides?

Text Box 1.

‘**Pesticide**’ – the act of killing a nuisance or plague. Synthetic chemical pesticides are chemical substances or mixtures used to control pests, including insects, fungi, moulds and weed plant species. These substances are also commonly known as ‘plant protection products’.

They are often categorised according to the target pest, for example:

Insecticides – to control insect pests.

Herbicides – to control weeds.

Fungicides – to control fungal pests.

Together, these groups cover a very large number of individual active ingredients, formulations and brand names. Pesticides are also categorized by their chemical class – for example, organophosphorus (OP pesticides), organochlorine pesticides (OC pesticides), carbamates, neonicotinoids.

1.1.1 Pesticide classes

• ORGANOCHLORINE PESTICIDES (OCPs)

Used for agriculture and public health purposes since 1950, though the uses of some have since been severely restricted or banned altogether because of their recognized toxicity to non-target species, including humans. Some organochlorine pesticides are very stable compounds and, therefore, extremely persistent in the environment because of their resistance to natural breakdown processes. For this reason several of the chemicals listed as Persistent Organic Pollutants (POPs) under the 2001 Stockholm Convention are OCPs. Although environmental levels of some organochlorines have fallen over time, many can still be found as contaminants in a wide range of ecosystem compartments, including soils, river sediments, coastal marine sediments reaching as far as the deep oceans and the poles (Willet et al. 1998).

KEY OCPs include: carbon tetrachloride; chlordane; DDT; DDE; dieldrin; heptachlor; β -HCH; γ -HCH. (NB: none of these are currently approved for use in the EU).

• ORGANOPHOSPHATE PESTICIDES (OPPs)

The insecticidal properties of certain organophosphate compounds were discovered during military nerve gas research and, since World War II, a number of organophosphate pesticides (OPPs) have been commercialized for agricultural use. OPPs include a diverse range of chemical structures. Their mode of toxicity makes them effective as pesticides as the chemicals inhibit a critical enzyme (acetylcholinesterase) in the central and peripheral nervous system, a property which also accounts for some of their observed toxicity to non-target species.

KEY OPPs include: acephate; chlorpyrifos; coumaphos; diazinon; dichlorvos; fonofos;

parathion; malathion; methyl parathion; phosmet. (NB: Chlorpyrifos and malathion are currently approved for use in the EU, banned for residential use in the US).

• CARBAMATES

Generally neurotoxic and are also acetylcholinesterase inhibitors. Some have been associated with adverse effects on human development, affecting both babies and children (Morais et al. 2012).

KEY CARBAMATES include: aldicarb; carbaryl; methiocarb; pirimicarb; maneb and mancozeb (both dithiocarbamates); EPTC (S-Ethyl-N,N-dipropylthiocarbamat). (NB: methiocarb, pirimicarb, maneb and mancozeb currently approved for use in the EU).

• SYNTHETIC PYRETHROIDS

These interfere with cell signaling (ion channels). Some have been associated with adverse effects on male reproductive health and are suspected endocrine disruptors (effects on hormone function) (Koureas et al. 2012).

KEY PYRETHROIDS include: cyhalothrin; cypermethrin; deltamethrin; permethrin. (NB: cypermethrin and deltamethrin are currently approved for use in EU).

• NEONICOTINOIDS

Newer class of pesticides; for example, imidacloprid was first commercially available in 1985. These substances are structured very like nicotine and block certain cell signaling pathways. They also have negative impact on neurodevelopment (Kimura-Kuroda et al. 2012). Due to suspected toxicity to wild and managed bees, some restrictions on use have been emplaced by the European Commission.

KEY NEONICOTINOIDS include: clothianidin; imidacloprid; thiamethoxam.

- **CHLOROACETAMIDES**

Can cause developmental abnormalities; both alachlor and metolachlor are no longer approved in the EU.

- **PARAQUAT**

Neurotoxic herbicide that inhibits photosynthesis. No longer approved for use in the EU.

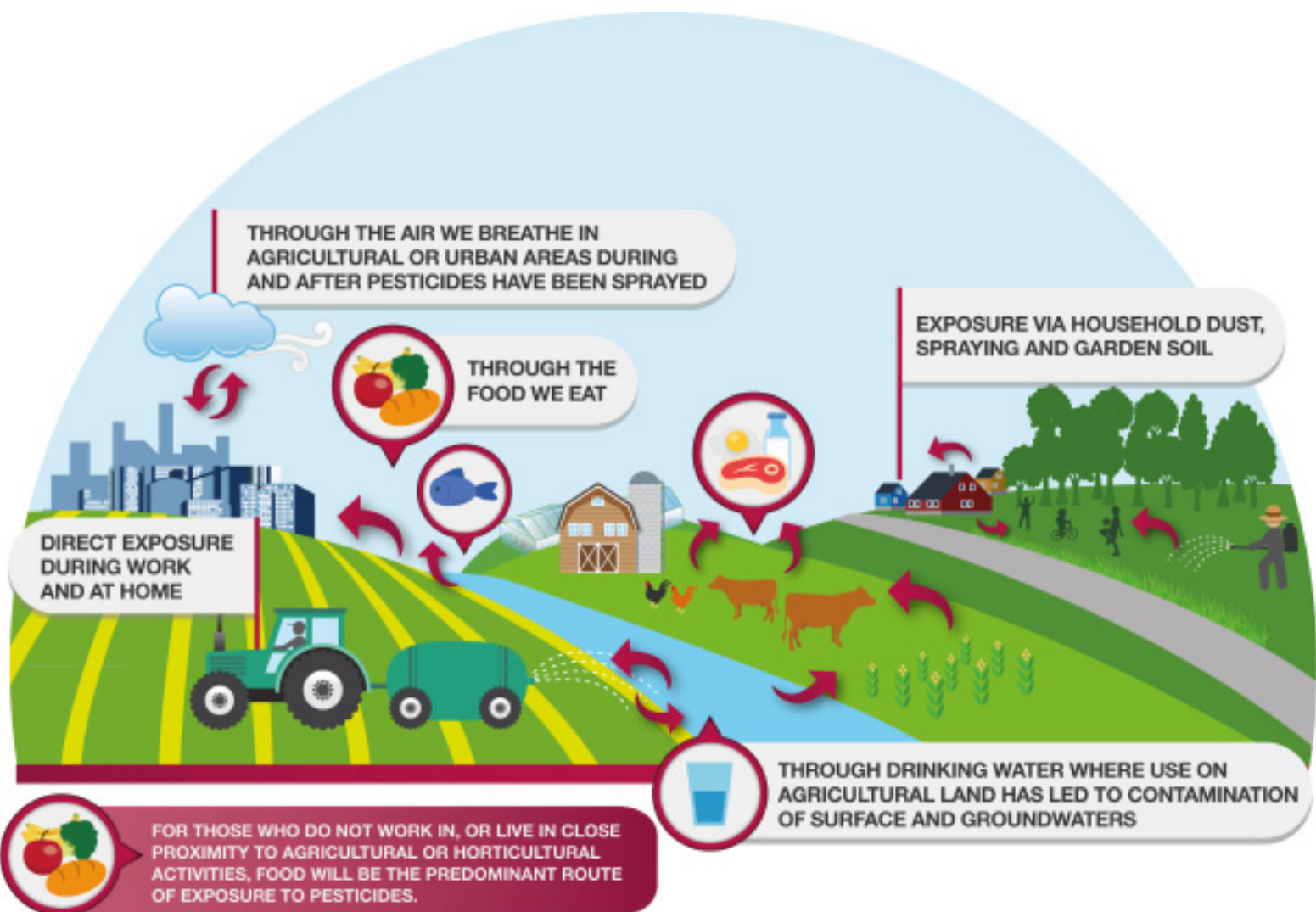
- **GLYPHOSATE**

The active constituent of Roundup acts by inhibiting a particular enzyme in plants. The health impacts remain disputed, however, the International Agency for Research on Cancer (IARC) recently classified glyphosate as Class 2A 'probably carcinogenic to humans (Guyton et al. 2015). This classification was based on limited evidence in humans (particularly on links to non-Hodgkins lymphoma) but a robust body of evidence in animals. Also potentially causes endocrine disrupting effects in human cells lines, and reproduction effects (Gasnier et al. 2009, Cassault-Meyer et al. 2014). Glyphosate is widely used globally and is the active ingredient in more than 750 different products relating to agriculture, forestry, urban and home application. Its use has increased sharply in conjunction with Roundup Ready crops that are genetically engineered to be resistant to the effects of glyphosate.

