

The Effect of Pesticides on Human Health and Environment

Negar Malekzadeh Moghaddam

2015

Biology department of BIHE

Supervisor : Shahram Berjis

Abstract

The use of toxic substance these days, like pesticides, is very popular all around the world especially in Third World countries. One can see pesticides not just in agriculture but in homes, schools, companies and lawns. Most of the people are in the exposure of these toxic substances without knowing anything about the effects on their health and their environment. As we use pesticides to kill bugs in our homes, spraying it easily all over the air, do we know the effects of them on human health? There are thousands of researches that show the different effects of pesticides on human and environment and also on animals. Gathering all of these effects together and presenting them to the readers is the goal of this paper. Scientists showed that there are lots of cancers and other diseases linked to pesticides. Besides, that they are dangerous for humans, can kill lots of animals, infect the water that we drink, and even our food. The awareness of these effects and diseases can help people to choose safe ways to kill the pests, or, by knowing each of the pesticide types, they can choose the one with the lowest toxicity and effects.

Table of content

Abstract	II
Table of content	III
List of figures.....	V
1. Introduction.....	1
2. Toxicity of pesticides.....	2
2.1 Acute and chronic toxicity.....	3
2.2 How are people exposed to pesticides?	4
2.3 Symptoms of pesticides poisoning	4
3. Pesticides groups.....	5
3.1 Insecticides	5
3.1. 1 Organophosphate.....	5
3.1. 2 Carbamates.....	7
3.1.2. A) Human exposure to carbamate residues	9
3.1.2. B) Risk assessment	10
3.1.3 Organochlorine.....	10
3.1.3 A) Influence of organochlorine pesticide on GH-IGF system	11
3.1.4 Pyrethroid and pyrethrins.....	12
3.1.4. A) Toxicity and symptoms	13
3.1.4. B) Treatment.....	14
3.2 Microbial biopesticides.....	14
3.2.1 What are the microbial biopesticides?.....	14
3.2.2 Why has there not been a higher uptake?	15
3.2.3 Bacteria	16
3.2.3. A) Introduction.....	16
3.2.3. B) Detailed example	16
3.2.4 Fungi	18
3.2.4. A) Introduction	18
3.2.4. B) Problem.....	18
3.2.4. C) Examples of fungal BCA.....	18
3.2.4. D) Future prospects	19
3.2.5 Virus	20
3.2.5. A) Introduction	20
3.2.5. B) Infection process	20
3.2.5. C) Classical control by the non-blocked baculovirus, orrycte rhinoceros virus.....	21
3.2.5. D) Future prospects	21
3.2.6 Nematode.....	21
3.2.6. A) Introduction	21
3.2.6. B) Advantages.....	22
3.2.6. C) General infection process	22
3.2.6. D) Classical control by Deladenussiricidicola	23
3.3 Plant- incorporated- protectants (PIPs)	23
3.4 Fungicides.....	25

3.4.1 Mobility in the plants	25
3.4.2 Role in the protection of plants.....	26
3.4.3 Breath of activity.....	26
3.4.4 Mode of action	26
3.4.5 Type of chemical	27
3.5 Herbicides.....	28
3.6 Rodenticides	29
3.6.1 Other rodenticides	31
3.6.1. A) Zinc phosphide.....	31
3.6.1. B) Bromethalin.....	31
3.6.1. C) Cholecalciferol.....	32
3.6.1. D) Strychnine	32
4. Effect of pesticides on human health and environment.....	33
4.1 Pollution of agricultural pesticides	33
4.1.1 Harmful human health and environmental effects	34
4.1.2 Causes of wrong use and/or risky use of agricultural pesticides	34
4.1.3 Strategies for reducing agricultural pesticide pollution	35
4.2 Non-cancer health effects.....	35
4.2.1 Asthma	35
4.2.2 Birth defect.....	39
4.2.3 Neurological effects	39
4.2.4 Hormone disruption	40
4.3 Cancer effects	42
4.3.1 Brain cancer.....	42
4.3.2 Breast cancer.....	43
4.3.3 Leukemia.....	43
4.3.4 Lymphoma.....	43
4.3.5 Prostate cancer	44
4.3.6 Soft tissue sarcoma	44
4.4 Effect on environment	44
4.4.1 Soil contamination	45
4.4.2 Water contamination	45
4.4.3 Effect on organisms.....	46
4.4.3. A) Soil organisms and processes.....	46
4.4.3. B) Soil invertebrates.....	46
4.4.3. C) Other soil species.....	47
4.4.3. D) Other non-target species.....	47
4.4.4 Aquatic life.....	48
4.4.5 Birds	51
5. Discussion	54
6. References	58
Appendix.....	66

List of figures:

Figure 1: Acute and Chronic exposure	3
Figure 2: How OPs can effect on nervous system	6
Figure 3: How Organochlroine passes through the food chain	9
Figure 4: Crystal of Bt toxin	14
Figure 5: Vine Weevil Adult	18
Figure 6: Steinernemakraussei	18
Figure 7: How PIPs work	20
Figure 8: Different kind of fungi, zone of their activity and application timing	22
Figure 9: How organophosphate can cause the ADHD disease	32
Figure 10: The contamination of water and soil by pesticides	35

Introduction

Pesticides are substances used for destroying pests—that includes any organisms considered harmful or troublesome to humans or to their property in some or all contexts— which can damage agricultural crops or can act as vectors to extend diseases. This includes any damaging, poisonous, or annoying insect, fungus, bacteria, organism, virus, rodent or other plant or animal. The Pesticide Management Regulatory Agency (PMRA) describes *pesticide* as “any product, device, organism, substance or thing that is manufactured, represented, sold or used as a means for directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest. Pesticide is a broad term that includes herbicides, insecticides, fungicides, antimicrobial agents, pool chemicals, microbial, material and wood preservatives, animal and insect repellents, and insect—and rodent—controlling devices” (The Policy and Research Committee 2003).

Because pesticides are marketed based on their toxic properties, they are the subject of particular health and environmental concerns. Probably the first known pesticide was elemental sulfur dusting used in Sumeria about 4500 years ago. In 15th century, toxic chemicals like arsenic, mercury, and lead were being applied to crops for killing pests. In 17th century Nicotine Sulfate was extracted from tobacco leaves and used as an insecticide. In the late 19th century synthetic organic chemicals appeared. The petrochemical industry, that today produces almost all such synthetic pesticides, first got started due to the near-extinction of whales in the 19th century. Also in 19th century two more natural pesticides, pyrethrum, which is taken from chrysanthemums, and rotenonem, taken from the roots of tropical vegetables, were introduced. But ecosystem’s pollution from pesticides is a more recent phenomenon. Before the World War II synthetic chemical pesticides were hardly used (Gupta 2008).

In the 1930s the use of synthetic pesticides began and became more general after the end of World War II. Nowadays there are several categories of chemical pesticides. From about 1945 to 1965, **Organochlorines** were used widely in all aspects of agriculture and forestry, for protecting wooden buildings and protecting humans from a vast diversity of insect pests. The other insecticides, **Carbamate**, came into use later; they are less widely used than the first. Their use is various; some are used more for forest protection, while others are used against potato and grain insect pests. In the 1970s the synthetic **Pyrethroid** group of insecticides came into existence. Synthetic pyrethroids are more stable to light and have an insecticidal activity about

ten times that of most organophosphates and carbamate insecticides. During the last two decades, because of their stability and activity, the use of pyrethroid increased, especially on fruits, vegetables, and corn. These chemicals have high insecticidal activity, so they allow applying just small amounts of them. (About 100g/Hectare).

Most of the groups above-mentioned are insecticides, but two of the best known pesticides, 2,4-D and 2,4,5-T, are Phenoxy herbicides. The first successful semi-selective herbicide to be expanded was 2,4-D [(2,4-dichlorophenoxy) acetic acid]. As well as the main chemical groups, there are many other pesticides on the market, such as aldehydes, amides, pyridil, isoxazol, etc.

From an environmental perspective, though some pesticides are species-specific, a great problem is that most of them don't differentiate between pests and useful organism. Pesticides can injure non-targeted species such as bees and birds, as well as soil and aquatic organisms. Pesticides have been known to move in the environment and have been found in nearby rivers and lakes (The Policy and Research Committee 2003).

Although there is no final epidemiological evidence proving that pesticides cause main health issues, there is a growing body of science that links pesticides with increased risk of reproductive problems, brain and nervous system affections, endocrine disruption and immune suppression disorder, and cancers, especially in children and old people (The Policy and Research Committee 2003).

In the Third World countries pesticides are very important to people and governments, and are used extensively both in agricultural and in public health programs. Almost 60% of the workers of these countries are employed in agriculture. Pesticides are used to control pests, so this percentage of people is in exposure of pesticides (Jeyaratnam 1985). Unfortunately most of these workers and their families don't know about the dangerous effects of pesticides, therefore I decided to write this paper and demonstrate not all, but most of these effects. I will present the human health and environmental effects, and the ways to reduce these risks.

Toxicity of pesticides

All the pesticides must be biologically active or toxic to be effective against the pests, and because of toxicity they are also hazardous to human health, animals and environment. So, the

people who use pesticides or regularly have contact with them must understand about their toxicity, potential health effects, and suppressive measures to reduce exposure to the products they use.

Pesticides consists of active ingredients—that is the part with the pesticidal effect, actually these chemicals kill living things—and inter ingredients which are mixed into the pesticide products as a carrier or sticking agent that are usually as toxic as the active ingredient itself. The measure of pesticide capacity or ability to cause injury or illness is called *toxicity*. The toxicity of a specific pesticide is determined by subjecting test animals to different dosages of the active ingredient. Depending on age, gender, individual sensitivity and other factors of people, the risk can be different for them. Although pesticides are intended to harm only target pest, if they are not used correctly they can be harmful for humans and the environment.

When users understand different levels of pesticides toxicity, they can reduce the potential hazard by selecting the pesticide with the lowest toxicity to control the pest.

Acute and Chronic Toxicity

There are two kinds of toxicity: acute and chronic. The chemical's ability to cause injury to a person or animal from a single exposure is referred to as an *acute toxicity*, and usually its effect is for a short time. Acute effects are the harmful effects that occur from a single exposure by any path of entry (Lorenz 2009). There are four paths of exposure: dermal or skin, inhalation or lungs, oral or mouth, and the eyes. Acute toxicity is measured as the concentration of a poison required to kill the 50 percent of the animals in a test population. This measure expressed as the lethal dose 50- LD_{50} or the lethal concentration 50 - LC_{50} . LD_{50} and LC_{50} are useful to compare the toxicity of different active ingredient and also different formulations that containing the same active ingredient. The lower the value of a pesticide product's LD and LC, the greater its toxicity to humans and animals. So, the pesticide with a high LD50 is least toxic to human if used according to the direction on the product label (Lorenz 2009). The *chronic toxicity* of pesticides is specified by subjecting test animals in long-term exposure to the active ingredient. The chronic effects are any harmful effects that are from small doses repeated over a period of time. The chronic effects from exposure to some pesticides consist of birth defects, toxicity to a

fetus, and production of benign or malignant tumors, genetic changes, blood disorders, nerve disorders, endocrine disruption, and reproduction effects. The chronic toxicity of pesticides is more difficult than acute toxicity to identify via laboratory analysis (Lorenz 2009).

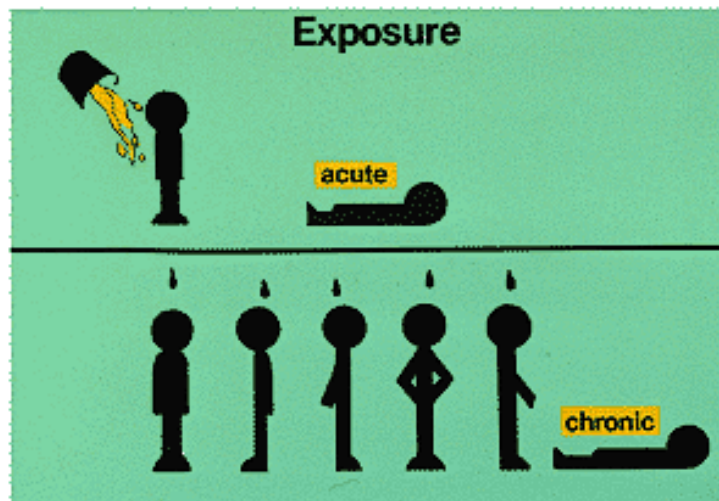


Figure 1

How are people exposed to pesticides?

In three ways people can be exposed to pesticides:

- **Breathing or inhalation exposure:** it can happen if you breathe air that has pesticide as a vapor, as an aerosol, or on small particles like dust.
- **Getting it into the mouth or digestive tract or oral exposure:** it can happen when you eat food or drink water that contains pesticide.
- **Contact with the skin and eyes or dermal exposure:** it can happen when your skin is exposed to pesticide. This can cause irritation and burns, and in the serious cases, the skin can absorb the pesticide inside the body and cause other health problems (California Department of Pesticide Regulation).

Symptoms of Pesticide Poisoning

The symptoms of pesticide poisoning can span from a gentle skin irritation to coma or even death. Different classes of chemicals can cause different types of symptoms. According to the level of chemicals, people can have a different sensitivity. The chemicals can cause very bad illnesses in some people. Due to possible health concerns, pesticide users and handlers should be able to recognize the common signs and symptoms of pesticide poisoning (Lorenz 2009).

The effect of pesticide poisoning can be widely specified as either topical or systemic. Topical effects usually expand at the site of pesticide contact, and are the result of the pesticide's irritant properties or an allergic response by the victim. The most commonly topical effect that is associated with pesticide exposure is inflammation or dermatitis of the skin. Reddening of the skin or rashes and/or blisters can be the symptoms of dermatitis. Some people "tend to cough, wheeze, or sneeze when exposed to pesticide sprays". Other symptoms are that eyes, mucous membranes of the nose, and even the sensitive linings of the mouth and back of the throat feel sore and scratchy. These symptoms normally come down in a few minutes after a person is removed from the exposure to the irritant. Symptoms of a true allergic reaction can be reddening and itching of the eyes and skin and also respiratory difficulty often like an asthmatic condition (Lorenz 2009).

Systemic effects are a little different from topical effects. They occur frequently far from the original point of contact as a result of the pesticide being absorbed into and distributed throughout the body. Systemic effects can include nausea, vomiting, fatigue, headache, and intestinal disorders. If the poisoning is very severe, the person may feel changes in heart rate, difficulty breathing, convulsion, and coma, which could cause death (Lorenz 2009).

Pesticides group:

Insecticides:

In the United States the greatest number of pesticide poisoning is caused by insecticides. These pesticides kill insects and other arthropods.

Organophosphate:

All the insecticides that contain phosphorus are called Organophosphate (Ops). All of them are derived from one of the phosphorus acids. Ops have two specific features, first they are generally more toxic to vertebrates than other classes of insecticides, second most are chemically unstable or non persistent. Organophosphate insecticide includes chlorpyrifos, diazinon, dimethoate, disulfoton, malathion, methyl parathion, and ethyl parathion. Many of organophosphates cause disorder in the nervous system. They affect the nervous system of insect

and also humans because there is a similarity between humans and insects in nerve impulse transmission.

To understand how is the effect of organophosphate on nervous system; we should actually understand how the nervous system works. The most complex system in the body is the nervous system that includes the brain, and millions of cells that make up a communications system inside the organism. Messages or electrical impulses move along this complex network of cells. The neurons or nerve cells don't physically touch each other; rather there is synapse or gap between them. The impulses must cross the synapses to keep the message moving along the whole network. When the impulse attains the synapse, the chemical acetylcholine is released to continue the message to the next cell. Acetylcholine is the first chemical that is responsible for transfer nerve impulses across the synapse of two neurons. After impulse is transmitted across the synapse, the acetylcholine is broken down by the enzyme cholinesterase. When this happens, the synapse is "cleared" and it is ready to receive a new transmission. Organophosphate insecticides block the activity of cholinesterase and so the concentration of acetylcholine rises up in the body. The result of acetylcholine increasing is that the nerve transmission between nerve cells will be an uncontrolled stream. The nervous system becomes "poisoned"; and the reposition of acetylcholine causes continues transmission of impulses across the synapses. The effect of organophosphate poisoning can result in systemic and topical symptoms. If the eye have a direct exposure for example, it will cause topical symptoms like constriction of the pupils, blurry vision, and eyebrow headache, and severe irritation and reddening of the eyes. Symptoms of systemic poisonings are almost completely due to the accumulation of acetylcholine at the nerve endings.