- **OTHER PESTICIDES OF VARIOUS CHEMICAL STRUCTURE**

Other pesticides approved for use in the European Union (but also used elsewhere) include: abamectin (aka avermectin); azoxystrobine; boscalid; captan; cyprodinil; dicamba; dinitrole; fipronil; pendimethalin and pyrimethanil. Substances which do not have approval for use in the EU (some of which may nevertheless still be approved for use or otherwise in use elsewhere) include: benomyl; carbon disulphide; ethylene dibromide (1,2 - dibromoethane); imazethapyr; trifluralin. Diethyltoluamide (DEET), used as an insect repellent and as a synergist in some pesticide formulations (including carbamates) is not listed under EU regulations.

1.2 How Are We Exposed to Pesticides?



1.2.1 Exposure via Food

Pesticide residues are commonly present in food that is grown through intensive industrial farming. Studies show that food often contains multiple residues and therefore pesticides are presented to us as mixtures or cocktails (Fenik et al. 2011). The toxic effect of these mixtures is particularly poorly understood, though it is recognised that some substances can interact synergistically in that their combined effect is greater than that of the individual components (Reffstrup et al. 2010). Assessing the toxicity of mixtures of pesticide residues is highly complex given the number of potential combinations and interactions which could occur.

Sutton et al. (2011) state that, as a result of pesticide residues in food produce, typical food consumption patterns in the US can result in potentially high cumulative exposure in the general population. This is likely true for other countries and may be of concern considering repeated consumption of pesticides, particularly those that are lipophilic (bind with fats) and bioaccumulate in the body over time.

PESTICIDES IN FRUIT AND VEGETABLES

Pesticides are used extensively in the commercial production of fruit and vegetables. Residues of the pesticides applied can persist within the tissues or on the surface of crops when they are brought to market. Over many years, scientists have developed a variety of techniques to quantify levels of pesticides in food, and results have suggested that continuous monitoring is necessary to ensure as far as possible that limit values set for pesticide residues are not exceeded in produce reaching the market place (Wilkowska and Biziuk 2011; Li et al. 2014). Most countries, either on a national or regional basis, maintain a threshold Maximum Residue Level (MRL) for each substance, above which the foodstuff is thought unacceptable for human consumption. For example, the European Union designates MRL limits that apply across the region.

Various literature published between 2007 and 2014 suggests that legumes, leafy greens and fruits such as apples and grapes frequently contain the highest levels of pesticide residues (Bempah et al. 2012; Jardim et al. 2012; Fan et al. 2013; Yuan et al. 2014). There is consistent evidence that these substances are regularly present as mixtures of multiple residues and, in many cases, at levels above MRL limits in certain countries (Latifah et al. 2011; Jardim et al. 2012). Among many other pesticides, cypermethrin, chlorpyrifos, iprodione, boscalid, dithiocarbamates and acephate are regularly detected in our food (Claeys et al. 2011; Lozowicka et al. 2012; Yuan et al. 2014). Whilst extensive research suggests that washing and cooking vegetables does reduce some of these residues that are on the surface of the plant, in some cases food preparation can actually concentrate levels (Keikotlhaile et al. 2010).

PESTICIDES IN FISH

Organotins have been widely used as fungicides and biocides in agriculture since the 1970s. Organotin compounds (primarily tributyltin, or TBT) were also commonly used as antifouling agents on boats and ships, contributing to widespread pollution of many coastal waters and leading to a global ban of this application by the International Maritime Organisation under the 2001 International Convention on the Control of Harmful Antifouling Systems on Ships (the AFS Convention, which entered into force in 2008).

A study of organotin pollution in global marine environments found that a triphenyltin compound (TPT), used as a pesticide on land, was also a common contaminant of sediments (Yi et al. 2012). Phenyltin compounds are not easily biotransformed by marine organisms and therefore bioaccumulate and potentially biomagnify through marine food web systems. Concentrations of organotins are particularly high in the blood of those people who consume greater amounts of seafood and it has been suggested that regular monitoring of the levels of these substances be carried out for public health purposes (Yi et al. 2012).

PESTICIDES IN ANIMAL PRODUCTS

Farmed animals can also accumulate pesticides from contaminated feed and from veterinary pesticide application. Whilst these substances are generally stored in the fat and muscles of the animals, some can also be found in the brain, liver, lungs and other offal (LeDoux 2011).

Insecticides and acaricides are often used to control ectoparasites such as red mites in poultry and egg production. Consequently, some of these pesticides



Pesticide Use on Apple Plantation near Hamburg/ Germany.
© Greenpeace / Christian Kaiser

accumulate in the muscle, fat and liver and can be detected in eggs even long after the chemicals have been eliminated from other tissues (Schenck and Donoghue 2000).

Milk and other dairy products also similarly contain a range of substances through bioaccumulation and storage in the fatty tissues of the animals. This is of particular concern as cows' milk is often a staple component of human diets, and is particularly widely consumed by children.

ORGANIC FOOD VERSUS THAT GROWN BY INDUSTRIAL AGRICULTURE

Studies have shown that the primary route of exposure to pesticides for most children is through their diet, such that children who are fed an organic diet may be expected to have consistently lower residues of pesticides in their urine than those that are given a diet grown through conventional industrial agriculture (Forman et al. 2012).

Lu et al. (2006) investigated OPP metabolites in the urine of children aged 3-11 years in Seattle, US. These children were given a conventional diet for 5 days, followed by an organic diet for 5 days. Monitoring showed that levels of the pesticides malathion and chlorpyrifos fell quickly to below detection limits after children consumed the organic diet in the latter 5 days. When a conventional diet was re-introduced to the children, the levels of these OPP metabolites in their urine increased again.

In this study, the organic food items in the children's diet consisted of fresh fruits and vegetables, processed fruit or vegetables such as juices, as well as wheat and corn-based items. Food in this area that was produced by industrial agriculture was routinely reported to contain OPPs and it was concluded that children were most likely exposed to chlorpyrifos and malathion through diet exclusively (Lu et al. 2006).

1.2.2 Exposure from Agricultural and Urban Pesticide Spraying

Pesticides sprayed on agricultural land, and in urban areas, become airborne during application and can drift for great distances in the air. For example, a study in the US found that several commonly used pesticides can be detected far beyond the sites of agricultural application. At distances of 10 m to 150 m away from the application sites some pesticides, such as diazinon and chlorpyrifos, still exceeded government safety levels (Reference Exposure Levels for air) (Sutton et al. 2011). People living in agricultural areas may therefore have a high exposure to pesticides because of inhalation of pesticide spray drift. Similarly, when pesticides are sprayed in parks and urban areas or in the home, people can be exposed if they breathe in the contaminated air.

1.2.3 Exposure via Household Dust, Spraying and Garden Soil

Household dust has been found to be contaminated with many chemicals including some pesticides, particularly if they are commonly used to control household pests (Naeher et al. 2010). The key substances used in domestic pest control are the pyrethroids permethrin and cyfluthrin, and in some cases chlorpyrifos. Ingestion, inhalation and skin contact with contaminated dusts can lead to continued and varied exposures to pesticides (Morgan et al. 2007, 2014; Starr et al. 2008). Homes situated in agricultural areas, particularly those that are in close proximity to pesticide-sprayed land, have been shown to be more contaminated (Harnly et al. 2009). However, contaminated dust is also a potential problem in urban areas where residues persist as a result of household application (Naeher et al. 2010; Muñoz-Quezada et al. 2012).



Spraying pesticides on Chinese Cabbage in Hebei / China

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An apple farmer sprays pesticides on his trees / India

© Greenpeace / Peter Caton



We are all exposed to pesticides at some levels, even if we take action to try to avoid them. Nevertheless, because of their specific situations and/or characteristics, some people are expected to be particularly highly exposed to pesticides, or particularly sensitive to their adverse effects. Some examples are given above.

1.3 Particularly Exposed or Vulnerable Populations

1.3.1 Agricultural Workers

Farmers and their families can have a higher exposure to pesticides than the general population. Farmers who spray pesticides (pesticide applicators) suffer the highest levels of exposure, though greenhouse workers can also be very highly exposed.

A study conducted in Europe that investigated residues found in the hair of agricultural workers discovered 33 different substances, including herbicides and fungicides. The most frequently found pesticides were pyrimethanil, cyprodinil and azoxystrobin and their detections corresponded to the types of cultivation and products used. Similar levels of p,p'-DDE and γ -HCH (no longer in current use) were found in all subjects, whatever their occupation on the



A worker without protective clothing only wearing a paper breathing protection sprays pesticides on vegetables in a greenhouse/ Spain
© Greenpeace / Ángel Garcia

farm, indicating an underlying longer term exposure from organochlorines that are highly persistent in the environment (Schummer et al. 2012). These results imply that, even when pesticide applicators are using the correct safety precautions, they are still subject to elevated levels of exposure that can be detected in their body tissues. The longevity in the body of some of the pesticides still in active use is not well known, though body residence times may be of lower significance if use and exposure is repeated regularly.