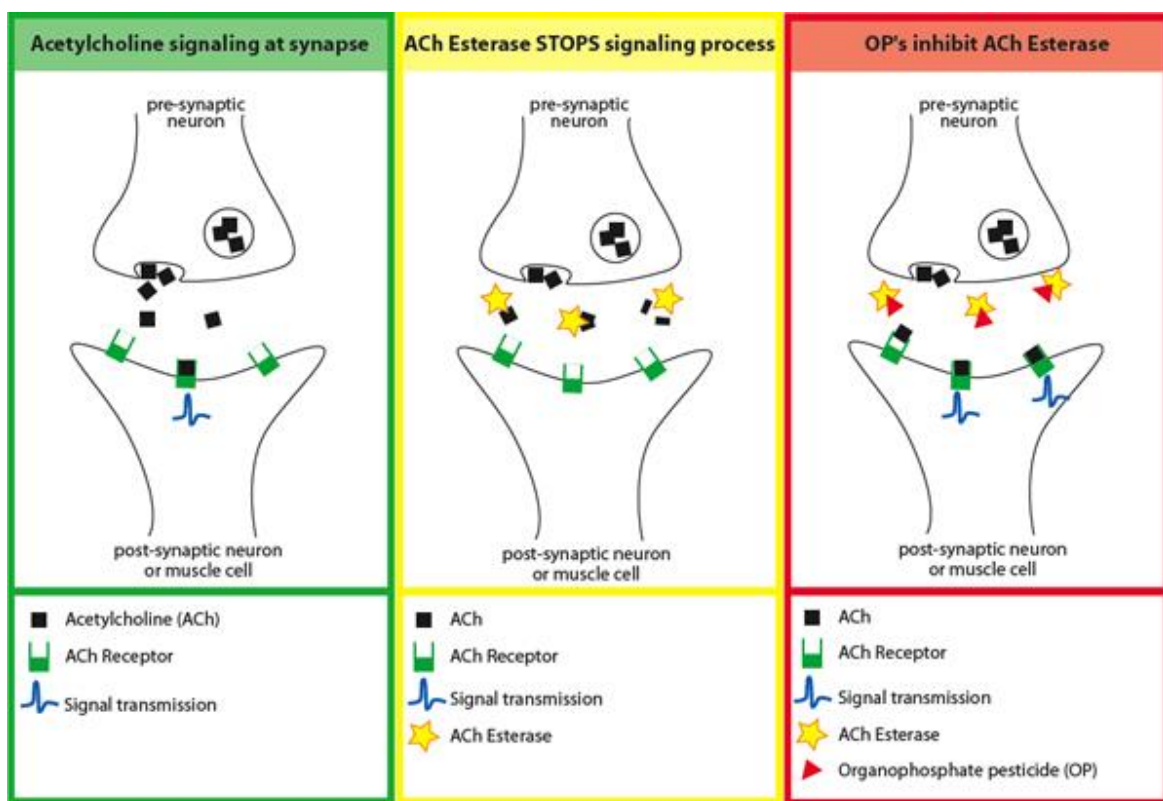


Figure 2: How OPs can effect on nervous system

Carbamate:

Carbamate insecticides are similar to organophosphates in chemical structure, but while OPs are derived of phosphoric acid, carbamates are derived of carbamic acid. Pesticides in this group are used for vector control in California, those consisting of carbaryl are used for dusting rodent burrows to control fleas; those with propoxur are used against insect pests, and certain kinds of bee and wasp control sprays. Carbamates also cause a relatively high risk for human poisoning.

The vast use of carbamate pesticides in modern agriculture has proposed serious public concern about the environment and food safety. Because of their wide range of biological activities, carbamates can be used as insecticides, fungicides, nematocides, acaricides, molluscicides, sprout inhibitors and herbicides. Carbamates represent one of the main categories of synthetic organic pesticides, since their introduction into the agrochemical market in the 1950s and are used yearly on a large scale worldwide. Though carbamates present low bioaccumulation potential and short-term toxicity, they are considered hazardous to the environment and human

health, being included in the priority list released by United States Environment Protection Agency. Apart from their pesticide attributes, the role of three carbamate insecticides – carbaryl, baygon and carbofuran—as possible cancer chemotherapeutic agents was recently explored on primary studies in vitro using trypsinized squamous cell carcinoma, since they inhibit cellular metabolism including energy, protein, and nucleic acid metabolism, thereby, causing cell regression and death. The mechanism of carbamates poisoning, excluding herbicidal carbamates, involves carbamylating of the active part of acetylcholinesterase (ChE) leading to the inactivation of vital enzyme that has an important role in nervous system of humans, and other animal species. Carbamates inhibit ChE like OPs do, and they act in almost the same way in biological system, but with two main differences. First, some carbamates are strong inhibitor of aliesterase, and their selectivity is sometimes more noticeable against the ChE of different species. Second, ChE inhibition by carbamates is reversible. When ChE is inhibited by carbamate, it is called Becarbamylated, like when an OP results in the enzyme are phosphorylated. In insect the effect of OPs and carbamates are firstly those of poisoning of the central nervous system. Herbicidal carbamates, like carbetamide, that represent a limited number of compounds, are not inhibitors of cholinesterase, they are cell division inhibitors.

Plants can metabolize carbamates, arylhydroxylation and conjugation, or hydrolytic breakdown, being the main ways of detoxification. The results of a number of studies suggest that carbamates are just distributed via the apoplastic system in plants. The acute toxicity of carbamates has different ranges, from highly toxic to only slightly toxic or practically non-toxic. Some carbamates are very toxic and others are less toxic in long-term studies. The beginning of clinical effects following carbamates exposure depend on the dose, route of exposure, type of carbamate involved, use of protective equipment and the premorbid state of the victim. Ingestion and inhalation of carbamates cause more and faster clinical effects in victims compared to dermal exposure. Just in severe exposure death could occurs where treatment is delayed or not enough atropine is given.

Health problems from pesticides in the absence of acute poisoning are also clinically important. According to the classification of USEPA (US Environmental Protection Agency) and IARC (International Agency for Research on Cancer) several carbamates are rated as possible carcinogens in humans. Epidemiologic studies illustrate that carbamates at high levels can induce

different types of cancer. For example, applicators with the highest LDs of exposure to aldicarb showed high occurrence of colon cancer, comparing to non-exposed workers. But melanoma was associated to carbaryl exposed applicators. There are some evidences today that show that both women and men can experience harmful reproductive effects from carbamates pesticides. When women are sufficiently exposed to certain pesticides, several types of adverse reproductive consequences may happen, and developmental problems in their children may result.

According to Frazier (2007), the main adverse reproductive effects associated to female exposure are neurodevelopmental or childhood behavioral problems (carbaryl), and possible childhood leukemia (propoxur). About male exposures associated with adverse reproductive effects, they are related with carbaryl, carbosulfan and carbofuran and consist in sperm aneuploidy and abnormal morphology in manufacturing workers (carbaryl); DNA fragmentation in men treated for infertility (carbaryl); chromosome aberrations and abnormal head morphology in mice spermatozoa (carbosulfan, carbofuran).

Human exposure to carabamate residues:

The existence of pesticide residues is a concern for users because carbamates are known to have potential harmful effects on other non-targeted organisms than pests and diseases. People have environmental exposures to pesticides mostly through diet, because of pesticide residues in food items is usually much higher than those related to water use and air inhalation. The assessment of pesticide residues in food is nowadays a preference objective to ensure food quality and to protect users against possible health risks. Fruits and vegetables are important ingredients of the human diet because they provide essential nutrients that are required for most of the reactions occurring in the body.

Carbaryl is one of the remnant most frequently reported in previous studies. Carbaryl can control a wide number of species of insects on fruits, and other crops, forests, as well as on hen, farm animals and pets. "Hassanzadeh et al (2010) studied the residue content of carbaryl applied on greenhouse cucumbers from Iran and its reduction by duration of a pre-harvest interval and post-harvest household processing. Carbaryl residues were detected in concentration ranges of 0.22-4.91 mg/kg indicating that residues in cucumber were higher than its European Union MRL (0.05 mg/kg) value 14 days after application." (Morais *et al* 2011) They suggested that a waiting

period of more than 14 days should be observed before harvesting or consumption of cucumbers, in order to protect consumer health. They concluded that household processing, such as washing and peeling and refrigeration storage, was effective in reducing the carbaryl residue levels. Peeling is the most effective way to reduce the carbaryl residue of the cucumber samples.

Risk assessment:

Commonly exposed professionals include pesticide applicators, those harvesting crops, and farmers. Humans can be also exposed to carbamates by over-exposure in home application, for example, in gardens and in the handling of household animals. Biological and environmental monitoring are the main tools now available for the “in-the-field” pesticide risk evaluation, however, some limitation must be considered, since effective activities occurs in an open air. Most people can be exposed to carbamates through diet, for example, using treated fruits, vegetable and polluted water.

Organochlorine:

The organochlorines (OCs) are insecticides that contain carbon, hydrogen, and chlorine. The chemical structure of organochlorine is varied, but they all have chlorine, that places them in a larger class of compounds called chlorinated hydrocarbons. OCs include insecticides DDT-derivatives (OC-DDTs), such as its metabolites (DDE,DDD) , other cyclodiene-derivative pesticides (OC-cyclodienes), like aldrin, dieldrin, and endrin, and hexachlorocyclohexanes, such as lindane. While organochlorines have the advantage of being cheap to manufacture and are effective against target species, they have serious unintentional consequences. They disrupt the movement of ions like calcium, chloride, sodium, and potassium into and out of nerve cells. But also, depending on the specific structure of the OC chemical, it can have an effect on the nervous system in another way. At one time organochlorines were ideal because they are very stable, slow to degrade in the environment, break down in fats – so they can easily be taken up by insects, and apparently safe for mammals. Unfortunately, it finally becomes clear that the resistance feature and fat solubility were actually very inappropriate: the organochlorine can pass through the food chain, where they bioaccumulate in the fat of large animals and humans and are passed on to the nursing child. Organochlorine such as DDT is now mostly prohibited in industrialized countries but they are still manufactured and used in developing countries.

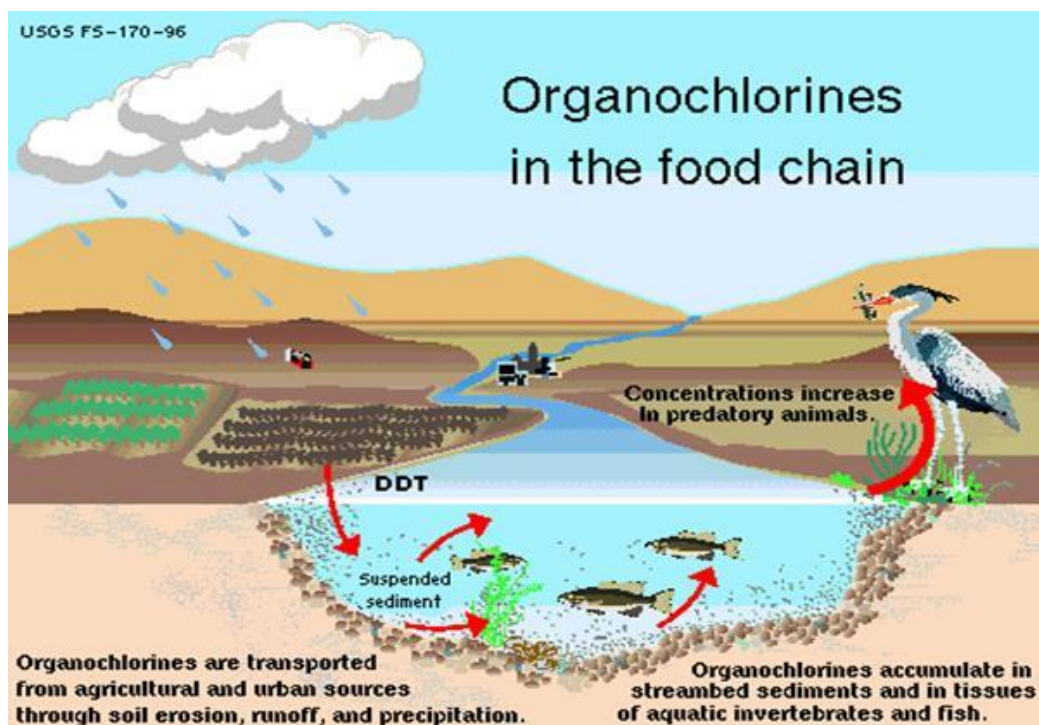


Figure 3: How Organochlorine passes through the food chain

Human body burden of organochlorine pesticides (OCs) is the result of universal presence of these contaminants in the environment and they are an issue of public health concern because they have been linked with the pathogenesis of cancer, asthma, diabetes, and growth disorder in children. Exposure of human begins to OCs largely derives from ingestion of polluted food although environmental, professional and other domiciliary exposure should not be disconsidered. Anyhow, it is well known that foods are the main source of human exposure to environmentally persistent pesticides, and group of DDT derivatives (OCs-DDT) is one of the groups of pollutants that are usually detected in foods all over the world.

Influence of Organochlorine Pesticide on GH-IGF System

Growth hormone (GH) is a glycoprotein that encourages anabolism and adjusts metabolism in a vast range of organs. In adult humans, GH is secreted into the bloodstream by anterior pituitary gland and acts directly on some tissues, but also indirectly through the production of insulin-like growth factors (IGFs). IGFs are called insulin-like because they have protein sequence

similarities with insulin and they also have insulin synergizing activity. The liver is the main source of IGFs. In fact, many of actions of GH are mediated indirectly through the up-regulation of systemic IGF release by the liver. Two distinct IGFs are important for human during adult life, IGF-1 and IGF-2, whereas IGF-2 seems to be more related to fetal development than adult life. Anyhow, correct functioning of the GH-IGF axis is required for successful human development as well as for maintenance of health in adults. IGF-1 has been established as a useful marker for monitoring the status of the GH-IGF axis.

Currently, human beings are potentially exposed to a wide range of structurally varied toxic compounds. Long-term exposure to these pollutants, mainly through environmental and dietetic means, potentially could deregulate the GH-IGF axis.

It has been suggested that exposure to environmental pollutants, such as organochlorine compounds, could be an exogenous factor that have ability in modulating the IGF system. There are relatively few reports on disruption of the GH-IGF axis by pesticides and other environmental pollutants, compared with the number of studies looking at their effects on reproductive endocrinology. Although most papers explore the effects of pesticides on GH/IGF system as a consequence of their estrogenic/antiandrogenic action, the possibility exists that pesticide could also influence GH-IGF system directly. So, environmental pollutants could alter (change) the normal synthesis or/and secretion of IGF-1, or could act altering the IGF signaling pathway in both, in vitro and in animal models. Because the liver is the main source of IGF-I in the circulation, there is a possibility to exist the inverse relationship between some OCs and IGF that could be an indirect effect of these environmental pollutants on liver tissue. In fact DDT and DDE have been related to increased risk of primary liver cancer. (Boada *et al.* n.d).

Pyrethroid and Pyrethrins:

More recent classes of insecticides are the Pyrethrins and the Pyrethroids that have replaced the use of cholinesterase-inhibiting insecticides, especially in the market's users. (Robert JR *et al.* 2012). The chemical structure of pyrethroids is totally different from organochlorines, organophosphate and carbamates but the main body part that suffers from its action is also the nervous system. (Katarina Lah 2011) The effect of pyrethroid is in the movement of sodium ions

(Na⁺) into and out of nerve cells, which cause the nerve cells to become hypersensitive to neurotransmitters. The difference between pyrethroids structures can change their toxic effects on specific insects and even mammals. (Katarina Lah 2011). These insecticides are used for control the pests in urban areas, also in gardening and agriculture for row crops and orchard, and even at home for pet sprays and shampoo (Robert JR *et al.* 2012). The pyrethrins are extracted from chrysanthemum plant. For the product's users, pyrethrins are usually combined with another active ingredient. Permethrin is one of the most known examples of pyethrin and is one of the few allowed products for use to apply in human skin, because of its capacity to kill lice.

Pyrethroids are synthetically derived compounds that are modified to be more stable in sunlight and heat, so they are used more for insect control, especially outdoors. Toxicity is very different among pyrethrins and pyrethroids. They are less toxic than cholinesterase insecticides but there is a subgroup of these compounds that has been modified with cyano side chain. This changing creates a compound that is more resistant to degradation and potentially more toxic than other pyrethroids. The chemicals that are usually used in this group consist of deltamethrin, cypemethrin, and fenvalerate (Robert JR *et al.* 2012).

Toxicity and symptoms:

As we mentioned before pyrethroids show their toxic effect by blocking the sodium channel in cell membrane. Most of the poisoning happens through extreme skin contact or ingestion or inhalation. The result is continued hyperpolarization- make the membrane more negative- so inhibit the cell function. Also some types of pyrethroids work at the other sites, like voltage-dependent chloride channels and γ -aminobutyric acid-gated chloride channels. This seems to be one of the reasons for variation of toxicity which is found among pyrethroid insecticides (Robert JR *et al.* 2012).

Pyrethroids with a cyano group, known as type II pyrethroids, cause most cases of human poisoning. Pyrethroids can absorb very well through the GI tract- digestive system- but limited penetration occurs across the skin barrier, which can limit acute toxicity. Usually after ingestion some pyrethroids can have a high acute toxicity. Pyrethroids have harmful effects on nervous system, GI tract and skin. Like OPs, muscle fasciculation, weakness, changing the level of caution and seizures can expand after exposure to some pyrethroids. Paresthesia, including burning, tingling, stinging, and finally numbness, are characteristic of pyrethroid exposure. The

paresthesia is dose-dependent and usually occurs in lower dosages of pyrethroid, if compared to what would cause systemic toxicity, thereby acting as a warning of exposure. The paresthesias are self-limiting when exposure is eliminated (Robert JR *et al.* 2012).

Treatment:

Pyrethroid toxicity is recognized by clinical history and knowledge of exposure to the factor. Fast diagnostic laboratory tests are not available. Most of the pyrethroids are metabolized to 3-phenoxybenzoic acid that can be recovered in the urine. CDC national studies provide biomonitoring information on pyrethroid urinary metabolites and can act as comparison for background measures of exposure in the general population. But in the clinical perimeter, metabolism levels results are usually taken from specialty laboratories and are not available as fast as possible, so, these results are not useful in acute clinical management (Robert JR *et al.* 2012).

Generally there is no antitoxin for systemic pyrethroid poisoning. Because they have similarities with cholinesterase inhibitor poisoning, some patients have been treated mistakenly with high atropine, sometimes with deadly results. Scientists tested several medications in animal models, but up to now none of them have been considered effective antidotes for systemic pyrethroid poisoning in humans. For important neurologic effects, patients should have standard decontamination, like GI tract decontamination, helpful respiratory care, seizure control with diazepam or lorazepam, and exact dosing of atropine for extreme salivation. Suitable recognition of the offending factor is necessary to differentiate these poisonings from OPs and often requires a high index of suspicion and a complete exposure history (Robert JR *et al.* 2012).

Microbial biopesticides:

What are microbial biopesticides?

Microbial biopesticides are a kind of biological control. Biological control is specified as the use of natural enemies such as predators, parasitoids, pathogens, and competing species to decrease a pest population (Harper 2006). Microbial biopesticides use microorganisms like bacteria, fungi, viruses and nematodes, which are naturally pathogenic to specific crop pests

insects. Entomopathogens are natural not synthetic, and in nature they make natural epizootics that provide the worth ecosystem service of controlling insect numbers and preventing pest prevalence.

Scientists have expanded ways and are continuing to search for new ways to use this antagonistic relationship as a tool for pest management. In 2003, biological control agents considered for 1.72% of total use for plant protection products, of which 41% of spending was on microbial biopesticides (harper 2006).

Why has there not been a higher uptake?

Microbial biopesticides are very specific and hence the market share is too small to recover the development and registration costs. Crop protection products regulation started in the 1960s after problems with pesticides were reported and some non-governmental organizations like Greenpeace and Pesticide Action Network changed public insight of pesticides (Ehlers 2011). Characteristics of products passable for publish onto the market were drawn by the European Pesticides Directive and based on guidance from agrochemical companies. As a result, the criteria focused firstly on effect. Regulation of biological control agents (BCAs) was hence evaluated based on criteria modeled on synthetic compounds.

Before the regulation, many BCAs were used and in all over their history of use, no negative effects had been reported. In spite of this, use of many BCAs stopped as registration costs were not justified. Though the regulatory system looks to be counterproductive, a preventative procedure was enforced due to past failures to prevent environmental damage. For example, the fungicide tolyfluanid was recently prohibited in the US because after microbial degradation in soil and entry into water system, ozone treatment converts it into the carcinogenic compound N-nitrosodimethylamine (NDMA) (Orosova et al 2010). Nevertheless, recently, people have begun to find out the potential of BCAs for use in agriculture, horticulture and forestry and thus the regulation and registration of microbial biopesticides has been reviewed. Regulation concentrates more now on ecological effects and the cost of registration has been reduced. For example in 2007 the cost of recording a biopesticide in the UK was £22,500 compared to £175,000 for recording a chemical pesticide (Chandler et al 2008). Commercialization of biological control

products is still mostly down to small companies. The microbial biopesticides consist of four groups: Bacteria, fungi, virus and nematodes.

Bacteria:

Introduction:

Generally bacterial entomopathogens have down virulence and are opportunistic. Bacteria belonging to the genus *Bacillus* have proved to be very efficient control agents, because they infect and kill a range of orders. The Gram positive bacteria, *Bacilli* make spores and are found plentifully in the soil. The bacteria naturally pass infection to the larval stage through ingestion and transmitted horizontally. But, absence of contact action means transmission is low and so *Bacillus* pathogens need frequent re-application. Fortunately, they are cheap to grow and produce.

Detailed Example:

Bacillus thuringiensis:

Bacillus thuringiensis (Bt) is the most widely used microbial biopesticide and is an example of inundative biological control. It has been considered the safest insecticide on the market by the World Health Organization (Ehlers 2011). Bt attacks species in the orders of Lepidoptera, Diptera, and Coleoptera, pests of vegetables, cotton, corn, rice and fruits. In the 1950s the Bt was first used and by 1998, about 200 Bt products were registered in America (Harper 2006, Lacey et al 2001).

Process of infection: the time of making spore, Bt produces a protein pro-toxin crystal, placed in parasporal inclusion bodies (Figure 1).

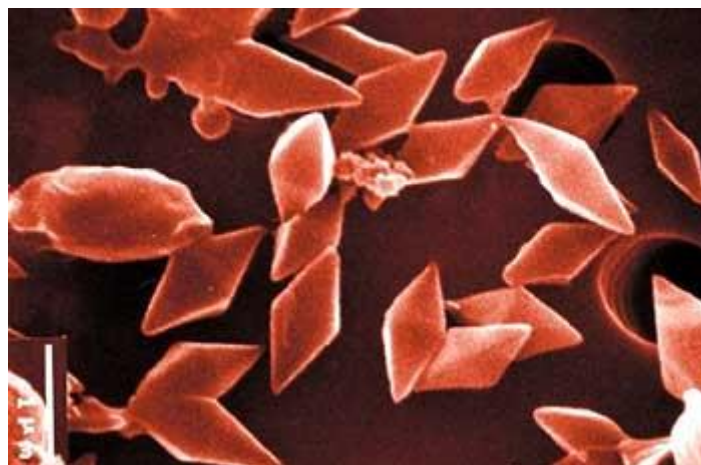


Figure 4: crystal of Bt toxin

The larvae ingest the crystal, then dissolve it within the alkaline midgut and they are cleaved by gut proteases to form delta-endotoxins. So Bt is selectively lethal to organisms with an alkaline gut. The toxin attach to specific gut receptors that damages the gut through pore formation and membrane transport cutting which result in cell paralysis. (Lacy et al 2001). So finally the insect stops eating and dies within 2-24 hours (Copping and Menn 2000). This infection is a dead end so the infection usually is not inherited by anew hosts. Crystalline proteins are coded by cry genes located on extra-chromosomal plasmids in the bacterial cell (Copping and Menn 2000). More than 200 genes have been recognized to code a different toxin in Bt. Each toxin is special for particular insect species because it binds to different gut receptors.

Other *Bacillus* species also are used as Microbial Control Agents or MCAs; these species are used on a lower scale than Bt, however they are still very important. First one is *Bacillus Papillae* attack to the order scarabaeids and especially cause “milky disease” in the Japanese beetle. This species was the first entomopathogen that have been released into the market in America and was registered in 1939. (Harper 2006). Second one is *Bacillus sphaericus*. It has beenused to kill mosquito larvae in Europe and Africa, in particular *Culex* species. (Copping and Menn 2000).

Fungi:

Introduction:

The important agents for a range of herbivorous insects are fungal entomopathogens. Until 2009, half of all reported classical introductions of pathogens were species of fungi (Hejek and Jr2010). Seven hundred and fifty species of pathogenic fungi have been found but only 1.5% has been analyzed better for use as microbial control agents (Lacey et al 2001). More researches in fungal entomopathogens is also essential in order to fully benefit from this untapped precious resource. *Beauveria*, *Metarhizium*, *Paecilomyces* and *Lecanicillium* are the common genera that are used for pest control because they can be grown on comparatively cheap artificial media and have a fairly long shelf life (Ehlers 2011). Their targets are a broad range of insects but individual fungal species are highly specific. Most species attack the insect via the cuticle or exoskeleton through spore contact, so don't have to be eaten. Also they are the only effective pathogen of "sucking sap feeders" like aphids and whiteflies.

Problem:

Even though most fungal entomopathogens are very specific, some of them infect non-target insects. For instance *Beauveria bassiana* used to control many greenhouse pests like spiders, crickets, grasshoppers, western flower thrips, and mites, can also make infection on ladybirds (Harper 2006). Ladybirds are useful biocontrol agents that are why it is a problem.

Examples of Fungal BCAs:

***Neozygites fresenii*:**

Neozygites fresenii make natural epizootics and they infect the cotton aphid, *Aphis gossypii* in South America. The fungi can decrease a population by 80% in 4 days (University of Warwick accessed online 2011). We cannot produce *N. fresenii* in vitro and produce in vivo is expensive. But Steinkraus and Boys (2005) have developed a method to harvest and keep great quantities of *N. fresenii* during a natural prevalence for future use in protection control. Besides, cotton farmers can forecast 10 days ahead if a natural prevalence will happen and also make aware decisions about whether to use expensive pesticides. (University of Warwick accessed online 2011).

Lagenidium giganteum:

Lagenidium giganteum is extensively used to control mosquitoes (Harper 2006). The spore detects the body of insect and then specific chemical cues stimulate germination and after that it penetrates the cuticle and finally it spread throughout the body. The insect becomes starved and in several days it dies. The fungi then produce a new generation of spores on the dead body that spread and infects new hosts. If there is no host, two spores will join and make a constant, long-lasting, dehydration resistant spore, till a host is present. Also the transmission is horizontal.

Metarhiziumanisopliae:

Since 1914 *Metarhiziumanisopliae* has been the most regularly used species in classical biological control. (Hajek and Jr2010). The species are used to control grasshopper, cockroaches, and termites, main pests in developing countries and also developed countries such as America, Australia, and Africa. It is easy to produce a huge amount of this factor because it can be grown on rice grains. Using oil, the green spores are simply spread to parts of the insect that have high relative moisture, for example where the cuticle is thin like on the neck or back or under the wings, where the fungi can germinate and grow. The fungi are very effective, for example it can kill 90% of grasshoppers in 7 to 21 days of application, depends on the number of infecting spores.

Future Prospects:

If scientists can develop stagnant spores and good mycelium, future use of entomopathogenic fungi will extend. Research in the genetic manipulation to raise virulence of fungi is increasing, however is not as widely investigated as bacteria and viruses. To have a better understanding of the abiotic and biotic interplays with entomopathogenic fungi is essential to determine the optimal amount and timing of application. Timing of application must consider the sensitive host stage, environmental conditions and agricultural practices.

Virus:

Introduction:

Baculoviridae, Polydnviridae and Ascoviridae are the three families that have been found to specifically make infection in insects (University of Warwick accessed online 2011). But viral entomopathogens only account for 1% of the global market for microbial biopesticides because of several limitations (harper 2006). Because the viruses are intracellular organisms, it is very difficult and expensive to grow them in laboratory. Also, because they are slow acting, sensitive to UV light and have a narrow host range frequently for individual species, the commercial use is limited (Lacey *et al* 2001). Viruses are very effective because they are resistant, highly malignant and produce secondary inoculums. They are safe to use because they don't infect vertebrates. Other advantage is that resistance is highly rare because the virus is living and also is able to evolve with its host. Typically viral pathogens used for inundative control.

Baculoviridae:

Baculoviridaefamily has the largest potential for use in biological control of insects because they are highly specific and very effective (Copping and Menn 2000). Currently there are sixteen products available based on *Baculoviruses* for use (University of Warwick accessed online 2011). *Nucleopolyhedrovirus* (NPV) and *Granulovirus* (GV) are two genera in this family. NPV aims Lepidoptera and Hymenoptera. For example *Helicoverpazea*NPV controls tobacco budworm and bollworms (Copping and Menn 2000). But GV just targets Lepidoptera, for example *Cydiapomonellagranulosis* virus control the codling moth, a universal, major pest of apple, plums and pear trees, and is used on 15% of Washington State orchards (Copping and Menn 2000).

Infection Process:

Baculoviruses make infection through ingestion by larvae. The obstruction bodies dissolve in the alkaline gut and free the virions. After that virions bind to gut receptors and invade the gut epithelial cells where it replicates and grows in the nucleus. Then the virus distributes across the body in the haemolymph and leads to the death of the larvae. Usually in Lepidoptera death occurs within four to five days after infection. After that a new generation of virus is released

from the dead body and it ready to invade a new host. Virus transferring within the host insect population can happen both in horizontal and in vertical form.

Classical Control by the non-blocked baculovirus, *Oryctes rhinoceros virus*:

Oryctes rhinoceros virus (OrV) infects the rhinoceros beetle (*Oryctes rhinoceros*) which are serious pests that cannot be controlled by pesticides and that destroy coconut palms in the Tropics (Huger 2005). In South Pacific countries, by 1968, the beetle caused serious crop damage, with an estimated loss of US\$1,100,000 (Bedford 1980). Because the adult eats the palm crown, they are responsible for the damage that lowers yield and kills saplings. Old rotting palm logs make a reproduction grounds for the beetle. OrV can persist at low host densities, which gives it its successful long-term control. To keep it stable and have an optimal control, the plantation hygiene, like removing breeding sites, is important. The adult stage is a very active vector for spreading the virus and spread can be raised by applying the virus to the mouth parts of caught beetles.

Future Prospects:

In the future, usage of viruses is expected to increase as scientists develop ways to control their limitations. For example in developing countries where cost of work is low, production of virus would supply employment and be a cheaper option than importing pesticides. Genetic manipulation of some viruses will also make their effect better, for example it can shorten the lag time between time of ingestion and death.

Nematode:

Introduction:

Nematodes are organisms about 0.6mm long, that live in the soil and have three life stages: egg, juvenile and adult. The most well-studied entomopathogenic nematodes are of the genera *Steinernema* and *Heterorhabditis*, which are lethal to many important insect pests that live in the soil. About 80 have been classified, but just twelve are used as biological control agents now. The second most widely used microbial control agents are nematodes after *B. thuringiensis*, with commercial sales at US\$2-3 million each year (Lacey *et al* 2001). Because of high production and formulation costs their use is limited to high value crops.

Advantages:

The nematodes can be clumped, cultured in vitro, applied using the same equipment like normal pesticides and are compatible with many synthetic pesticides. They don't make infection on plants, human or animals and also no safety equipment is needed.