The families of farmers living in agricultural areas may also have a slightly higher than average exposure to pesticides than other people. This is a result of pesticide sprays drifting through the air from fields near farmers' homes in addition to farm workers bringing their contaminated clothes and shoes back into the home after work. This is particularly of concern for infants and children because they may be more vulnerable to the toxic effects of some pesticides than adults (Arcury et al. 2007).

1.3.2 Children, Infants and Exposure in the Womb

When pregnant women and nursing mothers are exposed to pesticides, their children may also be exposed. Some pesticides can pass through the placenta to the developing fetus in the womb, and through breast milk to the nursing infant. During early development, the infant's organs are forming and growing, and can be very susceptible to the effects of toxic chemicals. A child's developing brain is more susceptible to neurotoxicants, for example, and the dose of pesticides per body weight is likely to be higher in children due to their small size (Weiss 2000). In addition, the overall levels and activity of certain enzymes that detoxify activate forms of pesticides are lower in children (Holland et al. 2006).

CONTAMINATION OF BREAST MILK

Breast milk is the best form of nutrition for babies before weaning, particularly in transferring key

elements of the disease protection system from mother to child. Given that breastfeeding occurs during some of the most sensitive times in the development of the young child, it is vital that contamination of breast milk with harmful chemicals be minimized or, as far as possible, avoided. Data from analysis of breast milk in various countries continues to show, however, that pesticide contamination remains a problem.

Organochlorine pesticides (OCPs), in particular, are known to bioaccumulate in the fat of the body and breast milk as a result of routine dietary intake and, as a result of their persistence in the environment, they continue to contaminate our bodies every day. These chemicals have been statistically associated with adverse effects on human development in epidemiological studies. A study in Taiwan detected OCPs in breast milk samples from women throughout the period 2000 to 2001 (Choa et al. 2006). Pesticides that were predominately found in the milk samples were p,p'-DDE, p,p'-DDT, α -chlordane, heptachlor epoxide, heptachlor, β -HCH, and γ -HCH. Similar results have been reported by studies in other parts of the world, including Colombia, Korea and Germany (Lee et al. 2013a; Raab et al. 2013; Rojas-Squella et al. 2013). Studies suggest that levels of these persistent OCPs in human milk may now be declining in many countries where these substances have been banned for some time (Ulaszewska et al. 2011). Diet remains a major factor regulating exposure, especially where fish consumption is high (Solomon and Weiss 2002).

Organochlorine pesticides that are still in common use in agriculture in many parts of the world include lindane and endosulfan. A study in India, published in 2003, detected high levels of endosulfan in breast milk samples of women from Bhopal (Sanghi et al. 2003). The World Health Organization (WHO) has established values for the levels of pesticides in breast milk which are deemed as 'acceptable' based on knowledge of their toxicity (known as Acceptable Daily Intake (ADI)). Sanghi et al. (2003) reported that endosulfan levels exceeded the WHO ADI at that time by 8.6 times. Lindane was also detected in breast milk of these Indian women.

Organophosphorus pesticides and synthetic pyrethroids are not considered to be persistent in the environment and consequently their levels in breast milk have been little studied. However, some studies have clearly shown that these pesticides do contaminate human breast milk and, whilst levels of OCPs may be declining, there has been a noted shift towards the detection of more OPPs and synthetic pyrethroids in breast milk as these substances have replaced more restricted pesticides (Sharma et al. 2014). Sanghi et al. (2003) found high levels of the OPP chlorpyrifos, as well as malathion, in the breast milk of women from Bhopal. In this study, chlorpyrifos levels in breast milk exceeded the WHO ADI by 4.1 times. A more recent pilot study in the US also detected chlorpyrifos, chlorpyrifos-methyl, and the carbamate insecticide propoxur in breast milk (Weldon et al. 2011).

Sharma et al. (2014) reported cyfluthrin, a synthetic pyrethroid, as the most frequently detected pesticide in a study of contaminants of breast milk in India. This study noted levels that would constitute a health risk to nursing infants. Furthermore, synthetic pyrethroids have now been detected in human breast milk samples that were collected from both urban and agricultural areas of Spain, Brazil and Colombia (Corcellas et al. 2012). These results suggested either that these pesticides can accumulate within the body, in contrast to the assumption that they are rapidly metabolized, or that contaminant levels are topped up through repeated exposure.

MULTIPLE ROUTES OF EXPOSURE

Young children and toddlers, spend much of their time at home on or close to the floor or outside on or close to the ground. They are in frequent contact with dust and soil and are more likely to ingest these chemicals as they regularly put their hands, toys or other objects into their mouths. From studies of contaminants found in the home, and direct monitoring of substances in the urine of children, it is clear that children, particularly toddlers, are likely to be exposed to substances through several pathways such as ingestion or inhalation of soil, carpet dust, diet and air (Naeher et al. 2010; Muñoz-Quezada et al. 2012; Morgan et al. 2014). There are likely geographic and seasonal differences in exposure patterns and, whilst scientists are currently attempting to evaluate both routes and rates of exposure, it is clear that children are under constant and varied exposure to many substances. Even at low individual substance levels, this continuous and combined exposure to complex mixtures of substances is of concern. Morgan et al. (2014) characterized exposure to various pesticides in preschool children in the US, through multiple routes including environmental sources (dust and air in the home and day-care centre dust and air), personal products (wipes) and food. Absorption rates varied for different substances and routes. However, the pesticides α -chlordane, γ -chlordane, heptachlor, chlorpyrifos, diazinon and permethrin were commonly found in these children's home and day-care environments, with diet being the major exposure route for chlorpyrifos and permethrin.

2. Health Impacts linked to Pesticide Exposure



Inside a greenhouse with growing vegetables being sprayed with pesticides / Spain.
© Greenpeace / Ángel Garcia

2.1 Effects of Prenatal (Fetal) & Infant Exposures

Human development is particularly vulnerable to effects of toxic chemicals, including pesticides (Text Box 2). Exposure of pregnant mothers to pesticides, and in some cases exposure of young children themselves, has been linked to adverse health outcomes for the children, including:

1. Reduced birth weights and lengths and occurrence of abnormalities
2. Lower intelligence
3. Altered behavior
4. Higher incidence of leukemia and other cancers
5. Higher incidence of miscarriage

These adverse impacts on children's health have been reported for children born to mothers who worked with pesticides whilst pregnant, though the health effects of pesticide exposure are a concern also for children from the general population, living both in agricultural regions and in the city.

Vulnerability of the very young to toxic pesticides

The developing fetus in the womb and the young infant can be particularly vulnerable to harmful effects from toxic pesticides. **The fetus is particularly vulnerable to chemical exposure due to the complexity of developmental processes and the high rate of growth.**

The developing nervous system can be particularly impacted upon by neurotoxic pesticides. Pesticides that are toxic to the nervous system include organophosphate pesticides (OPPs) and some carbamate pesticides, pyrethroids and neonicotinoids. Many such pesticides are known to cross the placental barrier; for example, OPPs have been detected in the amniotic fluid surrounding the fetus, posing a threat to the unborn child during a period of rapid brain development (Rauh et al. 2011).

The immune system of the fetus and infant are undeveloped and can also be adversely impacted upon by toxic chemicals. The newborn child and young infants have much lower levels of detoxifying enzymes than adults. For example, lower levels of the PON1 enzyme in newborns compared with adults suggests that infants may be especially vulnerable to organophosphate pesticide exposures – because they are slower to break down and detoxify these chemicals (Huen et al. 2012).

Young nursing infants are also at risk because breast milk, known to be contaminated with pesticides, is their only source of food and their metabolism is not mature enough to eliminate these pollutants (Corcellas et al. 2012). Moreover, both **nursing infants and small children are at a higher risk of pesticide toxicity than are adults** because the dose per body weight is higher in children due to their small size (Bouchard et al. 2011).

These same children are exposed not only to pesticides during their development, but also to other harmful chemicals, through a variety of pathways. The possible implications of such complex patterns of exposure are generally acknowledged but remain under-investigated and poorly understood.

2.1.1 Birth Defects

Levels of pesticides, such as the OPP chlorpyrifos, detected in blood extracted from fetal umbilical cords of babies born in New York, US, suggest that higher pesticide exposure in the womb may impair growth of the fetus (Whyatt et al. 2004). Barr et al. (2010) reports similar results for metolachlor and also suggest that pesticide burdens may be associated with birth outcomes, although causality could not be inferred from the data in the study.