General Infection Process:

The nematodes are entomopathogenic, owing to their symbiotic relationship with bacteria of the genera *Xenorhabdus*, for steinernematids, and *Photorhabdus*, for heterorhabditids (Lacey *et al*2001). Steinernematids enter the insect through the natural openings and mate whilst heterorhabditids enter through the cuticle and are hermaphrodites. The bacteria are very malignant and fast acting—in contrast to other microbial biopesticides—, and cause death by septicaemia in 24-48 hours after infection. The bacteria degenerate the insect body that the juvenile nematodes feed on before developing into adult and reproducing. There is symbiosis with specific bacteria for each species of nematodes. Infection transferring is horizontal. There are two examples of inoculative biological control, first is *Phasmarhabditis hermaphrodita* is used to kill slugs and the second is *Steinernema kraussei*, which is used to kill vine weevils (*Otiorhynchus sulcatus*) (Figure 2 & 3).



Figure 5



Figure 6

Classical Control by *Deladenussiricidicola*:

The wood wasp- *Sirexnoctilio*- is native to Eurasia and Northern Africa. It is an invasive species in Australia and New Zealand, where it is freed from natural enemies and as a result causes significant damages to the economically important Monterey pine. The female wood wasp can kill the trees by injecting toxic mucus and its symbiotic fungus *Amylostereumareolatum* when egg is laying inside the tree (Hurley *et al* 2007). The developing larvae feed from fungus. *S. noctilio* mostly make infection on stressed trees, so many silvicultural practices are implemented to keep the health of the forests. Parasitic wasps are also used to control this pest, but inoculative introduction of the nematode *Deladenussiricidicola* is seen as the primary biological control agent, having greatest success in Australia (Hurley *et al* 2007). The nematode is especially effective as it actively seeks out its host using chemoreceptor - like parasitoids- thus detecting effective larvae, and is also very resistant.

Plant-incorporated- protectants (PIPs):

Plant-incorporated protectants, or PIPs, are plants with genes inserted in such a way that they cause the plants to produce a pesticide inside its own tissues. When plants are genetically improved to make pesticides in this method, the Environmental Protection Agency (EPA) regulates them as pesticides. When the plant genes are modified to create plants that tolerate some herbicides such engineering is not regulated as pesticides (National Pesticides Information Center 2013).

For instance, scientists are able to take the gene for a specific Bt (*Bacillus thuringiensis*) pesticidal protein and insert the gene into the plant's genetic material. After that the plant makes the pesticidal protein, when the pest feeds on the plant it control the pest. The genetic material and protein are regulated by EPA, but the plant itself is not regulated.

Before the pesticide can be registered by EPA there must be enough data indicating that it will not present unreasonable risks to human health or the environment when is used according to label directions. When evaluating the potential risks of genetically engineered plant-incorporated protectants, EPA needs vast studies examining many factors, like risk to human health, potential for gene flow, non-target organisms and the environment, and the requirement for insect resistance management plans. In 1995 before the first PIP production was registered, EPA demandedthat PIP production be completely tested against human safety standards before they were used in human food and livestock food products. Based on the lots of reviews of the scientific studies and frequently peer reviews by the Federal Insecticide, Fungicide and Rodenticide Scientific Advisory Panel, EPA found out that these genetically engineered PIP products, when used in following with approved label directions and use restrictions, would not constitute unreasonable risk to human health and the environment during their time-limited registration (U.S.A Environmental Protection Agency 2015).

Plant Incorporated protectants (PIP)

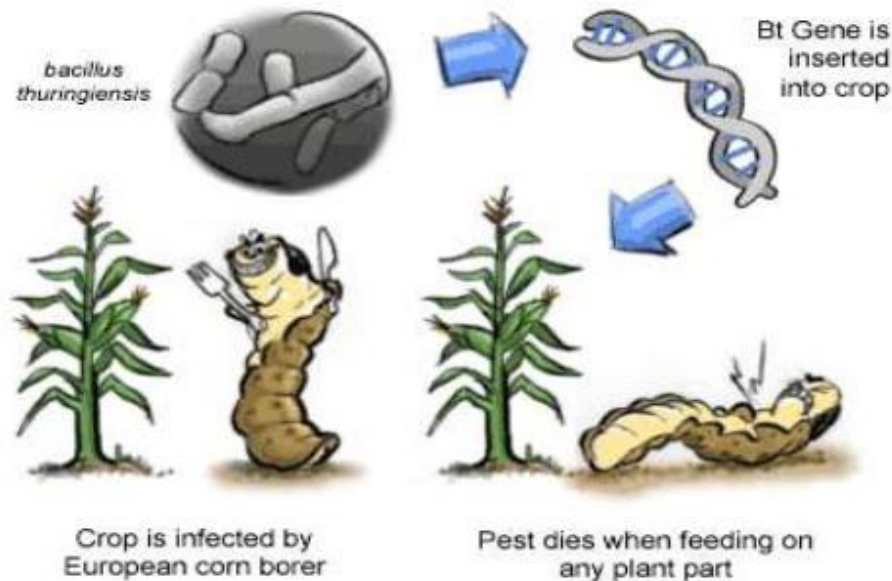


Fig. Showing the mode of action of cry protein crystal produced by genetically modified plant

1. <http://permaculturenews.org/2012/08/14/bt-toxicity-confirmed-flawed-studies-exposed/>

9

Figure 7: How PIPs work

Fungicides:

The biocidal chemical compounds or the biological organisms that are used to kill or prevent fungi or fungal spores from growing are called fungicides. Scientists classify fungicides in different ways: first, mobility in the plant; second, role in the protection of plants; third, breadth of activity; fourth, mode of action; and, fifth, chemical group. Some fungicides can be in more than one of these categories (Muller 2013).

1) Mobility in the plant:

There are two groups, contact and systemic fungicides. Contact fungicides are the ones which stay on the surface where they are applied, but which do not go deeper. These fungicides don't have after-infection activity. When a new plant grows, the application should be repeated in order

to protect the plant and also to replace material that has been washed off by rain or irrigation or degraded by sunlight. On the other hand, systemic fungicides are absorbed into the plant tissues and can make some after-infection activity. Actually, there are very few fungicides that are truly systemic, for example, which can go more freely all over the plant; some are upwardly systemic: they move only upward in the plant through xylem tissue; and some are locally systemic: they move into treated leaves and distribute again to some degree inside the treated portion of the plant.

2) Role in protection of plants:

Fungicides can have a preventive activity. It occurs when a fungicide is available on the plant as a protective barrier before the pathogen comes or starts to develop, so that it can prevent infection from happening. They have also early-infection activity; it happens when the active ingredient of a fungicide can go deeper in the plant and stops the pathogen in the plant tissues. Most fungicides that have early-infection activity also have preventive activity, and they are more effective when applied before infection happens. The other role of fungicides is eradication. This is defined as an ability to stop disease development after the appearance of symptoms. Very few fungicides have this ability, and producers will probably not depend on this as a means of disease control. The last role of fungicides is anti-sporulate activity. This is the ability to stop fungi from making spores. In this case, the development of disease is continuing, but spores are not being made or released, so that the amount of inoculum assessable to infect surrounding plants is decreased.

3) Breadth of activity:

There are single-site and multi-site fungicides. The single-site fungicides are active against just one point in one metabolic pathway in a fungus or against a single critical enzyme or protein needed by the fungus. They are less toxic for plants and have systemic features. Multi-site fungicides have effect on a number of different metabolic sites inside the fungus.

4) Mode of action:

Fungicides cause the death of fungi by damaging their cell membrane, inactivating important enzymes or proteins, or preventing the continuation of key processes like energy production or respiration. Others affect specific metabolic pathways like the production of sterols or chitin. For instance, phenylamide fungicide bind and inhibit the function of RNA polymerase in oomycetes, while the benzimidazole fungicides prevent the formation of beta

tubulin polymers that cells use during nuclear division. If we know how exactly a fungicide have an effect on a fungus, it helps us to select the best product. First, the mode of action points to what fungi will be affected by a fungicide and what diseases can be controlled by using that fungicide. Second, in disease management programs fungicides with different modes of action are necessary to fungicide resistance development.

5) Type of chemical:

Fungicides can be classified according with their chemical composition, be it organic or inorganic. Chemically, those with carbon atoms in their structure are called organic, and the ones without carbon are inorganic. A large amount of the first fungicides that were used were inorganic compounds based on sulfur or metal ions like copper, tin, cadmium and mercury that are toxic to fungi. Copper and sulfur are still widely used. Most of the fungicides that are used today are organic, and, so, contain carbon. The word “organic” that is used here is based on chemistry terminology and it is different from “organic” as used to describe a system of agriculture that tries to be holistic, pesticide-free, and to improve eagroecosystem health.

Fungi can cause severe harm in agriculture, resulting in critical losses of product, quality and benefit. Fungicides are used in agriculture and also to destroy fungal infections in animals. There are chemicals that are used to control oomycetes, but they are not fungi, even though they use the same mechanisms that fungi use to infect plants. (Latijnhouwers M et al 2003).

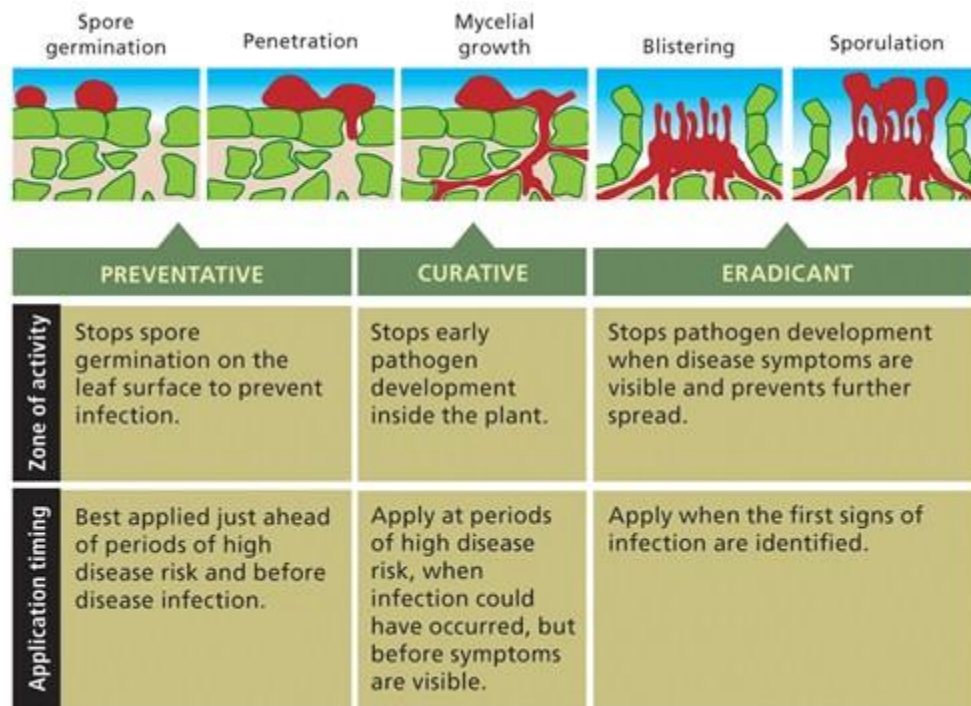


Figure 8: Different kind of fungi, zone of their activity and application timing

Herbicides:

Chemicals that are used to handle or control undesirable vegetation are called herbicides. The most common application of herbicides happens in row-crop farming, where before or during planting they are applied to make more crop productivity by reducing other vegetation. Also they can be applied to crops during fall to make harvesting better. In forest management herbicides are used to prepare logged areas for replanting; the volume of application and the area covered is greater than in farming, but the alternation of application is much less frequent (Todd and Suter 2012). In suburban and urban areas, herbicides are applied to lawns, parks, golf courses and other areas. Also herbicides are applied to water bodies to control aquatic weeds. The possible effects of herbicides are powerfully influenced by their toxic mode of action and their method of application. They can act by inhibiting cell division, photosynthesis, amino acid production, or by mimicking natural auxin hormones that regulate plant growth, and cause malformation in new growth. Herbicides are applied in several methods like spraying onto the plant leaves, applying to soils, and applying directly to aquatic systems. Herbicides can cause biological impairments of water bodies if they happen in water or sediment in enough concentrations. Most generally, they

enter surface water in runoff or leachate, however, because they have relatively low toxicity to fish and invertebrates, acute toxicity is probable to happen only when they are intentionally or accidentally applied directly to water bodies. Direct applications can have a result in direct toxicity to non-target plants and animals or indirect effects like the death and decay of plants. Impairments also are more possible when herbicides are applied together or with other pesticides. Scientific tests using the earthworm (*Eiseniafetida*) show that Atrazine actssynergistically with Chlorpyrifos, and organophosphate insecticide: the mixture is seven times more toxic than the two individual pesticides individually. Atrazine showed that it can increase the effects of other pesticides in mosquito larvae, fruit flies, houseflies and midge flies.

Herbicides must be absorbed by plants, adequately making contact with plants, than moving inside the plants and being active until the site of action, in order to have a toxic level at the site of action, being thus effective. The method of application that is used decides whether the herbicide will contact germinating seedlings, roots, shoots, or leaves of plants.

Rodenticides:

The pesticides that kill rodents are called Rodenticides. Rodents include rats, mice, squirrels, woodchucks, chipmunks and other animals. Even though rodents play important role in nature, they sometimes may need control. They can harm crops, break housing codes, transfer disease, and in some cases cause ecological damage (U.S.A Environmental Protection Agency 2004). The body of all mammals – like rodents, human, dogs and cats – work in very similar way. Rodenticides can have the same effect when ingested by any mammal. They can also have effect on birds. Usually Rodenticides are formulated as baits to attract the animals. Seasoning can include fish oil, molasses or peanut butter. Baits that use in agriculture and natural areas may contain ground meat, vegetables, grains or fruits (Erickson W and Urban D 2004). These can attract children and pets, so they should be used and/or stored far from their reach.

There are lots of different active ingredients registered as rodenticides in the US. According to how they work, they can be thus grouped. Anticoagulants: these rodenticides can stop normal blood clotting. The examples of this group are: Bromadiolone, chlorophacinone, difethialone, diphacinone, brodifacoum, and warfarin. One enzyme that is made by our livers allows our bodies to recycle vitamin K. The body uses vitamin K to make the blood clotting agent so that it

prevents the body from bleeding too much. Anticoagulants stop the work of this enzyme. The body provides an extra store, but if the exposure to anticoagulant increases, the store will run out and internal bleeding can happen (Campbell A and Chapman M 2000). There are some rodenticides that are not anticoagulants, they work in different ways. More examples are Zinc Phosphide, Bromethalin, Cholecalciferol and strychnine.

All rodenticides when ingested by rodent can be toxic. Most of them also can be toxic when inhaled and/or when have contact with the skin. Warfarin is a special case, since its toxicity is low when the exposure is by inhalation or skin contact. Cholecalciferol, strychnine and zinc phosphide are of low toxicity upon skin contact. Bromethalin is quite toxic in dermal exposure.

The first anticoagulant rodenticide was Warfarin (U.S.A Environmental Protection Agency 2004). It was registered in 1950. It was found in musty sweet clover that had caused sickness in a herd of cattle. Before many rodents become resistant to warfarin, it was the most widely used rodenticide. After that the new rodenticides developed (Murphy, M. J. and Talcott, P. A 2006). Warfarin, diphacinone and chlorophacinone usually need that an animal ingests several doses of the bait over several days. These are called multiple-dose anticoagulants. There are also single-dose anticoagulants like brodifacoum, difethialone and bromadiolone that are more toxic. One day of feeding can release the toxic dose (U.S.A. Environmental Protection Agency 1998).

The single-dose anticoagulants bind more firmly to the enzyme which makes blood clotting agents that is why they are more toxic than multiple-dose rodenticides. Single-dose anticoagulants are not simply fended from the body; they can be kept in the liver. Selling most of these kinds of rodenticides to non-licensed applicators is prohibited, especially for residential use. As previously mentioned exposure to anticoagulants can provoke uncontrolled bleeding in any part of the body, but this is not always clear. Some other symptoms have been seen in animals that were poisoned with anticoagulant rodenticide such as difficulty in breathing, weakness and lethargy. There are some less common signs like coughing, blackened stools, paleness, seizures, shaking, vomiting, and bleeding from the gums. The signs of contamination may delay for up to five days after exposure because the stored clotting agents have to run out. Because children normally eat small amounts of the product, they may never show signs of

poisoning. In people the signs of poisoning are quick bleeding from nose, gums or skin. Also internal bleeding can happen.

Other rodenticide:

There are some of rodenticides that work in other ways. Currently these are used in the U.S.A: zinc phosphide, bromethalin, cholecalciferol and strychnine. Each of them works in a different way.

Zinc phosphide :

It was first registered in 1947 (U.S.A Environmental Protection Agency 2004). If water and acid be present, it changes to phosphine gas. Phosphine gas is very toxic because it blocks the energy production in the cells of the body, causing their death. Exposure to phosphine is especially damaging to the brain, kidney, heart and liver. In Michigan, zinc phosphine poisoning has caused random deaths of non-target species. Wild turkeys have been the most severely affected. Exposure to humans is rare, being restricted to the touching of bait material. If suitable attention is taken, the rodenticide can be safely used and its impact on non-target species kept down.

Zinc phosphide can cause vomiting in an hour after ingestion. But symptoms of toxicity may delay up to four hours, and in some cases longer than eighteen hours. Other symptoms of toxicity are anxiety, difficulty breathing, weakness, discomfort leading to frantic pacing and convulsions. In humans, also vomiting, excitement, chills, shortness of breath and even coma can happen.

Bromethalin:

This rodenticide was registered by U.S.A environmental protection agency (EPA) in 1984(U.S.A. Environmental Protection Agency 1998). Bromethalin stops the energy production of cells in the central nervous system. As the nerve cells swell, it makes pressure on the brain, and after that paralysis and death will happen. The main breakdown product of bromethalin is more toxic than bromethalin itself. It can be more toxic to some animals than others because the

ability to break down bromethalin is different in different species (Roder, J. D., 2001). Bromethalin is a single-dose rodenticide (U.S.A. Environmental Protection Agency 1998).

Ingestion of bromethalin can cause muscle tremors, seizures and raise the sensitivity to light or noise. The start of signs depends on the dose. If the animals eat a lethal dose, signs can develop 8 to 12 hours or several days after ingestion, and can move forward over a period of a week or longer. In this case the animals won't be able to control their hind legs. They also may vomit, lose interest in food, or fall in coma. People can also have changed mental condition.

Cholecalciferol :

Cholecalciferol was registered in the U.S.A in 1984. It is vitamin D. Vitamin D helps the body to keep calcium balance by increasing absorption of calcium from the gut and kidneys. Toxic doses of cholecalciferol cause too much calcium in the blood that can have effect on central nervous system, the digestive tract, muscles, kidneys and cardiovascular system. The ability of the body to keep suitable calcium levels must be overwhelmed before cholecalciferol becomes toxic. This rodenticide is multiple-doses; it means the rodents should eat several doses of it. Pets can get sick by eating cholecalciferol, but poisoning of people is very rare.

From routine or one-time exposure, cholecalciferol can be toxic. Symptoms in animals are weakness, depression and loss of appetite. Symptoms develop to include constipation, vomiting, increased thirst, more repeated urination and dehydration. The ones who survive can have permanent damage to kidneys and muscles. Cholecalciferol can be kept in the body and its breakdown products are removed slowly; that's because the symptoms of poisoning may remain for weeks. The experience of people who were exposed to cholecalciferol was unusual thirst and increased urination. If the increasing of calcium levels keeps long enough, they can suffer from heart and kidney damage.

Strychnine:

It was also first registered in 1947, but had been used for many years before 1947. It can just be used illegally. The products that have more than 0.5% of strychnine are strictly controlled; they are just sold to certified applicators. Strychnine comes from the seeds of *Strychnosnux-*

vomica and *Strychnosignatii* plants (Talcott, P. A. Strychnine 2006). It affects the spinal cord by causing nerve cells to fire more willingly, and that leads to muscle spasms. Enough doses can cause breathing paralysis and death.

Poisoning from strychnine can cause involuntary muscle spasms in animals and also people. The spasms can be intense, and include “extreme extension of the limbs.” After the ingestion of strychnine the signs of poisoning begin in fifteen minutes in people and in two hours in animals.

Effect of pesticides on human health and environment:

The effect of pesticides can be different in various people. Children can be more sensitive to some pesticides than adults, because their body is developing so it cannot break down some chemicals as effectively as adults. Besides that, they play on the floors and lawns or put objects on their mouth, and this increases the chance of their exposure.

People who have asthma or other chronic diseases can get sick after pesticide exposure more easily than healthy people. Some people are more sensitive to the odor or other irritant effects of certain pesticides.

However, no matter what their individual sensitivities are, people in “the greatest dangers of pesticide illness are those whose exposure is highest” like workers who mix and apply pesticides. People who use pesticides in their home can also be overexposed and become ill, especially if they don’t carefully follow the directions on the product label. Also people living near agricultural fields are more likely than urban residents to be exposed to farm chemicals.

Pollution of Agricultural pesticide:

Agricultural pesticide pollution results from the use or wrong use of agricultural pesticides, and manifests itself as harmful effects on human health and the environment. An agricultural pesticide is any substance or mix of substances intended for preventing, destroying, or reducing the effects of any pest that may affect the growth or productivity of any agricultural product.

The development and construction of agricultural pesticides became universal after World War II, as wartime scientific knowledge was applied to several technological inventions including the production of agricultural pesticides. These chemicals were introduced to U.S.A agriculture and later on to other parts of the world. They were touted as miracle technology that would eliminate hunger in the world. While agricultural pesticides may not have eliminated hunger and starvation

in the world, these chemicals has lived up to their expectation in increasing agricultural productivity and crop yield, and reduced post-harvest losses. For instance, pesticides were used for the control of insect and fungal pests of potato in the U.S.A in the 1940s, also in the early 1950s in Japan were used for control of insect pests of rice, and the control of boll-weevil in El Salvador in 1953 (Ibitayo 2011).

Harmful human health and environmental effects:

Agricultural pesticides are purposely made as poisons to destroy agricultural pests. By the same token, these chemicals may result in wide damage to human health and the environment. Harmful human health symptoms of agricultural pesticides pollution may consist of headache, body weakness, blurred vision, vomiting, irritability, impaired concentration and abdominal pain. Other symptoms include the repression of the human immune system, non-institutional depression, asthma, reduced sperm concentration and power, blood and liver diseases and nerve damage.

The harmful effects of agricultural pesticide pollution are not limited to human health but expand to the environment. Pesticide remnant may enter streams by run-off and put dangers to fish, birds, wild animals and plants in the aquatic habitat. Also, resistant pesticides like DDT may bioaccumulate, move through the food chain and finally be ingested by and adversely affect birds, wild animals and domestic livestock.

Causes of wrong use and/or risky use of agricultural pesticides:

The incidence of agricultural pesticide pollution or poisoning is exacerbated through misuse or unsafe use. The common factors of agricultural pesticide misuse or unsafe use in developing countries consist of the absence of accurate regulations and the lack of implementation of existing ones, the failure to follow label instructions and guideline, and the importation of toxic agricultural pesticides that have been prohibited or are severely restricted in developed and industrialized countries. The others include the use of leaking equipment, exposure to pesticide drift, negligence to wear personal protective equipment (PPE) like gloves, long pants and respirators, and scheduled application of pesticides regardless of the level of pest infestation.

Other dangerous actions that are especially common in developing countries include storage of pesticides in family bedrooms and in unlocked cabinets that children can access easily,

inappropriate disposal of empty pesticide containers, the use of empty containers for household purposes, for example, storing foodstuffs and water for both humans and animals. But misuse or unsafe use of agricultural pesticides is not limited to developing countries. In some developed and industrialized countries there exists the use of outdoor-destined agricultural pesticides for indoors, to control household pests (Ibitayo 2011).

Strategies for reducing agricultural pesticide pollution:

Some strategies that have been suggested to decrease agricultural pesticide pollution and the effects, include: 1) extensive risk communication and education programs, 2) the use of suitable personal protective clothing, 3) selection of disease-resistant hybrid specimens, 4) admission of Integrated Pesticide Management (IPM). IPM emphasize non-chemical and cultural cultivation of pest control strategies, like removing the infected parts of plants, crop rotation that may interrupt the life cycle of pests, and biological control like the use of insect predators.

Non-cancer health effects:

1: Asthma, 2: Birth Defects, 3: Neurological Effects, 4: hormone disruption.

1) Asthma:

There are two words in explaining the asthma problem: *cause* and *trigger*. To understand better we should know the difference between these two. A *cause* is a fundamental reason why people get asthma or other diseases. The accurate causes of asthma are unknown, but specialists have shown that exposure to cigarette smoke, allergens and air pollution can cause high levels of asthma in populations. On the other hand, a *trigger* is something that causes an asthma attack in persons who already suffer from the disease. There are lots of known triggers of asthma attack, like cigarette smoke, perfume, air pollution, wood smoke and so on. As it is clear regarding cigarette smoke, pesticides have also been shown to both cause and trigger asthma attacks.

Asthma is a serious chronic disorder of the lungs which manifests itself by repeated attacks of bronchial constriction that cause coughing, wheezing and breathlessness. In most of the cases asthma is a dangerous disease and it can threaten life. Researchers have found that pesticide exposure can make a poisoning effect connected to asthma. Asthma has both genetic and environmental aspects. Some people are genetically predisposed to asthma and allergies. But, the

fast increase in asthma rates in recent years cannot be explained just by genetic causes, and also asthma rates are increasing between people without family history of asthma and allergies.

There is obviously an important environmental component to the increasing asthma rate. There exists, up to now, no study that can conclusively prove that a certain pesticide causes asthma, but studies have shown the evidence that exposure to pesticides is associated with higher rates of asthma. For example, in one research focus was on farmers and pesticide applicators; they were exposed to higher levels of pesticides than the rest of the population. Studies have shown that these groups have higher rates of asthma and also other respiratory problems because they used pesticides. But pesticide exposure because of work is only one part of the problem, Household and community exposure to pesticides can also cause respiratory problems. A study done in the 1960s in Hawaii discovered that recurrent household use of insecticides is related with an increased prevalence of respiratory problems, like asthma and chronic bronchitis. Most of the pesticides used were insect sprays for flies, cockroaches and mosquitoes.

As well as being a basic cause of asthma, pesticides can also trigger asthma attacks in people who already suffer from the disease. Asthma is determined by extreme sensitivity of the lungs to different motives, which can trigger an asthma attack. There are many things which can trigger asthma attacks, like allergens, irritants, pesticides and other chemicals, tough exercise and air pollution.

People who have asthma are very sensitive to pesticides and there is a risk of attack even with a small amount of exposure. A lot of pesticides are made of small molecules that can make asthma symptoms worse and more serious. Also pesticides increase airway hyper-reactivity that can trigger asthma attacks, which makes the airway more sensitive to any allergen or other causes. Researchers have shown that pesticides in some ways change the nerve function controlling the smooth muscle lining of the airway, causing the airway to condense and hold airflow, which is exactly what happens during the asthma attack. Also pesticides damage directly the cells that line the lungs and so trigger asthma attacks.

Not all the pesticides are associated with asthma, however most of them are. The following is list of some generally used pesticide and how they contribute to asthma:

Herbicides:

➤ **Glyphosate :**

One of the most generally used pesticides on lawns and landscapes is glyphosate. The asthma-like symptoms and some breathing difficulty can happen after exposure. The glyphosate have been linked to pneumonia and also mucous membrane tissue's damages and upper respiratory tract problems.

➤ **2,4-D and Chlorophenoxy Herbicides:**

In U.S.A 2,4-D is generally use as a lawn herbicide in home and garden. Chlorophenoxy compounds like 2,4-D are softly irritating to respiratory linings. People who have asthma should avoid exposure, as it can make the condition worse and trigger an asthma attack.

➤ **Atrazine:**

In landscapes, golf courses, agriculture and lawns applicators use atrazine. Because large group of pesticide applicators use atrazine, it is associated with wheezing. Also, exposure to atrazine can increase breathing rate and lung congestion.

Insecticides:

➤ **Pyrethrum and Pyrethrins:**

Pyrethrum and Pyrethrins are made from raw plant extracts; these extracts have impurities that can be allergenic or irritating. Since 1930s Pyrethrum has been known to cause asthma, allergies and respiratory irritation. A more purified form of these extracts is Pyrethrins; since it has small amount of impurities. Nevertheless, it can causes asthmatic reactions and sensitization in persons exposed to it. Usually the products of Pyrethrum and Pyrethrin are formulated with PiperonylButoxide (PBO). Inhalation of PBO can cause hard breathing and induce fluids to accumulate in the lungs; it is also linked to cancer.

➤ **Synthetic pyrethroids (Permethrin, Cypermethrin, Cyfluthrin, Sumithrin, Resmethrin):**

The others chemically formulated versions of Pyrethrum are synthetic pyrethroid that are engineered to be more toxic and longer lasting. Synthetic pyrethroid exposure can cause hyper sensitization. They are usually formulated with PBO.

➤ **Organophosphates (Chlorpyrifos, Diazinon, Malathion, Methyl Parathion):**

Organophosphates or OP are used in houses for termite control, as a mosquito spray, and also in agriculture and on golf courses. OPs are neurotoxic and exposure can cause respiratory muscles weakness, bronchoconstriction, wheezing, bronchial secretions and respiratory failure. OPs exposure can cause short and long term respiratory effects.

➤ **Carbamates (Carbaryl, Carbofuran):**

One of the insecticides is Carbamates, which is widely used in gardens, agriculture and homes. Carbamates also cause respiratory problems, just like OPs.

Fungicides

➤ **Fungicides:**

Lots of different fungicides are cause cases of occupational asthma among workers. Also fungicides cause hypersensitivity in workers who deal with them; as a result their airways become very sensitive and show reactions to inhaled fungicides, like wheezing and breathlessness.

Asthma will not disappear on its own because it is a serious epidemic problem. Parents should limit their children from exposure to pesticides at home, community and school, whether they have asthma or not. There are easy steps that everybody can take to avoid pesticides and their consequences, and also reduce the risk of getting asthma. For example, EPA has shown that almost 85% of total daily exposure to pesticides comes from the air inhaled inside the house. So, parents and house owners should avoid applying any pesticides inside the house, and also on lawns and gardens. Instead, people can try to solve their pest problems using non-toxic controls and preventive actions. Children are also at risk of exposure to pesticides in schools. To protect children's health, schools should pursue non-toxic management methods. On the other hand, adults spend most of their time in office buildings, and studies show that, on average, 40% to 55% of office workers have had an experience of headache, cough, fatigue and wheezing on a weekly basis. Office building also should adopt an integrated pest management program that depends on non-toxic practices.

2) Birth defect

Exposure to pesticides and problems like birth defects and altered fetal death are linked together by strong evidence (Sanborn M *et al.* 2007). The generally used pesticide, chlorpyrifos, has been shown to cause intense birth defects in four children exposed in the uterus. Chlorpyrifos is largely used as an agricultural chemical, and also is the most common pesticide used indoors to kill termites, fleas, roaches and in pest control strips.

The case that brought into the public knowledge that there is a connection between birth defects and pesticide exposure was the births of three babies in Florida in 2005 with very bad birth defects. Their mother worked for Ag-Mart produce, a company that produces chemically-treated tomatoes and other agricultural products. Birth defects are defined as structural or functional abnormalities present at birth that make physical or mental disabilities in a range of mild to fatal. Scientists have recognized thousands of several types of birth defects. Currently, birth defects are the major causes of death in the first year of life of infants. In April 2009 the medical journal *Acta Paediatrica* published reports that indicate that in the U.S.A the highest rates of birth defects arise when gestation happens during the months of spring and summer, because during these months the use of pesticides increase and there is high concentrations of pesticides in surface waters (Winchester D *et al.* 2009). Scientists found a strong relationship between higher rates of birth defects like cleft lip, clubfoot, spina bifida and Down's syndrome, among women who become pregnant when nitrates, atrazine and other pesticides were at the high end of their seasonal changes. Agent orange or Herbicide orange is a combination of 2,4-D and 2,4,5-T, has been related with genetic effects and bad health in Malaya and also Vietnam (Ngo AD *et al.* 2006).