In the US, women who regularly used pesticides in and around their homes were two times more likely to give birth to children with neural tube defects (Brender et al. 2010). Other birth defects in newborns whose mothers were consistently exposed to higher levels of pesticides include circulatory, respiratory, urogenital and skeletal defects (Garry et al. 1996). It has also been reported in the US that mothers living in close proximity (<500 m) to corn fields of 2.4 hectares or more were more likely to give birth to babies with limb defects (Ochoa-Acuña and Carbajo 2009). However, this association was not evident for those living in similar proximity to soya fields and it is not fully understood whether this correlation is as a result of the use of specific agrochemicals or application techniques or rates in corn cultivation or toxicity related to the presence of a mycotoxin that is found in contaminated corn.

2.1.2 Neurotoxicity

Increasing evidence suggests that pre-natal pesticide exposure (i.e. exposure of the unborn child during pregnancy) may have a permanent effect on children's behavior and intelligence. Organophosphorus pesticides in particular have been implicated. In a review of 27 published studies of children exposed to pesticides in food and in the home at a very young age, all but one study showed some negative effect of organophosphate pesticides on development of the child's brain and nervous system (Muñoz-Quezada et al. 2013). Developmental impacts were mainly described as

cognitive or behavioural, particularly those related to attention deficit disorders and motor skills.

IMPAIRED INTELLECTUAL DEVELOPMENT

In agricultural regions, exposure of mother and child to pesticides is likely to occur through a combination of diet and exposure to airborne agrochemicals sprayed in fields near to homes. A study in the agricultural region of the Salinas Valley, California, documented prenatal exposure to organophosphate pesticides through levels detected in the urine of pregnant women (Bouchard et al. 2011). High levels of these pesticides in mothers' urine were statistically associated with poorer intellectual development in the children when they reached 7 years of age. Children of the most highly exposed mothers had an average deficit of 7 IQ points compared to children of those with the lowest exposure. These cognitive effects occurred in children whose mother's urine had levels of organophosphate pesticides that were near the upper end of the range typically found across the general US population.

Organophosphorus pesticides are still used in urban areas for pest control. Until 2001, the use of the OPP chlorpyrifos was particularly heavy in urban areas. Rauh et al. (2011) describes exposure of pregnant women in New York City to chlorpyrifos and the potential impacts on their children. Umbilical cord blood samples taken at birth showed that prenatal exposure to chlorpyrifos in the womb was statistically associated with poorer intellectual development when the children reached 7 years of age. A higher exposure to chlorpyrifos in the womb was associated with deficits in Working Memory Index and deficits in IQ at age 7. These results are consistent with those of the Salinas Valley study in which the children exposed in the womb to OPPs also had deficits in working memory and IQ. These deficits are likely to contribute to long-term problems for these children as impairments in working memory are thought to interfere with reading comprehension, learning and academic achievement and may have considerable economic implications (Rauh et al. 2011).

These findings are also consistent with results from a study examining brain structure in New York City children (Rauh et al. 2012). Researchers found structural changes in the developing human brain that were statistically associated with prenatal exposure to chlorpyrifos. Brain structure was examined in 40 of these children between 6 to 11 years old using magnetic resonance imaging (MRI). Those children who were exposed to higher levels of chlorpyrifos in the womb had more abnormalities in brain structure in the regions of the brain associated with certain cognitive and behavioral processes. Changes in brain structure were visibly apparent across the brain surface, with abnormal enlargement of some areas and thinning in others. Links between prenatal exposure to chlorpyrifos, altered brain structure and deficits in cognitive development suggested that these neurotoxic effects are long-term, extending into childhood. Moreover, these findings are consistent with those of controlled laboratory experiments that suggest that similar adverse impacts in animals may be irreversible (Rauh et al. 2012).

This clearly has serious public health implications. The levels of exposure to chlorpyrifos experienced by the children in the study reported by Rauh et al. (2012) were within the same range as those experienced by the general population. Therefore, it is of great concern that organophosphate pesticides, including chlorpyrifos, are still used for pest control in agriculture throughout the world. Although restrictions are in place for home use of chlorpyrifos, and there are regulations on its use in public spaces (e.g. buffer zones), this product is still in use as an insecticide in public spaces such as golf courses and some parks.



Spraying of genetically engineered soya / Argentina
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ADVERSE BEHAVIORAL EFFECTS

Adverse effects on the behavior of children (mainly related to attention problems) have been linked with prenatal exposure to OPPs in both the agricultural region of the Salinas Valley, California, and in New York City (Marks et al. 2010; Muñoz-Quezada et al. 2013).

Attention deficit/hyperactivity disorder (ADHD) is a complex disorder and the precise causes are unknown. Around 8-9% of school-age children are thought to have ADHD in the US (Pastor and Reuben 2008). Such marked attention problems in children are known to disrupt learning and social development (Marks et al. 2010).

Bouchard et al. (2010) examined exposures of 8-15 year olds in the US to OPPs, mainly from diet, and reported that children with higher urinary OPP metabolites were more likely to be diagnosed with ADHD. The study concluded that OPP exposure, at levels commonly found in the US may contribute to ADHD prevalence in children (Bouchard et al. 2012). These findings are also supported by Jurewicz and Hanke (2008) in a review of prenatal and childhood exposure to pesticides and neurobehavioural development. Though the conclusions of some studies differed, taken together it was found that children's exposure to pesticides resulted in impaired neurobehavioural development.

OTHER EVIDENCE OF NEUROTOXICITY

There are some indications that prenatal exposures to organophosphate pesticides have an adverse impact on motor skills (the control of muscle movement). In northern Ecuador, floriculture in greenhouses is intensive and OPPs are commonly used. A study of children (6-8 years old) whose mothers had worked in the greenhouses whilst pregnant, suggested consistent deficits in motor speed and coordination as well as general mental functioning in comparison to other children, whose mothers were not exposed to pesticides during work (London et al. 2012). These effects were associated with a developmental delay in the children equivalent to 1.5 to 2 years, even at levels of exposure that produced no acute adverse health outcomes in their mothers.

CHILDREN EMPLOYED IN AGRICULTURE MAY BE PARTICULARLY AT RISK

Children themselves employed in agricultural work and using pesticides may be particularly vulnerable to the toxic effects of pesticides. One study in Egypt investigated children (aged 9-15) and adolescents (aged 16-19) who were employed as pesticide applicators in cotton growing (Rasoul et al. 2008). Organophosphorus pesticides were commonly used. The study found that, for both age groups, those who were more highly exposed to OPPs scored significantly worse on neurobehavioral tests than children who did not work with pesticides. It was reported that the longer the time the children spent working as pesticide applicators, the worse were the cognitive deficits.

CONCLUSIONS ON DEVELOPMENTAL NEUROTOXICITY

Taken together, these various lines of investigation indicate that, while the situation for those employed in agriculture is understandably more acute and severe, some level of negative impact on the developing brain and nervous system may also be detectable in the wider population as a result of lower levels of exposure to organophosphate pesticides. Much of the evidence from both animal and human studies is robust and considerable concerns have been expressed by scientists working in the field. Given the substantial impact of neurodevelopmental abnormalities in society and the potential link to pesticide exposure it is critical that this exposure be minimized and, as far as possible, prevented through effective measures to greatly restrict and ultimately prohibit the use of these harmful pesticides

Based on existing research, many other widely used pesticides should also be considered to be neurodevelopmental toxicants including carbamates (particularly aldicarb and methomyl), most pyrethroids (e.g. permethrin), ethylenebisdithiocarbamates (e.g. maneb and mancozeb), and chlorophenoxy herbicides (2,4-D) (Ragouc-Sengler et al. 2000; Bjørling-Poulsen et al. 2008; Soderlund 2012; van Thriel 2012). There is also emerging evidence using cell cultures and laboratory animals that indicate that neonicotinoid pesticides (particularly imidacloprid) potentially disrupt brain development and neurotransmissions in humans (Kimura-Kuroda et al. 2012; Vale et al. 2012). Therefore, exposure prevention is vital in protecting those living and working in agricultural areas.

2.1.3 Childhood Leukemia and Other Cancers

A review of recent evidence suggests that there is a higher risk of leukemia in children if their mothers were exposed to pesticides whilst pregnant, either from agricultural work, or from use of pesticides in their homes and gardens (Alavanja et al. 2013). Early life exposure to certain substances is suspected to be a significant additional risk factor for various childhood leukemias. Given that rates of certain childhood cancers have been increasing since the 1970s, the potential for increased risk arising from exposure to pesticides is clearly of substantial concern.

EXPOSURE TO PESTICIDES AT WORK

Van Maele-Fabry et al. (2010) analysed the results of 10 studies detailing work-related exposure to pesticides in women before, during and after pregnancy and the health outcomes of their children. Occupational exposure to pesticides in mothers was associated with an increased risk of their children developing leukemia. The risk for developing leukemia was reported to be 1.6 fold greater than for children whose mothers were not exposed to pesticides in their work.