3) Neurological Effects

Pesticides can be strong neurotoxins. When people are exposed to neurotoxins as short-term effects, they might feel dizzy, lightheaded, confused, and may have reduced coordination and ability to think. Long-term exposure can result in reduced IQ and learning disability, associated with fixed brain damage. In spite of vast reporting of harmful symptoms, until recently few studies could link stable brain damage to such exposures. There is new evidence that long term

exposure to pesticides in areas where they are used in great amount there can happen permanent brain damage to children who live in these areas (Children's Environmental Health Center n.d).

There is ample literature suggesting that pesticide exposure may increase risk of Parkinson's disease (PD). Lots of studies have found that PD risk is related to living in village areas, drinking well water and farming as a job. More specifically, many case-control studies have observed that pesticide exposure is related with increased PD risk. In the study of Le Counter et al. (1999), were noted that 12 of 20 studies found a positive association. In most of these studies, exposure was widely outlined as any exposure to any pesticide that might reduce the association (Vergucht, S. *et al.* 2006).

Some of the studies of pesticide exposure and PD risk have been able to show the risk offered by specific pesticides. Several studies found increased risk associated with exposure to either insecticides or herbicides, several studies have showed paraquat, and one study suggested that risk was raised by exposure to organochlorines, organophosphates or carbamates. In addition to analytical studies, several case reports have described PD in individuals exposed to organophosphate, glyphosate, paraquat, diquat, maneb and other ethylene bis-dithiocarbamates (Vergucht, S. *et al.* 2006).

The EPA completed a ten year review of the organophosphate pesticides following the 1996 Food Quality Protection Act; however, of neurotoxic effects, drawing powerful critique from inside the agency and from outside researchers (Phillips ML 2006).

4) Hormone disruption

Endocrine Disruption:

Pesticides, plastics, detergents and disinfectants are the common products which are used in households; the ingredients inside these chemicals can enter the body and disrupt hormones and cause harmful diseases and also developmental and reproductive problems. Because they interact with the endocrine system, they are known as endocrine disruptors.

A set of glands like the thyroid, the gonads, the adrenal and the pituitary glands make the endocrine system; they produce hormones like of estrogen, testosterone and ect. These

hormones help guide the development, reproduction, growth and behavior. Hormones act as signal molecules; they travel via bloodstream and elicit responses in other parts of the body (Owens *et al.* 2010). The endocrine system is serious in both animals and humans. Disruption of hormone function may change normal development of fetus and child forever. Also there are some pesticides that can be toxic to the immune system in animals (Natural Resources Defense Council 1998).

The endocrine disruptors work basically as follows: 1) By imitating the action of naturally produced hormones like estrogen or testosterone, they elicit the same chemical reactions in the body. 2) They prevent the action of normal hormones by blocking hormone receptors in cells, or 3) they have effect on the transport, synthesis, metabolism and excretion of hormones, so changing the concentration of natural hormones in the body. There are some diseases linked to endocrine disruptors like Attention Deficit Hyperactivity Disorder (ADHD), Alzheimer's and Parkinson's diseases, diabetes, obesity, infertility, cardiovascular disease, early puberty and childhood and adult cancers. The European Union has identified more than fifty active ingredients in pesticides that work as endocrine disruptors (Owens *et al.* 2010).

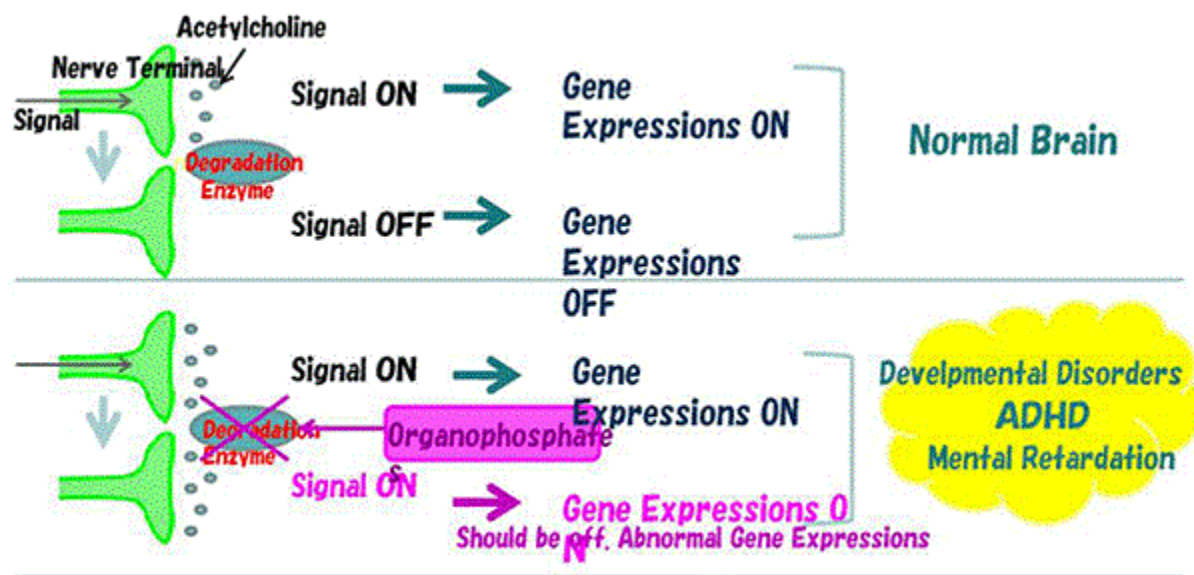


Figure 9: How Organophosphate can cause the ADHD disease

Lots of pesticides currently in use are known to interfere with the normal function of hormone in animals. For instance, common fungicides like vinclozolin and iprodione, both decompose

into a metabolite that intervene in function of testosterone and other androgens. Different organochlorine pesticides like DDT, endosulfan, dicofol and methoxychlor, imitate estrogen. It's common to use Lindane to cure head lice, especially in children, but it can act as an anti-estrogen and also can be toxic for the nervous system. The common herbicide Atazine can interrupt ovarian function and make breast tumors happen in animals. Until now there are no studies to show the effects of these chemicals on endocrine system in humans, but the endocrine system in animals is almost the same as in humans, so making it probable that effects observed in animals may be also related to human health risks.

Most of the epidemiological studies about pesticide exposure and children's health were done on the non-farming population. Maybe they minimize the health impacts on farm children. It is very important to recognize the sources and levels of exposure to pesticides to protect the most highly exposed children from impact of these dangerous chemicals on their health (Natural Resources Defense Council 1998).

Cancer effects:

For a long time the link between pesticides and cancer has been a concern. While agriculture has traditionally been attached to pesticide-related sicknesses, nineteen of thirty generally used lawn pesticides and twenty eight of forty generally used school pesticides are related to cancer. In recent years there are lots of evidences linking environmental exposure to cancer, but in May 6, 2010 a report released by the President's Cancer Panel found out that the true burden of environmentally caused cancer is minimized very much. Scientists found out that there is an association between cancer and use of pesticides in agriculture and all over the urban environment in homes, public places and schools. There are some cancer linked to pesticides exposure include brain, breast, lymphoma, leukemia, soft tissue sarcoma, prostate cancer and lots of other cancers (Owens *et al.* 2010).

Brain cancer:

Brain cancer appears in two main types: primary and metastatic. Primary brain cancer begins in the brain, but metastatic brain cancer first starts somewhere else in the body and then moves to the brain. As reported by American Brain Tumor Association, the most solid tumors in children are brain tumors. The second main reason of cancer-related deaths males under 40 and females

under 20 is brain tumors. Scientists believe that insecticides, which aim the nervous system, can play role in the development of brain tumors. There are several studies that show adults with brain cancer are more likely to have been exposed to pesticides (Owens *et al.* 2010).

Breast cancer:

As doctors estimate, one in eight women will be diagnosed in their life with breast cancer. Breast cancer is one of the deaths cause in North America for women in ages 35 to 50. In five to ten percent of these cases genetics can be considered as the causation factor. According to the Breast Cancer Fund, growing body of scientific evidences suggests that toxic chemical exposure like pesticides in the environment are contributing to high breast cancer rates. Some pesticides can be breast carcinogens and others can act by mimicking hormones in the body, so they can also cause breast cancer (Owens *et al.* 2010).

Leukemia:

Leukemia is the cancer of blood-forming cells of the bone marrow, and it is one of the most common childhood cancers. Many studies show a “critical window of exposure” to pesticides. Children’s exposure to pesticides that are used in their homes, or from parental occupational use, is associated with leukemia in them. Also the pesticide exposure during the mother’s pregnancy may cause high risk of leukemia in children. Several studies link leukemia to agricultural and residential exposure to pesticides, for children, adults and fetuses (Owens *et al.* 2010).

Lymphoma:

Cancers that arise in the lymph system are referred to as lymphomas and consist of Hodgkin’s lymphoma (HL) and non-Hodgkin’s lymphoma (NHL). In the U.S.A the most common blood cancer are lymphomas. Lymphoma is the 3rd most common cancer in children and 7th in adults. The occurrence of NHL has been growing over the past several decades. The Lymphoma Foundation of America reported that 75 out of all 99 epidemiologic studies done on lymphoma and pesticides showed a link between these two. These reports show that the people who were in states and locations with the high pesticides use, developed lymphoma more than the others (Owens *et al.* 2010).

Prostate Cancer:

The prostate is a gland in the male reproductive system. The second most common cancer among American men is prostate cancer. Researches show high rates of prostate cancer in Vietnam veterans exposed to Agent Orange and also farmers that had exposure to pesticides. International Journal of Cancer published a study in 2003 and showed that people who work in agriculture have a higher 40% of chance to having prostate cancer compared with other people. Some other studies suggest that endocrine disruption can be the mechanism for developing this type of cancer (Owens *et al.* 2010).

Soft Tissue Sarcoma:

Soft tissue sarcoma starts in the muscle, fibrous tissue, fat, blood vessel and other body's supporting tissue. It is an uncommon type of cancer and the risk can increase by the exposure to certain chemicals and radiation therapy. In a study of Denver children in 1995 it was found that yard pesticide applications are linked to increasing the risk of soft tissue sarcomas. And ten other studies showed that living near agricultural areas can be associated with this type of cancer.

There are lots of pesticides on the market and a great number of possible combinations for exposure. Scientists link different types of cancers to pesticides. According to President's Cancer Panel almost 40 chemicals are arranged by the International Agency for research on Cancer (IARC) in categories known as being possible human carcinogens, yet they are used in EPA, now on the market. These chemicals offer the risk of lots of cancer like: lungs, eye, mouth, esophagus, bone, pancreas, colon, bladder and etc. (Owens *et al.* 2010).

Effects on environment:

The only groups of chemicals that are consciously applied to the environment with aim to repress plant and animal pests and to protect agricultural and industrial products are pesticides. But most of the pesticides do not specifically target the pest only, and during their application they also affect non-target plants and animals. "Repeated application leads to loss of biodiversity" (Pesticide Action Network 2010). Many pesticides are not degrade easily, they "persist in soil, leach to groundwater and surface water" and make wide environmental

contamination (Pesticides Action Network 2010). Environmental effects of pesticides are in different media:

- 1) **Soil contamination:** pesticides enter the soil through spray drift during leaves treatment, wash from treated leaves, release from granulates or from treated seeds in soil. Some pesticides like soil fumigants and nematocides are applied directly into the soil to control pests and plant diseases that exist in soil. Depending on the pesticides' chemical properties, and also physical, chemical and biological properties of the soil; transport, durability, or degradation of pesticides can be vary. All these factors affect sorption/desorption, volatilization, degradation, uptake by plants, run-off, and leaching of pesticides. (Pesticides Action Network 2010).
- 2) **Water contamination:** During pesticides spraying, they can go into water through drift, by runoff from treated area, leaching through the soil. In some states pesticides can spread directly onto water surface like for control of mosquitoes. Water pollution depends mostly on the nature of pesticides, soil properties, weather conditions, landscape and also on the distance from an application place to a water source. Quick transport to groundwater can be caused by heavy rain at any moment after application of the pesticide to wet soil. (Pesticides Action Network 2010).

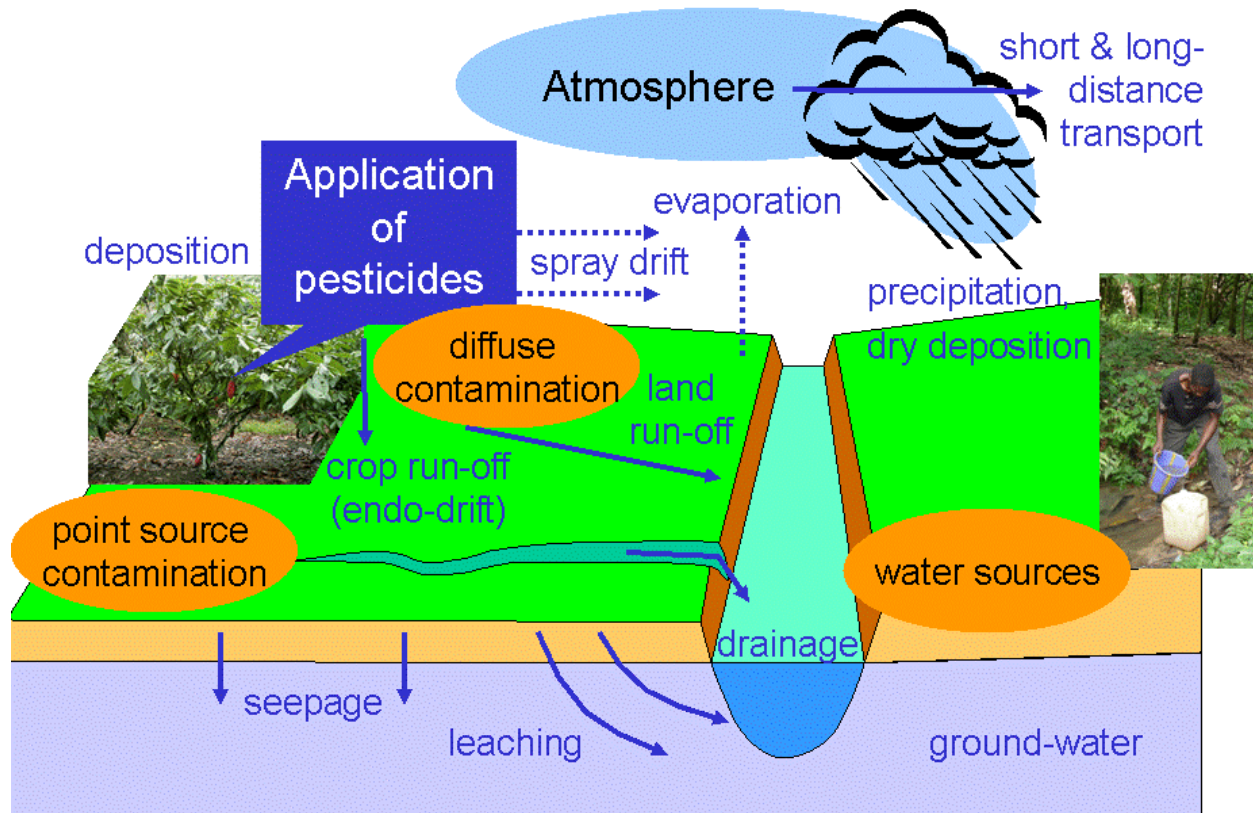


Figure 10: The contamination of water and soil by Pesticides

3) Effects on organisms :

- a) **Soil organisms:** soil microorganisms play a key role in soil. They are necessary for maintenance of soil structure, alteration and mineralization of organic materials, and making nutrients available for vegetables. Also soil microorganisms are able to metabolize and degrade lots of pollutants and pesticides. But then, microbial degradation can make more toxic and persistent metabolites. Soil microbial population is determined by fast flexibility and adaptability to changed environmental conditions, but the application of pesticides – especially long-term ones –can cause important irreversible changes in their population (Pesticides Action Network 2010).
- b) **Soil invertebrates:** nematodes, springtails, mites and other micro-arthropods, earthworms, spiders, insects and all these small organisms make the soil food web and enable decomposition of organic compounds like leaves, manure, plant residues, and

they also “prey on crop pests”. Soil organisms increase soil density and porosity and so “increasing infiltration and reducing runoff” (Pesticide Action Network 2010).

Earthworms play a very important role in soil ecosystem and also they are the greatest part of biomass of terrestrial invertebrates. Earthworms are determined by high ability to accumulate a lot of pollutants from soil in their tissues, so they are used for studying bioaccumulation potential of chemicals (Pesticides Action Network 2010).

- c) **Other soil species:** glyphosate affect predatory arthropods like spiders and ground beetles in agricultural fields, they also cause behavioral changes and even an exposure to residues can have influence on long-term surviving. Herbicides can have an effect on the arthropods’ community dynamic, as distinguished from their impact on plant community, and may influence biological control in agroecosystem (Pesticide Action Network 2010).

- d) **Other non-target species:** bees, butterflies and natural enemies:

Broad-spectrum insecticides such as carbamates, organophosphate and pyrethroids, can cause population reduction of useful insects like bees, spiders, or beetles. Many of these species play an important role in the food web, or as natural enemies of pest insects. Since 1970, insect numbers in cereal fields in Sussex, England, have dropped by half. The number of bugs, spiders and beetles were significantly higher in untreated fields. In British organic farms, numbers and species affluence of butterflies was greater than in usual farms. The number of carabid beetles and spiders was usually higher on organic farms. Standard management practice appeared to affect natural enemies far more than other insects or target pests. Moths were significantly more abundant on organic farms and species richness was higher. In arable fields, insecticide use was an important factor influencing communities of epigeic spiders. On the place with an increased pesticide input, communities of bugs, wild bees, and spiders were more equal, showing less exchange between communities in areas with “hard” agriculture.

Bees do the very necessary pollination. Honey bees are under pressure from parasitic mites, viral diseases, habitat loss and pesticides. Intensified agricultural practices, habitat loss, and agrochemicals are considered to be among the chief environmental threats to Europe’s honey and wild bees. Agricultural policy must reduce these

pressures to make sure about enough pollinator populations. On organic farms in the USA, with near natural habitat, various native wild bee communities provided full pollination services, while diversity and numbers of native bees were greatly reduced in other farms. In the UK, 95 cases of bee poisoning—where the cause could be identified—have shown that, between 1995 and 2001, organophosphate caused 42%, carbamates 29%, and pyrethroids 14% of cases. In the last decades in the UK, insecticides which poisoned bee colonies included bendiocarb (a carbamate) and three pyrethroids: cypermethrin, deltamethrin and permethrin. Synergistic effects between pyrethroids and EBI fungicides (imidazole or triazole fungicides) can increase the risk to honeybees.

Clothianidin and imidacloprid are highly toxic to bumble-bees and other wild bees. These two neonicotinoid insecticides are used to remedy corn and sunflower seeds. In 2008, clothianidin caused many bee poisoning and colony deaths in southern Germany. When imidacloprid-treated seed is grown, a large enough amount can enter the environment to poison bees. Residues of imidacloprid in corn pollen grown from treated seed can be a high risk to bees due to sublethal effects. Even at low doses of imidacloprid, bees' foraging behavior was negatively affected (Isenring 2010). Lately, use of clothianidin in seed treatment caused extensive bee poisoning. Residues of imidacloprid in plants can negatively change the behavior of bees.

e) Aquatic life:

When environmental pollution such as that caused by pesticides affect the health of aquatic organisms like fishes and other organisms, aquatic toxicity can happen. The capacity of pesticides to injure fish and aquatic animals is mostly a function of its toxicity, dose rate, exposure time and stability in the environment. Pesticides' exposure of fish and other aquatic animals rely on its bioconcentration, biomagnifications, bioavailability and stability in the environment.

Bioconcentration is the reposition of pesticides in animal tissue at levels more than the ones in the soil or water to which they were applied. Some fishes can localize some pesticides in their body tissues, like fats and organs, at levels ten million times more than in the water.

Biomagnifications is the reposition of pesticides at each consecutive level of the food chain. Certain pesticides bioaccumulate in the food chain. For instance, if a pesticide exists in water, water plants can absorb it and then it can be eaten by insects and minnows. They also become polluted. In the food chain, at each step the pesticide's concentration can increase. When a fish, like trout, constantly eat polluted animals, they bioconcentrate high levels of pullutants in their body fat. The poison can pass on to human by fish.

Bioavailability refers to the pesticide's amount in the environment accessible to fish and wildlife. Some pesticides breakdown quickly after application, but some bind firmly to particles of soil suspended in the water column or stream bottoms, so that their availability is reduced. Some of them are diluted fast in water or evaporate quickly into the air and are less available to aquatic life. The plants and insects inside the water are the habitat and food for fish and other aquatic animals, Pesticides can reduce their availability in aquatic environment.

When pesticides are applied, insects that fishes eat are killed, and they can thus lose a significant amount of their food supply. When the insects supply for fishes become inadequate suddenly, it forces them to range farther to search food, where they may risk more exposure to predation. Also, the reproductive success of fishes and aquatic animals can be reduced by the spraying of herbicides. For many fishes the shallow, weedy nursery areas supply plentiful food and shelter for young fishes.

Aquatic plants provide almost 80% of the soluble oxygen essential for aquatic life in lakes and ponds. Killing the aquatic plants by spraying herbicides can have a severe result as low oxygen level and the asphyxiation of fish. The pollution of a river, lake or pond with herbicides can significantly reduce fish habitat, food supply, soluble oxygen and fish productivity.

The way of exposure to pesticides for fish and aquatic animals is almost the same as for humans. There are three principal ways: **First**, dermal: during swimming in pesticide-polluted water, direct absorption can happen through the skin; **Second**, breathing: by direct uptake of

pesticides via the gills during respiration, and **Third**, orally: with drinking the pesticide-polluted water or eating the pesticide-polluted prey.

There is also secondary poisoning, that happens when fish eat animals that have been poisoned and killed by a pesticide. For example, fish eating dying insect poisoned by insecticides can themselves be killed if the insects they eat contain large quantities of pesticides, or their toxic byproducts.

There are some ways to reduce the risk of using pesticides. Before the use of pesticides one should consider some points that can help to cause less toxicity to environment.

1. Only use a pesticide when it's extremely necessary: if there are different ways for treating the problem, use them. Owners should consider the costs and consequences of pesticide treatment to the problem.
2. Use the pesticides with less toxicity: one of the ways to reduce the pesticides effects on aquatic systems is using the chemicals which are least poisonous to aquatic life.
3. Use secure and reasonable application methods: the first rule to use pesticides is to read the pesticide label and follow the directions exactly. If the label be confusing for the user and he or she does not understand it, the user can contact the Extension Agent, the provider or the pesticide company to get more information. Attention should always be paid to warning statements about environmental hazards on the label. It is essential to check if the application equipments are working well. Never should one wash equipment used for the spray of pesticides in lakes, ponds or rivers. And, finally, one should try to keep and store containers of pesticides according to the label instructions. (Virginia Cooperative Extension 2009).

f) Birds:

Chemical relatives of DDT, the organochlorine insecticides are still killing birds. The same happens with carbamate and organophosphate insecticides, although they are not as resistant as organochlorine. Because they are degraded more quickly by light and microbes, their high acute toxicity and extensive use make them an important problem to birds. Some extremely toxic herbicides also kill birds. There are some associations between bird mortality and each of pesticide's classes.

Organochlorines:

When DDT's registered uses were cancelled, the organochlorine threat to birds didn't go away. Several organochlorine pesticides like the miticidedicofol (that also causes eggshell thinning in birds) are still used in USA. DDT and related compounds are still used in many countries around the world. Birds that migrate to other countries can bring back residues store in their tissue to the origin country. Some analysis showed that these birds brought back the residues of pesticides to America. For example, analysis found high levels of the DDT metabolite DDE and dicofol ad methoxychlor in great horned owls. The owls don't migrate, so the organochlorine residues could have come from the birds' migratory prey, resistant residues from prior years carried by the long-lived birds. Because there are several ways for contamination, it's not possible to determine the source (Cox 1991).

Organophosphates:

As we mentioned before, organophosphate insecticides inhibit the enzyme acetylcholinesterase in the nervous system. Since we all have similar mechanisms of nerve transmission, in target insect, birds and mammals, this mode of action is similar. Most of the organophosphates are extremely toxic to birds even at very low doses. A recent research about acute lethal doses (LD50) for the mallard duck showed that sixteen of twentyorganophosphate

were extremely toxic at doses less than twenty milligrams per kilogram of body weight. Well attested bird kills have been caused by the organophosphate diazinon, chlorpyrifos and isofenphos. All four organophosphate, phosphamidon, fenitrothion, acephate, and trichlorofon, which reviewed in aerial forestry application review, caused reductions in the abundance of singing males, the number of species present, or the number of birds present (Cox 1991).

Carbamates:

Because the mode of action of carbamates is similar to the organophosphate, some carbamates insecticides kill birds at low doses. The best known example is cabofuran that has been estimated to kill one to two million birds per year in the U.S.A. There are three carbamates, aldicarb, carbofuran, and bendiocarb, they are granular formulation, and it means they are made of small particles that birds can eat. Over half of house sparrows, when fed these pesticides, were killed by ingestion of just one granule and only five to ten granules killed red-winged blackbirds. But, a research of effects on bird population as a result of a forestry application showed that both the abundance of birds and the number of bird species present was reduced by aerial spraying of carbaryl. There are some other studies of forestry carbaryl application that found no important effects on birds, but researchers noted that this research lasted longer and used larger spray blocks than the studies that found no effects (Cox 1991).

Herbicides:

Although one would expect that herbicides be less extremely toxic to birds or even other animals than insecticides, the fact is that some herbicides are fatal to birds even in small doses. A dinitrophenol herbicide called Dinoseb, gets involved in the basic energy metabolism in both animal and plant cells, kills wild birds at low doses and is as extremely toxic to birds as some of the most toxic insecticides. Paraquat herbicide is very toxic to human and animals; it can kill adult birds, and also can kill nestling kestrels. Some nestling died because they were fed paraquat. The herbicide dinitro-ocresol, also is quite toxic to birds.

As long as humans use pesticides, these toxic chemicals will continue to kill birds, reduce their food resources and disrupt their normal behaviors. The only way to remove the pesticide effects on birds is to use “nonchemical resource management techniques”. Everywhere where pesticides are used, like farms, forests or lawns, managers should find that these techniques work well and make economic sense (Cox 1991).

Discussion:

Pesticides are highly effective substances that can control pests and vectors of human diseases. After World War II the application of pesticides in agriculture increased substantially, aiming at the multiplication of crops yields, and the production of high quality products to satisfy the increasing food demands all over the world.

The over-increasing use of pesticides brought concerns about their effects on human health and environment. Due to the ability of pesticides to kill living organisms, it also means that they have toxicity to humans and to non-target organism in environment. There are different groups of pesticides, and they are differentiated by their chemicals structures, and each of them has a special effect on a special target. Insecticides are the ones which kill insects and the other groups of arthropods. Organophosphate is one the insecticides and it's very toxic to vertebrates and chemically unstable. They make disorder in the nervous system by blocking the activity of cholinesterase at the nerve endings.

Carbamates have a range of biological activates and that's because they become a serious public problem. They can also have effect on nervous system and in high levels they can cause cancer. The people who work on agriculture like the ones that do harvesting or pesticides applicators are more in the exposure of these chemicals.

Organochlorine effects on nervous system by interrupting the calcium ion channels in nervous system, and also because they are stable, they can pass through the food chain and make disease in human and animals. The effect of these pesticides on growth hormone system in human is also one of the worries in public health.

Prythroid and Pyrethrins are the newest group of insecticides that has less toxicity and danger for human and environment. They block the sodium channel in cell membrane and if they make systemic poisoning generally there is no antitoxin for it. The insecticides are all synthetic pesticides and due to their poisoning feature they can be more dangerous and should be more concern about them. People who use pesticides should try to don't use these chemicals and instead using safe ways to destroy the pests.

Other groups of pesticides are microbial pesticides they are actually biological controls. By using the microorganisms like virus, bacteria and so on, we can destroy most of the pests. Because they are very specific and most of the times making and producing them is expensive, using of these pesticides are not very popular yet. Depends on what group you want to use, you

can choose the cheapest one like bacillus thuringiensis that producing them is easy and fast, but in the other hand viruses are expensive and hard to grow them in vitro. By time passing on if scientists can find a better and cheaper ways to produce these pesticides would be very helpful with less hazardous features.

New generations of pesticides are PIPs. These interesting pesticides are actually the gene of the bacteria inserted inside the plant's gene, so as the plant grow and do the metabolism; it makes the pesticides in its own tissues. So if the pest feeds on plant, it will die. These pesticides have a great and bright future in the agriculture.

As we use fungi to destroy the pests, we also need fungicides for the ones which make disease on plants. Fungicides are in different groups according to their way of action. If you know what effects each fungus makes on organisms or plants you can choose the best fungicide product and have the best result.

Herbicides and rodenticides are also the pesticides that we use to kill the weeds and rodents. These ones can be more dangerous for animals because they are more using in their living environment. They can be eaten by them and make lots of diseases or even kill them. So we should be careful about the way of using and also storing them to keep them far from living animals and young humans.

The effect of pesticides on human health is serious, and they can cause several diseases. These diseases can be cancers and non-cancers. Most of the diseases are dangerous and fatal, especially for developing and young children, those with chemical sensitivities, and those with compromised immune systems.

Asthma is one the health effects. Most of the pesticides are like dusts or small pieces, if you spray them on to the air or ground. These dusts can go to your respiratory system and cause or trigger the asthma. So using mask and proper cloth is necessary while using them. There are some evidence showed not all but most of the groups of pesticides like herbicides, insecticides, organophosphates and fungicides are contributing to asthma. Strong evidences link pesticides to birth defects. Pregnant mothers who were on the exposure of pesticides, especially during spring, had babies with different kind of birth problems. These can show that these toxic chemicals can go through the blood and also can transfer from mother to babies and make dangerous disease. As we talk about it most of the pesticides are having effect on nervous system, so they are strong neurotoxins. They can disrupt the action of nervous cells and cause harmful effects, like

Parkinson's disease. These chemicals can also go inside the body and interact with endocrine system. As we see these days most of the young men and women have infertility problems and they cannot have baby. Using of pesticides in our food and living environment raise our exposure to these toxic chemicals and they cause some problems in our health that sometimes is irreversible.

Pesticides and cancers were linked together for a long time and it was always a concern for public health. Although they are linking lots of cancers like brains cancer, breast cancer, leukemia and so on, and but still there is no certain evidence that can prove that pesticides are carcinogens for sure. In the other side according to President's cancer panel almost 40 chemicals are arranged by the IARC in categories known as being possible human carcinogens.

Also, pesticides affect the environment and organisms in it. They can cause pollution on soil, like fumigants that they are injected inside the soil to kill the termites and bedbugs or nematocides which are applied directly inside the soil. These chemicals can move through the soil and kill most of the useful organisms. Also they pollute water; this can happen by runoff from soil or treated area and also sometimes can spray directly to the water. This can be dangerous for aquatic life, because they destroy most of the good aquatic plants that they are the living environments of fishes and other aquatic organisms and can have serve result of low oxygen level. They can also destroy little organisms which they are fish's food.

Making pollution on air, killing birds, fishes and organisms in the soil are the other dangerous results of using synthetic pesticides. They can pollute our food and water that we drink and in this way they can transfer these chemicals to human and other animals.

Although there are not unquestionable proofs for most of the diseases that are linked to pesticides, still there is abundant evidence that allow us to recognize a very strong link between pesticides and a vast array of illnesses, both in humans and animals and plants. Despite many efforts to show and diagnose the diseases, more research is needed to find and develop the ways of preventing them and to present the results to the entire world. The ailments that have been found in animals and humans have several similarities between them. Persons who use these substances, or who are exposed to them, must know about the health risks and the ways of reducing these risks. Also, governments should have a ban on the non-essential use of pesticides

and suggest that the sale and use of these chemicals be regulated to minimize the possibility of damage to human and environmental health.

References:

B. Todd, G.W. Suter II (2012) 'Herbicides' **CADDIS: The Causal Analysis/Diagnosis Decision Information System** 2, EPA: Environmental protection Agency [online]. Available at: http://www.epa.gov/caddis/ssr_herb_int.html (Accessed :18/02/2015).