A meta-analysis of literature describing maternal and paternal occupational exposure to pesticides and links with childhood leukemia examined pesticides by broad group, i.e., insecticide, herbicide etc. (Wigle et al. 2009). This analysis found that childhood leukemia was associated with prenatal maternal exposure in all studies, although links to paternal exposure were weaker and less consistent. The increased risk of children developing leukemia after maternal occupational exposure to insecticides had an odds ratio of 2.7 times in comparison to non-exposed children. For those exposed to herbicides the odds ratio was increased to 3.6.

EXPOSURE TO PESTICIDES IN THE HOME AND GARDEN

Turner et al. (2010) analysed the findings of 15 studies that examined home and garden use of unspecified insecticides and herbicides and the link to childhood leukemia. Taken together, these studies suggested that, if mothers were exposed to these substances during pregnancy, there was an increased risk of their children developing leukemia. For example, the likelihood of a child developing leukemia as a result of their mothers being exposed to insecticides was 2 times greater than for children whose mothers did not use pesticides in the home.

OTHER CANCERS

There is some evidence to suggest that pesticide exposure during pregnancy may elevate the risk of cancer of the brain and bones in children (Wigle et al. 2009). Exposure of fathers to pesticides (broadly grouped in a meta-analysis) at work, or at home, has also been associated with increased risk of brain cancer in children, possibly due to pesticide-induced genetic damage to paternal germ cells (which produce sperm), or from household contamination with pesticides brought home on the father's work clothes (Vinson et al. 2011). In their meta-analysis of 40 studies, Vinson et al. (2011) also note that exposure to pesticides has been associated with increased risks of childhood leukemia and lymphoma.

Flower et al. (2004) identified 50 childhood cancers (from a total of 17 357 children) and suggested that parental exposure to pesticides at work was associated with an increased incidence of all cancers, including lymphomas, e.g. Hogkin's lymphoma. Of the 16 specified pesticides used by fathers prenatally, aldrin, dichlorvos and ethyl dipropylthiocarbamate were thought to increase the odds of cancer in children, although results were based on small sample sizes.

2.1.4 Miscarriage and Preterm Delivery

Several studies have suggested that exposure to pesticides at work whilst pregnant may lead to miscarriage, but the evidence is as yet inconclusive. Research suggests that it may be the lipophilic nature (tendency to combine with fats) of organochlorine pesticides that disturbs the normal estrogen-progesterone balance which is particularly important in the maintenance of pregnancy (Sharma et al. 2012). Pathak et al. (2009) reported that high β -HCH levels in cord blood were associated with pre-term labour, and Pathak et al. (2010) also suggested that high γ -HCH levels are associated with a higher risk of recurrent miscarriage.

Bretveld et al. (2008) studied women in the Netherlands working in flower greenhouses where large amounts of pesticides such as abamectin, imidacloprid, methiocarb, deltamethrin and pirimicarb were routinely used. These substances are all currently approved for use in the EU. The study reported that the risk of miscarriage among these women was increased 4-fold.

Text Box 3.

Pesticides may affect future generations through gene expression

Experimental studies have shown that some substances can promote the inheritance of disease through epigenetic transgenerational inheritance. Epigenetics is the study of inherited changes in gene expression (switching on/off of genes) that occur without changes in the DNA sequence.

In the case of disease, a pregnant female, if exposed to substances such as permethrin or DEET, may not only have an increased likelihood of disease herself but may also transmit an increased risk to her grandchildren, even if they have never been exposed to these toxins. This has been observed experimentally in animals, and is likely to be linked to this switching on or off of certain genes (Manikkam et al. 2012). Anway and Skinner (2006) reported that exposure of rats to vinclozolin (anti-androgenic fungicide) had significant negative effects to the subsequent four generations of offspring. This is also mechanistically possible in humans and a number of studies have noted that pesticides do affect patterns of gene expression (Collota et al. 2013). It is, therefore, possible that this is one of the mechanisms by which pesticides can affect human health.

2.2 Pesticides and Cancers in Adults

The Agricultural Health Study (AHS) was initiated in 1993 to study potential impacts of pesticides on farmers, pesticides applicators and their families in Iowa and North Carolina, USA (Alavanja et al. 1996). Both cancer and non-cancer health risks were monitored over many years in approximately 75,000 people, 77% of which were registered pesticide applicators. The AHS has received criticism from a number of scientists due to the inability to quantify firmly the exposure intensity and other confounding factors such as lifestyle and the mixtures of substances that these workers were exposed to. Also, the numbers of incidences of these cancers as sometimes small in the sample observed, such that the scientific robustness of the studies has been called into question. However, a review of evidence from the published studies relating to the AHS suggested that work-related exposure to 12 pesticides was related to an increased risk of developing all types of cancers (Weichenthal et al. 2010). Animal toxicity experiments also support the biological plausibility of carcinogenicity in a number of pesticides, including alachlor, carbaryl, metolachlor, pendimethalin, permethrin and trifluralin (Weichenthal et al. 2010).

Whether a given pesticide causes an increased risk of a particular cancer is very difficult to ascertain in that there are often multiple confounding factors involved in any experiment or population study. Nevertheless, Alavanja et al. (2013) states that, given evidence from studies relating to both the AHS and other robust literature on pesticides and their association with cancer, there is a significant public health problem linked to the use of pesticides. Furthermore, there is evidence to suggest that the risk of contracting cancer may be elevated not just for pesticide applicators, but also for the general population when living in the areas of higher environmental pesticide exposure (Parrón et al. 2013).

Whilst direct causal evidence relating pesticide exposure to cancer therefore remains somewhat equivocal, there do seem to be patterns of association between certain pesticides and a number of cancers (Table 1). These substances are designated with various WHO classifications from 'risk unlikely' to 'extremely hazardous'. However, none are clearly classed as having carcinogenic properties. This highlights the difficulty in providing unequivocal evidence in order to change policy, and many of these substances continue to be used in agriculture.

Table 1. Pesticides with a significant association with particular cancers in farm workers/pesticide applicators in literature published as a result of the Agricultural Health Society (Weichenthal et al. 2010), and WHO classification as stated in the IUPAC Pesticides Properties Database*. WHO classification is denoted by U = unlikely to cause harm, O = obsolete, SH = slightly hazardous, MH = moderately hazardous, EH = extremely hazardous. Data on restrictions in Europe based on that given by European Commission EU Pesticides Database**.

Pesticide	Class	Type of cancer	WHO classification	Restricted in Europe
Alachlor***	OCP	all lymphohematopoietic****	MH	Yes
Aldicarb***	carbamate	colon	EH	Yes
Carbaryl***	carbamate	melanoma	MH	Yes
Diazinon***	OPP	all lymphohematopoietic, lung and leukemia	MH	Yes
Dicamba***	Benzoic acid	lung, colon	MH	No
Dieldrin	Chlorinated hydrocarbon	lung	O	Yes
Chlordane	OCP	rectal, leukemia	MH	Yes
Chlorpyrifos***	OPP	all lymphohematopoietic, lung, rectal, brain	MH	No
EPTC*** (S-ethyl-N,N-dipropylthiocarbamate)	thiocarbamate	leukemia, colon, pancreatic	MH	Yes
Fonofos	OPP	leukemia, prostate (for applicators with family history)	O	Yes
Imazethapyr***	Imidazolinone	colon, bladder	U	Yes
Metolachlor***	chloroacetamide	lung	SH	Yes
Pendimethalin***	dinitroaniline	lung, rectal, pancreatic	MH	No
Permethrin***	Synthetic pyrethroid	multiple myeloma	MH	Yes
Trifluralin***	dinitroaniline	colon	U	Yes

* <http://sitem.herts.ac.uk/aeru/ppdb/en/index.htm>

** http://ec.europa.eu/sanco_pesticides/public/?event=homepage&language=EN

*** Evidence of carcinogenicity noted in March 2009 by US Environmental Protection Agency where pesticide displayed a significant exposure-related response relationship with at least one cancer.

**** Includes all lymphomas, leukemia and multiple myelomas.

2.2.2 Prostate Cancer

Several studies, including research on agricultural workers, suggest that increased risk of prostate cancer may be associated with pesticide use, particularly OCPs (Band et al. 2010). The risk of prostate cancer was greater for those exposed to OCPs who also had a family history of the disease (Alavanja et al. 2003; Alavanja and Bonner 2012; Mills and Shah 2014).

2.2.3 Lung Cancer

As most of all lung cancer is related to cigarette smoking, it is particularly difficult to study the impact of other substances. Therefore, studies must adjust for the effect of smoking to identify the contribution of other chemicals. In general, although it is suspected that agricultural workers smoke less than other population groups as a result of their outdoor and physical lifestyle, in the case of prolonged exposure to certain pesticides (e.g. chlorpyrifos), there is some evidence to suggest that these workers suffer a higher incidence of lung cancer (Lee et al. 2004a; Lee et al. 2004b; Alavanja and Bonner 2012).

2.2.4 Rare Cancers

There are certain, more rarely diagnosed, cancers for which there is some evidence of association with various occupational health hazards. Amongst the many other substances that people are exposed to, long-term occupational use of pesticides is thought to be associated with increased risk of multiple myelomas, bone sarcoma and Ewing sarcoma that develops in the bone and surrounding tissues (Merletti et al. 2006; Perrota et al. 2008; Vinson et al. 2011; Pahwa et al. 2012; Charbotel et al. 2014). Some incidence of Hodgkin's disease (a lymphomal cancer) may also be related to pesticide exposure, particularly from chlorpyrifos (Khuder et al. 1999; Orsi et al. 2009; Karunanayake et al. 2012).

Leukemias (blood cancers) are a diverse group of cancers and, whilst there is less knowledge on the types of pesticides that are associated with specific forms of the disease, it is thought that there may be some association between occupational exposure to pesticides in general and acute myeloid leukemia (Van Maele-Fabry et al. 2007; Alavanja et al. 2013). This type of leukemia is, though rare, the most common type to affect adults. Increased risk of another rare disease, hair-cell leukemia, is also thought to be associated with occupational exposure to OCPs and OPPs (Orsi et al. 2009).

2.2.5 Genetic Susceptibility

The mechanisms by which pesticides can cause cancer are numerous. Direct damage to the DNA (genotoxicity) is thought to occur in agricultural workers in contact with organophosphates, carbamates, pyrethroids and complex pesticide mixtures, though there may also be other mechanisms involved (Bolognesi 2003; Bolognesi et al. 2011). Some people within a population may be at a greater risk than others due to variations in their genetic characteristics. There are several genes which code for enzymes known to detoxify pesticides, and others that are specifically involved in DNA repair. Some individuals carry variants of these genes that code for enzymes that are not as effective and, as a consequence, their bodies are less able to cope with these chemicals when exposure occurs. This is thought to be part of the mechanism involved in putting some individuals at a greater risk of developing cancer than others, though uncertainties in this field remain high.

Alavanja et al. (2013) noted that the genetic susceptibility to the cancer-causing (carcinogenic) effects of some pesticides appears to be an important aspect of the disease mechanism. Furthermore, individuals with this genetic susceptibility are common throughout current human populations, such that identifying them and attempting to eliminate their exposure is not a practical option.

Text Box 4.

Increased susceptibility to DNA damage in some farmers

The increased susceptibility of some people to pesticide exposure was, for example, reported as part of a study on fruit farmers in Central Taiwan (Liu et al. 2006). These farmers were exposed to almost 30 different pesticides in their daily work. The study investigated whether the farmers' exposures to pesticides were related to observed levels of DNA damage, and whether any farmers were more susceptible to DNA damage due to certain variations in their genes.

It is known that one particular family of genes, known as the GST genes, code for enzymes which detoxify organic substances, including various pesticides. The research by Liu et al. (2006) on farmers indicated that **individuals who carried a GST gene variant (known as GSTP1 Ile-Ile) were at a greater risk of DNA damage**, particularly if they were amongst the most highly exposed groups.

2.3 Pesticides and Damage to the Nervous System

Many pesticides, particularly insecticides, are specifically designed to target the nervous systems of pests. For this reason, these substance can also be neurotoxic to non-target animals, including (in some cases) humans and other mammals (Bjørning-Poulsen et al. 2008). The neurodevelopmental effects of significant pesticide exposure on children are well documented. The link between pesticides and certain neurodegenerative diseases in adults is less well known, though it is thought that their development may be due to a combination of both environmental factors and genetic predisposition. Whilst aging almost certainly represents the greatest risk factor, low-dose/long-term exposures to pesticides have been implicated as a further factor. Understanding the underlying mechanisms in the inter-play between such environmental and genetic components is an important area of future research (Baltazar et al. 2014).

2.3.1 Parkinson's Disease

Parkinson's disease is a common neurodegenerative disease that is characterized by neuron loss in the mid-brain. Movement-regulating cells in this area of the brain are disabled, causing the person to suffer from tremors and slow movement, balance problems and sometimes behavioral changes (Chhillar et al. 2013). The causes of Parkinson's disease are complex – it is associated with aging, gender and genetic factors, upon which environmental factors such as pesticide exposures are superimposed (Wang et al. 2014).

Several studies have, nevertheless, found that exposure to pesticides in farm workers and pesticide sprayers is statistically associated with an increased risk of developing Parkinson's disease (Van Maele-Fabry et al. 2012). Van der Mark et al. (2012) reviewed 46 studies on the association between pesticides and Parkinson's disease, concluding that summary risk estimates strongly suggest that the risk of developing Parkinson's disease is increased by exposure to pesticides, particularly herbicides and/or insecticides.

Chlorpyrifos and OCP insecticides may have a stronger influence on Parkinson's disease development, although just as with establishing a link with exposure and cancer, it is difficult to establish a causal relationship definitively (Elbaz et al. 2009; Freire and Koifman 2012). In a population living in northern India, higher than average levels of β -HCH and dieldrin were found in the blood in populations associated with an elevated risk of Parkinson's disease (Chhillar et al. 2013).

In a study in an agricultural region of California, exposure to OPPs as a result of living or working in the area was also reported to be associated with an increased risk of developing Parkinson's disease (Wang et al. 2014). All 26 OPPs that were assessed by this study were associated with an increased risk of developing the disease. Pezzoli and Cereda (2013) suggested that occupational exposure to the herbicide paraquat is also associated with a 2-fold risk for developing Parkinson's disease; this substance is still registered for use in many countries around the world, though is now banned in the US and Europe.

GENETIC SUSCEPTIBILITY AND PD

As with cancer, population level studies have reported that people with particular variants of genes that are involved in breaking-down pesticide chemicals in the body are more susceptible, in that they have a greater risk of developing Parkinson's disease after exposure to pesticides. These genetic variants are common within the human population.

Fong et al. (2007) reported that farmers in southwestern Taiwan with a variant of two particular genes (MnSOD and NQO1) have an increased risk of Parkinson's disease compared to the general population. Those with variants of these genes make defective enzymes and this may increase the risk of brain tissue damage leading to increased susceptibility to Parkinson's disease. This risk of developing Parkinson's disease for these people is increased 2.4-fold compared to people with normal genes. Farmers with particular variant of both genes had a 4-fold risk of developing Parkinson's disease.

Another enzyme, paroxonase 1, which is coded for by the gene PON1, is key in detoxifying organophosphate pesticides in the body (Manthripragada et al. 2010). Those with certain variants of the PON1 genes are common within the general population. These people are less efficient at detoxifying organophosphates. Again, individuals living and working in an agricultural region of California and who had a particular variant of both genes had the highest likelihood of developing Parkinson's disease (2.8-3.5 times greater than those with normal genes that live outside the region with no exposure to pesticides) (Lee et al. 2013b).

Variations in the GSTP genes (particularly GSTP-1) may also produce proteins that, instead of detoxifying particular pesticides, may actually increase the toxicity of the substrate and form a more toxic metabolite with the potential to cause further damage in the brain. In these cases, those with certain GSTP-1 variations also have a higher susceptibility to Parkinson's disease (Menegon et al. 1998).

PESTICIDES IN THE HOME AND PD

As well as occupational use of pesticides, those using them in and around the home may be more susceptible to Parkinson's disease as a result of this exposure. Narayan et al. (2013) found that use of pesticides in the homes of the US public, specifically OPPs, was associated with a 70-100% increased odds of developing Parkinson's disease. Again, frequent users of organophosphate pesticides in the home that carried a particular variant of the PON1 gene had a 2.6-3.7 times higher risk of developing Parkinson's disease.

2.3.2 Dementia and Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia. Genetic factors account of up to 70% of the risk associated with contracting AD, as well as obesity, smoking, inactivity, hypertension and diabetes (Ballard et al. 2011). In addition to these well-known factors, there is an emerging body of evidence to suggest that exposure to certain pesticides, particularly chronic exposure to OPPs, may contribute to the risk of developing AD (Zaganas et al. 2013). For example, some studies have shown that there is an increase in cognitive, behavioural and psychomotor dysfunction with increased long-term exposure (Costa et al. 2008). Risks of vascular dementia, another common form of dementia, may also be increased by pesticide exposure. As with other degenerative diseases, there appears to be a genetic susceptibility to these types of dementia and pesticide exposure, most probably as a result of the role of detoxifying enzymes and their encoding by particular genes (Zaganas et al. 2013).

2.3.3 Other Nervous System Impacts

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

ALS is a rare condition affecting 1-2 people per 100,000 and is a rapid neurodegenerative disease where the motor neurons of the brain and spinal cord are affected. Around 10% of cases have a family history, but environmental factors such as exposure to solvents, metals and OCPs are thought to increase the risk of developing the disease (Kamel et al. 2012). Acute poisoning by OPPs may also be linked to the development of ALS, and further research is required in order to focus on quantifying the exposure of people to different pesticide classes and to test the strength of correlation with development of the disease (Baltazar et al. 2014).

GENERAL IMPAIRED NEUROLOGICAL FUNCTION

Farm workers who spray pesticides are sometimes involved in incidents in which they are accidentally exposed to high levels of pesticides. Such 'high pesticide exposure events' (HPEEs) can be relatively common amongst pesticide applicators. This may occur as a result of equipment malfunction, poor working practices during mixing, loading or applying pesticides or during repair of equipment (Starks et al. 2012a). Individuals in the Agricultural Health Study (US) who had a history of such HPEEs (broadly categorised as 'pesticides') recorded, on average, slower responses in two neurobehavioral tests of visual scanning. Starks et al. (2012a) concluded that these events may be associated with long-term adverse neurological function.

Farm workers and pesticide applicators who have worked for some time in their occupations may be subjected to lower-level yet long-term pesticide exposure. This exposure, particularly to organophosphate pesticides, may adversely affect both the central nervous system (brain and spinal cord) and peripheral nervous system (nerves which connect the organs and limbs to the brain and spinal cord). Ismail et al. (2012) reviewed 17 published studies that together suggested that chronic low-level exposure to OPPs in agricultural workers may be related to adverse effects on brain functioning, including changes in attention, speech, sight, memory and emotional aspects (including incidence of conditions such as depression).

Starks et al. (2012b) reported that long-term exposure to ten OPPs was associated with poorer peripheral nervous system function assessed using certain medical tests. In particular toe proprioception (the inability to sense whether the toe is being moved up or down when the eyes are closed) was linked with a history of use of the pesticides chlorpyrifos, coumaphos, dichlorvos, fonofos, phosmet and tetrachlorvinphos.

These results are consistent with the findings of a meta-analysis of 14 studies (1600 participants),

all coherently designed to statistically test the association between low-level organophosphate exposure and impaired neurological function (Mackenzie Ross et al. 2013). This review stated that these studies found significant, small to moderate impacts on cognitive functions (particularly psychomotor speed, memory, visuospatial abilities) as a result of prolonged, yet low-level, organophosphate exposure. Further, Mackenzie Ross et al. 2010, found significant deficits in neurological functioning in sheep farmers exposed, at low-levels, to organophosphates through routine parasite control ('sheep-dips'). The impact of these substances, particularly at low exposure levels had hitherto been underestimated and this has serious implications for those working in other industries such as in aviation where aircraft fuel is mixed with a number of organophosphates used as lubricants.

2.4 Immune System Impacts

Results from the numerous studies conducted on the immunotoxicity of pesticides paint a complex picture. Differing experimental design, challenges in the identification of suitable control (non-exposed) groups and difficulties in accurately quantifying pesticide exposure make inferring causation problematic. However, studies in animals do suggest that the immune system may be an additional target of pesticide action, through mechanisms of relevance also to humans, leading either to an increase in hypersensitivity to certain chemical (immunostimulation) or in some cases to immunosuppression, particularly in children (Corsini et al. 2013).

For example, there is some evidence to suggest that occupational exposure to multiple agricultural chemicals may be linked to both onset of allergic asthma and allergic rhinitis, although results are rather inconclusive (Corsini et al. 2013). For example, those farm workers involved in the Agricultural Health Study in the US, were assessed to have a 2-fold increase risk of developing asthma, with the implication that this may have been linked

to elevate exposure to a number of pesticides, including coumaphos, heptachlor, parathion, ethylene bromide and mixtures comprising carbon tetrachloride and carbon disulphide (Hoppin et al. 2009). In addition, Slager et al. (2010) reported that use of the pesticides glyphosate, diazoxon, chlorpyrifos, dichlorvos, malathion, carbaryl, permethrin and captan may contribute to increased episodes of allergic rhinitis in farmers. The use of specific pesticides (pendimethalin and aldicarb) may exacerbate symptoms in those already known to be asthma sufferers (Henneberger et al. 2014)

Autoimmune diseases that may potentially be linked to home and work-related pesticide exposure in postmenopausal women include rheumatoid arthritis and systemic lupus erythematosus (Parks et al. 2011).

2.5 Hormone System Impacts

2.5.1 Thyroid Disease

Experimental research has indicated that many pesticides are endocrine disruptors that can disturb the functioning of various hormones throughout the body (Mnif et al. 2011; Mandrich et al. 2014). Thyroid hormone production is thought to be inhibited by substances such as amitrole, cyhalothrin, fipronil and pyrimethanil. Floriculture workers who were exposed to various OPPs, showed altered levels of thyroid hormones in their bodies (Lacasaña et al. 2010).

Other pesticides may also alter thyroid hormone levels and potentially lead to thyroid disease. In the US Agricultural Health Study, wives of pesticide applicators living and/or working in an agricultural region had increased levels of thyroid disease compared to the general population (Goldner et al. 2010). The increased incidence of thyroid disease in these women was thought to be linked to their exposure to various organochlorine insecticides and the fungicides benomyl and maneb/mancozeb (carbamates).

In an area of Brazil that has been shown to be heavily contaminated with OCPs, Freire et al. (2013) found that, within the study population of 608 adults (303 men, 305 women), there was an increased prevalence of hyperthyroidism. There were also gender-specific differences; whereas women showed higher levels of thyroid hormones, the levels in males were actually lower than observed in the general population.

2.5.2 Pesticides and Sex Hormones

Experimental studies conducted in vitro (in a test-tube or cell-line culture) support observations that the balance of sex hormones can be disrupted by exposure to certain pesticides (Kjeldsen et al. 2013). Andersen et al. (2008) reports that the sons of women that have been exposed to pesticides whilst pregnant during their work in greenhouses can suffer impaired development. Conversely, girls whose mothers worked in greenhouses in Denmark during the first trimester of pregnancy have been shown to develop breasts earlier than in other populations, even though hormone levels appeared similar when the girls reached school age (Wohlfahrt-Veje et al. 2012).

There is also evidence that fertility of both men and women may be reduced with increased pesticide exposure (Abell et al. 2000; Oliva et al. 2001). This may be a particular problem for those people who have existing genetic or medical factors that have already compromised their fertility.

2.6 Pesticide Poisoning

The data available are too limited to allow a full analysis of the full health impacts of pesticides due to chronic exposures, despite the large amount of evidence of serious impacts. In 2002, however, deliberate self-poisoning by pesticides was estimated to have resulted in 186,000 deaths, although some estimates placed this as high as 258,000 (Pruss-Ustun et al. 2011). In 2002, intentional (suicidal) poisoning from pesticides accounted for approximately one third of the world's suicides, and in 2004, 71% of the unintentional poisonings were considered preventable through improving chemical safety methods (WHO 2008; Gunnell et al. 2008). The group most at-risk from unintentional pesticide poisoning are children, especially between the ages 0-4 years (Perry et al. 2014). In the case of fatalities caused by insecticide poisoning, most were due to ingestion of OPPs. Severe cases of OPP poisoning are manifest in 'cholinergic syndrome' where various central nervous system effects include blurred vision, headache, slurred speech, coma, convulsions and blocking of the respiratory centre. In some cases poisoning can induce delayed neuropathy where nerve cells degenerate over time, though the mechanism by which this occurs is not well understood (Bjørning-Poulsen et al. 2008). In this sense, there is strong evidence that survivors of acute OPP poisoning may suffer long-term adverse effects to the nervous system.



Pesticide spraying in Yunnan / China
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3. Industrial Agriculture - Impact On Wild Habitats



Monoculture landscape in France.
© Greenpeace/ Emile Loreaux

The focus of this report is the threat to human health posed by pesticides, both during use and as a wider consequence of that use. This threat is, of course, by no means the only problem arising from our current over-reliance on pesticides and the unsustainable systems of industrial farming which they are used to underpin.

Pesticides released into the environment have long been known also to impact on many species groups throughout the environment. The widespread use of organochlorine pesticides in the 1960s and 70s caused dramatic declines in wildlife populations in many parts of the world, perhaps most vividly illustrated by the documented impacts on and declines in birds of prey (Köhler et al. 2013). DDT, dieldrin and other toxic organochlorine pesticides that impacted birds and other wildlife at that time, have subsequently been banned from agricultural use. Since then, however, declines in the populations of birds and wild bees, as well as changes in aquatic communities (Beketov et al. 2013; Kennedy et al. 2013; Hallmann et al. 2014) have been linked to the widespread and repeated application of newer generations of pesticides brought in as replacements. Pesticides are found in every habitat on earth and are routinely detected in both marine and terrestrial mammals (Carpenter et al. 2014; Law 2014).

The spread of industrial farming methods in Europe has caused widespread loss of wildlife habitat on farms for a variety of reasons, not just because of the industrial scale use of pesticides. Hedgerows, woodland, and field margins, which were

once nesting and foraging habitat for many species, have been destroyed in pursuit of larger field sizes characteristic of industrial agriculture. The loss of this habitat has compounded the decline of many species including bees, other pollinators, predatory invertebrates and farmland birds (Kennedy et al. 2013; Goulson 2014; Hallmann et al. 2014; Allsopp et al. 2014).

Insecticides may not only kill the target pest species but also other invertebrate species, on which birds rely on for their food. Furthermore, herbicide applications designed to control weed species can also kill many beneficial plant species in fields, both within and bordering crops, species that provide both shelter and food for birds and other wildlife.

Amphibians are now considered to be the most threatened and rapidly declining species group on the planet and are fast disappearing from habitats on a global scale. Research by Brühl et al. (2013) has suggested that frogs are extremely sensitive to the toxic impacts of pesticides at levels that are currently used in agriculture.

Christin et al (2013) sampled northern leopard frogs, a species within the most common frog group of North America, and found that those individuals that were living in agricultural regions (mainly intensively grown corn and soya) were smaller and had altered immune systems that made them potentially more vulnerable to disease and infections.

These are just a few illustrative examples of the impact of pesticide pollutants on wildlife and ecosystems, issues which are explored further in other reports. It is evident, however, that while the need to provide a greater protection for humans from pesticide exposure is in itself a compelling reason to move towards a more sustainable system of ecological farming, it is by no means the only justification for such a shift, nor the only benefit which would arise.

4. Conclusions



Various Pesticides Packages
Collected from Asparagus
Lettuce Fields in Hebei / China
© Greenpeace / LiGang

The health of agricultural workers and of the wider public, including children, is being threatened by the pesticides used in agricultural areas and potentially by those found in the food we consume.

There is widespread evidence that exposure to certain pesticides is a significant additional risk factor in many chronic diseases, including different forms of cancer, neurodegenerative diseases such as Parkinson and Alzheimer's, and diseases of the newborn. There is also circumstantial evidence that pesticide exposure is associated with disruption in the immune system and hormone imbalances. Though there are inherent problems in conducting large-scale experiments and directly assessing causation of these human health problems, the statistical associations between exposure to certain pesticides and the incidence of some diseases are compelling and cannot be ignored. The mechanisms by which these chemicals may induce disease may not yet be fully understood, though research suggests key roles for the impairment of the function of detoxifying enzymes, as well as impacts mediated through ion channels and receptors throughout the body (Mostafalou and Abdollahi 2013).

Moreover, some members of the population have an inherent genetic susceptibility to the health effects of pesticide exposure and are therefore likely to be more at risk than others. The challenges involved in identifying such differences and developing policy approaches which can ensure a high level of protection for everyone may

well remain insurmountable for as long as we continue to rely on routine application of pesticides.

Furthermore, future generations that have not been exposed to these substances may also be at risk of these diseases due to epigenetic transgenerational inheritance.

Many synthetic pesticides used in agriculture are persistent and pervasive in the environment and, as a result, we are exposed to a cocktail of chemicals through the food we consume and the environment in which we live. Evidence suggests that much of this exposure is presented as multiple mixtures of chemicals, the toxic effect of which are unknown, particularly over longer time scales (Reffstrup et al. 2010). In some cases these substances can interact such that mixtures may have unpredictable and higher toxicities than the individual components themselves. Whilst attempts have been made to describe the toxicity of these interactions, there are no accepted international guidelines in evaluating such risks. Pesticides are, of course, not the only hazardous chemicals to which our bodies are exposed on a daily basis.

There is, therefore, a compelling case and an urgent need to reduce and, wherever possible, avoid human exposures to hazardous chemicals. In the case of agrochemicals, this will require us to fundamentally rethink and change our farming systems to eliminate our exposure to synthetic pesticides and protect the health not only of particularly highly exposed and/or vulnerable groups, such as agricultural workers and children, but also the general population and wild ecosystems.

5. The Solution



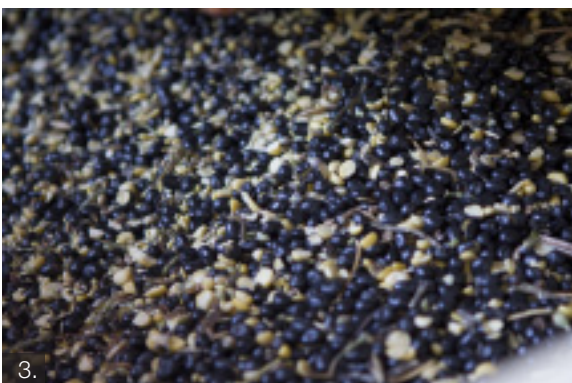
Vegetables on an organic farm in Hungary.
© Greenpeace / Bence Jardany

Strategies to simply reduce the use of selected pesticides will not be protective of human health as there is such a vast range of pesticides that are implicated in adverse effects on health and ecosystems in general. Phasing out the use of synthetic pesticides completely – in moving away from industrial agriculture – and moving to the implementation of ecological farming is crucial in avoiding these risks.

Crops must be protected through a multi-level approach that increases heterogeneity of the landscape so as to provide habitat for pollinators and natural pest control species. This functional biodiversity can be increased through active vegetation management. Diversity of crop types and cultivars, rotation and fallowing increases the fertility of soils and increases resistance to pests. Natural bio-control agents such as beneficial bacteria, viruses, insects and nematodes have been used successfully in improving crop protection (Forster et al. 2013).

NATIONAL AND GLOBAL STRATEGIES SHOULD INCLUDE:

1. Phase out the use of synthetic-chemical pesticides in agriculture.
[Priority should be given to banning pesticides that have carcinogenic properties, are mutagenic or toxic to reproduction (CMRs category I and II), and interfere with the hormone system (EDCs) as well as chemicals with neurotoxic properties].
2. Ensure proper implementation of the Sustainable Use Directive.
[By making sure that member states put in place concrete national measures and targets leading to a substantial reduction in the use of chemical pesticides in agriculture].
3. Improve the EU risk assessment process for pesticides.
[Ensure that safety controls take into account all direct and indirect, medium and long term health and environmental impacts caused by the exposure to cocktail of chemicals].
4. Shift public research spending to ecological farming contributing to the concrete uptake of ecological farming practices by farmers. [Moving away from the current reliance on synthetic-chemicals towards biodiversity-based tools controlling pests and enhancing farmlands and ecosystems' health].



1: Organic apples on a market in Germany © Greenpeace / Sabine Vielmo
2: Close-up of potatoes in ecological shop in Friesland / Netherlands © Greenpeace / Ben Deiman
3. Ecological broad beans, protein plants in Greece © Greenpeace / Panos Mitsios
4. Vegetables on an organic farm in Hungary © Greenpeace / NAGY Szabolcs

Ecological Farming

Ecological agriculture is the only effective and workable solution to protect human health and the environment. Ecological farming is already being successfully practiced in many areas of the world and world experts agree that agriculture must become more sustainable. The recent increase in organic farming practices in Europe demonstrates that farming without pesticides is entirely feasible, scalable, economically profitable and environmentally safe. Land under organic cultivation increased from 5.7 million hectares in 2002 to 9.6 million hectares in 2011, and includes arable crop and orchard as well as animal sectors (European Commission, 2013).

Food produced by ecological farming is safe for our health. No synthetic chemical pesticides are used and sustainable practices boosts plant and animal (functional) biodiversity in agricultural landscapes.

With the implementation of ecological farming it is possible to create a toxic free future and a safer environment for children. Implementation of ecological farming across the world will provide the ability for communities to feed themselves and ensures a future of healthy farming and healthy food to all the people.

Greenpeace seven principles of ecological farming are:

1. FOOD SOVEREIGNTY
2. REWARDING RURAL LIVELIHOODS
3. SMARTER FOOD PRODUCTION AND YIELDS
4. BIODIVERSITY
5. SUSTAINABLE SOIL HEALTH
6. ECOLOGICAL PEST PROTECTION
7. RESILIENT FOOD SYSTEMS



Vegetables on an organic farm in Hungary
© Greenpeace / NAGY Szabolcs

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