Bedford, G.O. (1980) 'Biology, Ecology, and Control of Palm Rhinoceros Beetles' **Annual Review of Entomology** 25, pp. 309-339. Available at: <http://www.annualreviews.org/doi/abs/10.1146/annurev.en.25.010180.001521?journalCode=ento> . (Accessed:15/01/2015)

Beyond Pesticides (n.d). **Pesticide-Induced Diseases: Asthma/Respiratory Effects**. Available at: <http://www.beyondpesticides.org/health/asthma.php> (Accessed : 20/12/2014).

Boada L.D, Henríquez-Hernández L.A, Zumbado M, Almeida-González M, Valerón P.F, and Luzardo O.P (n.d.). Influence of Organochlorine Pesticides on GH-IGF System. In: Prof. Milan Jokanovic. *The impact of pesticides*. Academy publish.org, p 143-153.

California Department of Pesticide Regulation (n.d). 'What are the potential Health Effects of Pesticides' **A community guide to recognizing and reporting pesticides problems**. pp: 27-29. Available at: <http://www.cdpr.ca.gov/docs/dept/comguide/> (Accessed :20/12/2014).

Campbell, A.; Chapman, M. (2000) Anticoagulant rodenticides. *Handbook of poisoning in dogs and cats*; Blackwell Science pp 64-73. Available at: http://www.armchairpatriot.com/HomeVet/Handbook_of_Poisoning_in_Dogs_and_Cats.pdf (Accessed :10/03/2015).

Chandler, D., Davidson, G., Grant, W.P., Greaves, J. and Tatchell, G.M. (2008) 'Microbial Biopesticides for Integrated Crop Management: an Assessment of Environmental and Regulatory Sustainability'. **Trends in Food Science & Technology** 19, pp. 275-283. Available at: <http://wrap.warwick.ac.uk/1388/> . (Accessed :18/02/2015).

Children's Environmental Health Center (n.d). ***Health Effects of Pesticides***. Available at:
<http://www.kidsforsavingearth.org/mnchec/articles/pesticides.htm> (
Accessed :20/12/2015).

Copping, L. G. and Menn, J. J. (2000) 'Review Biopesticides: a review of their action, applications and efficacy'. ***Pest Management Science***, 56(8), pp. 651-676.

Cox Caroline (1991). 'Pesticides and Birds: From DDT to Today's Poisons'. ***Journal of Pesticides Reform*** 11(4) pp: 2-6. Available at:
http://eap.mcgill.ca/MagRack/JPR/JPR_14.htm (Accessed :12/03/2015).

Ehlers, R. ed. (2011) 'Regulation of Biological Control Agents'. **London: Springer**, pp. 3-32.

Erickson, W.; Urban, D. (2004). ***Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: a Comparative Approach***, U.S.A Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances. Available at:
www.pesticideresearch.com/site/.../EPAComparisonRodenticideRisks.pdf
(Accessed :12/03/2015).

Gunsolus Jeffrey L, Durran William S. (1999). 'Herbicide Mode of Action and Injury Symptoms', ***North Central Regional Extension Publication 377***. Available at:
<http://www.cof.orst.edu/cof/fs/kpuettmann/FS%20533/Vegetation%20Management/Herbicide%20Mode%20of%20Action%20and%20Injury%20Symptoms.htm> (Accessed :18/02/2015)

Gupta Abhik (2008) 'Impact of Pesticides on Human and Ecosystem Health: Scientific, Ethical and Policy issues'. ***academia.edu*** [online]. Available at:
http://www.academia.edu/1001825/Impact_of_Pesticides_on_Human_and_Ecosystem_Health_Scientific_Ethical_and_Policy_Issues (Accessed :28/03/2015).

- Hajek, A.E. and Jr, I.D. (2010) 'Fungal Pathogens as Classical Biological Control Agents against Arthropods'. **BioControl** 55, pp. 147-158. Available at: <https://books.google.com.br/books?id=LFnD2-zWofEC&pg=PA147&lpg=PA147&dq=Fungal+Pathogens+as+Classical+Biological+Control+Agents+against+Arthropods&source=bl&ots=AVSD0ELEKZ&sig=uAA7Xwe-BJ2CmYmhjQE2qvyxgyE&hl=pt-BR&sa=X&ei=iz93VcKhLoSZgwTMrIDgBw&ved=0CDUQ6AEwAg#v=onepage&q&f=false>. (Accessed :10/03/2015).
- Harper, D.R. (2006) 'Biological Control by Microorganisms'. Encyclopedia of Life Sciences (ELS) John Wiley & Sons, Ltd: Chichester. Available at: <http://www.els.net/WileyCDA/ElsArticle/refId-a0000344.html> . (Accessed :10/03/2015).
- Huger, A.M. (2005) 'The *Oryctes*virus: Its detection, identification, and implementation in biological control of the coconut palm rhinoceros beetle, *Oryctes rhinoceros*' (Coleoptera: Scarabaeidae). **Journal of Invertebrate Pathology** 89, pp. 78-84 .
- Hurley, B.P., Slippers, B. and Wingfield, M. J. (2007) 'A Comparison of Control Results for the Alien Invasive Woodwasp, *Sirexnoctilio*, in the Southern Hemisphere' **Agricultural and Forest Entomology**, 9, pp. 159-171. Wiley Online Library [Online]. Available at: <http://onlinelibrary.wiley.com/doi/10.1111/j.1461-9563.2007.00340.x/abstract> . (Accessed :28/02/2015).
- Ibitayo O (2011). **Agricultural Pesticides Contamination**. Available at: <http://www.eoearth.org/view/article/149910/> (Accessed : 12/03/2015).
- Isenring Richard (2010) 'Pesticides and the loss of biodiversity: How intensive pesticide use affects wildlife populations and species diversity' **Pesticide Action Network Eroup** [online] Available at: <http://www.paneurope.info/Campaigns/biodiversity.html> (Accessed :12/03/2015).

James R. Roberts, MD, MPH, Catherine J. Karr, MD, PhD, Council on Environmental Health. (2012). 'Technical Report: Pesticide Exposure in Children'. *Pediatrics*. 130(6). Available at: <http://pediatrics.aappublications.org/content/130/6/e1765.abstract>. (Accessed: 18/02/2015).

Jeyaratnam J (1985). 'Health problems of pesticides usage in the Third World'. *British Journal of Industrial Medicine* 42(8): 505-506. *PMC* [online]. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/4016001> (Accessed :20/12/2014).

Lacey, L. A., Frutos, R., Kaya, H. K. and Vail, P. (2001) 'Insect Pathogens as Biological Control Agents: Do They Have a Future?' *Biological Control* 21(3), pp. 230-248. Available at: people.ufpr.br/~microgeral/BIOMED2013InsectPathogensasBiolog.pdf

Lah Katarina. (2011) *Biological properties of insecticides*. Available at: <http://www.toxipedia.org/display/toxipedia/Biological+Properties+of+Insecticides> (Assessed: 20/03/2015).

Latijnhouwers M, de Wit PJ, Govers F. (2003) 'Oomycetes and fungi: similar weaponry to attack plants'. *Trends in Microbiology* Volume 11, pp 462-469. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14557029> (Accessed :12/03/2015).

Lorenz E.S (2009). *Potential Health Effects of Pesticides*. Available at: <http://extension.psu.edu/pests/pesticide-education/applicators/fact-sheets/pesticide-safety/potential-health-effects-of-pesticides> (Accessed :03/02/2015).

McGrath, M.T. (2004). 'What are Fungicides?' *The Plant Health Instructor*. The American Phytopathological Society [Online]. Available at: <http://www.apsnet.org/about/Pages/default.aspx> (Accessed :12/03/2015).

Michigan Department of Natural Resources (n.d). **Zinc Phosphide**. Available at:
http://www.michigan.gov/dnr/0,1607,7-153-10370_12150_12220-26326--,00.html
(Accessed :28/02/2015).

Morais S, Dias E and Lourdes Pereira M. (2011). Carbamates: Human exposure and health effects. In: Prof. Milan Jokanovic. **The impact of pesticides**. Academy publisher.org, p21-38.
Mueller, Daren. (2006) **Fungicides:Terminology**. Available at:
<http://www.ipm.iastate.edu/ipm/icm/2006/5-15/fungicides.html> (Accessed :03/02/2015).

Murphy, M. J.; Talcott, P. A. (2006) Anticoagulant rodenticides. *Small Animal Toxicology*, 2nd ed.; Elsevier Saunders: St.Louis, MO, pp 565, 570-571.
National Pesticides Information Center (2013). **Plant Incorporated Protectants (PIPs) / Genetically Modified Plants**. Available at: <http://npic.orst.edu/reg/pip.html>, (Accessed: 02/04/2015).

Natural Resources Defense Council (1998). **Trouble on the Farm Growing Up with Pesticides in Agricultural Communities**. Available at:
<http://www.nrdc.org/health/kids/farm/farminx.asp> (Accessed : 02/04/2015).

Ngo AD, Taylor R, Roberts CL, Nguyen TV (2006). ‘Association between Agent Orange and birth defects: systematic review and meta-analysis’ **Int. J. Epidemiol** 35(5) : 1220-1230. **Oxford Journals** [online]. Available at: <http://ije.oxfordjournals.org/content/35/5/1220.short> (Accessed : 10/03/2015).

Orosová, M., Holečková, B., Šiviková, K. and Dianovský, J. (2010) ‘Effect of Fungicide Euparen Multi (tolylfluanid) on the Induction of Chromosomal Aberrations in Cultivated Bovine Lymphocytes’. **ActaBiologicaHungarica** 61(4), pp. 411–422. Available at:
<http://www.ncbi.nlm.nih.gov/pubmed/21112833> (Accessed: 12/03/2015).

Owens K, Feldman J, and Kepner J (2010) 'Wide range of diseases linked to pesticides'. *Pesticides and You* 30 (2): 13. *Beyond Pesticides* [online]. Available at: www.beyondpesticides.org/health/pid-database.pdf (Accessed : 15/01/2015).

Pesticides Action Network (2010). *Environmental Impacts of Pesticides*. Available at: <http://www.pan-europe.info/Campaigns/pesticides.html> (Accessed :15/01/2015).

Phillips ML (2006). 'Registering skepticism: does the EPA's pesticide review protect children?' *Environmental Health Perspectives* 114 (10): A592-A595. *PMC* [online]. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626397/> (Accessed :26/01/2015).

Reuters (2008). *Study confirms Parkinson's-pesticides link*. Available at: <http://www.reuters.com/article/2008/04/18/us-parkinsons-pesticides-idUSCOL87119020080418> (Accessed :02/04/2015).

Roder, J. D. (2001). *Veterinary Toxicology*; Butterworth Heinemann: Boston, pp 84, 106-108, 123.

Sanborn M, Kerr KJ, Cole DC, Bassil KL, Vakil C, Kaur J.S (2007). 'Cancer Health Effects of Pesticides: systemic review'. *Can Fam Physician* 53(10): 1704-1711. *PMC* [online]. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17934034> (Accessed : 16/04/2015).

Sanborn M, Kerr KJ, Sanin LH, Cole DC, Bassil KL, Vakil C (2007) 'Non-cancer health effects of pesticides: systematic review and implications for family doctors' *Can Fam Physician*. 53 (10): 1712-1720. *PMC* [online]. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2231436/> (Accessed :16/04/2015).

Steinkraus, D. C. and Boys, G. O. (2005) 'Mass Harvesting of the Entomopathogenic Fungus, *Neozygites fresenii*, from Natural Field Epizootics in the cotton aphid, *Aphis*

gossypii'. **Journal of Invertebrate Pathology** 88, pp. 212-217. Available at:

<http://www.ncbi.nlm.nih.gov/pubmed/15955339> (Accessed: 12/03/2015).

The Policy and Research Committee, MWC (2003). 'Pesticides background paper'.

Muskoka Watershed Council [online]. Available at:

<http://www.muskokawatershed.org/resources/position-papers/> (Accessed : 20/12/2014).

University of Warwick.(n.d). **Entomopathogens and Biological Control** available

at:http://www2.warwick.ac.uk/fac/sci/lifesci/research/entomopathogenicfungi/entomopathogens_and_biological_control.pdf (Accessed: 18/02/2015).

U.S.A. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic

Substances, Office of Pesticide Programs (1998). **Reregistration Eligibility Decision (RED)**

Rodenticide cluster. Available at: <http://www.epa.gov> (Accessed :26/01/2015).

U.S.A Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic

Substances (2004). **Analysis of rodenticide baits use**. Available at: <http://www.epa.gov>

(Accessed : 16/04/2015).

U.S.A Environmental Protection Agency (2015). **Plant Incorporated Protectants**. Available

at: <http://www.epa.gov/opppbpd1/biopesticides/pips/index.htm> (Accessed: 02/04/2015).

Vergucht S, Voghel S, Misson C, Vrancken C, Callebaut K, Steurbaut W, Pussemier L,

Marot J, Maraite H, Vanhaecke P. (2006). **Health and environmental effects of pesticides**

and type 18 biocides. Available at: www.crphyto.be/pdf/heepebi.pdf (Accessed :

12/03/2015).

Virginia Cooperative Extension (2009). **Pesticides and Aquatic Animals: A Guide to**

Reducing Impacts on Aquatic Systems. Available at: [https://pubs.ext.vt.edu/420/420-](https://pubs.ext.vt.edu/420/420-013/420-013.html)

[013/420-013.html](https://pubs.ext.vt.edu/420/420-013/420-013.html) (Accessed : 16/04/2015).

Winchester, D.; Huskins, J.; Ying, J. (2009). 'Agrichemicals in surface water and birth defects in the United States' *Actapaediatrica* 98 (4): 664-669. **PMC** [online]. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2667895> (Accessed : 02/04/2015).

Appendix

The following table summarizes the information about some important pesticide's groups mentioned in the article and their symptoms on human, and the ways of their treatment.

Type of Pesticides	Chemical Family	Sign and Symptoms	First Aid and Treatments
Organophosphate	Diazinin	headache, nausea, dizziness, pin-point pupils, blurred vision, tightness in the chest, difficulty in breathing, muscle weakness or twitching, difficulty in walking, vomiting, abdominal cramps, and diarrhoea. Effects on the central nervous system may include confusion, anxiety, drowsiness, depression, difficulty in concentrating, slurred speech, poor recall, insomnia, nightmares, and a form of toxic psychosis resulting in bizarre behavior.	Fresh air rest. Artificial respiration if indicated. Refer for medical attention.
	Dimethoate	Dizziness. Sweating. Laboured breathing. Nausea. Weakness.	Fresh air rest. Artificial respiration if

		Pupillary constriction muscle cramp excessive salivation. Redness. Pain in eyes. Abdominal cramps. Convulsions. Diarrhoea. Unconsciousness. Vomiting.	indicated. Refer for medical attention. First rinse with plenty of water for several minutes (remove contact lenses if easily possible) then take to a doctor. Induce vomiting (ONLY IN CONSCIOUS PERSONS!). Rest. Refer for medical attention.
	Disulfoton	Convulsions. Dizziness. Sweating. Laboured breathing. Nausea. Unconsciousness. Pupillary constriction muscle cramp excessive salivation. Abdominal cramps. Diarrhea. Vomiting	Fresh air rest. Half-upright position. Artificial respiration may be needed. Refer for medical attention. Rinse mouth. Induce vomiting (ONLY IN CONSCIOUS PERSONS!).

			Refer for medical attention
	Malathion	headache, nausea, vomiting, abdominal cramps, diarrhea, generalized muscle weakness and twitching, slurred speech, pinpoint pupils, excessive secretions, and shortness of breath.	Fresh air rest. Refer for medical attention.
	Methyl parathion	Convulsions. Dizziness. Sweating. Laboured breathing. Nausea. Unconsciousness. Vomiting. Pupillary constriction muscle cramp excessive salivation. Symptoms may be delayed. Muscle twitching. Eye Redness. Pain. Blurred vision. Pupillary constriction. Abdominal cramps. Diarrhea. Labored breathing. Nausea. Unconsciousness. Vomiting. Pupillary	Fresh air rest. Refer for medical attention. Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention. First rinse with plenty of water for several minutes (remove contact lenses if easily possible)

		constriction. Muscle cramps.	then take to a doctor. Induce vomiting (ONLY IN CONSCIOUS PERSONS!). Rest. Refer for medical attention.
Carbamate	Carbaryl	Convulsions. Dizziness. Laboured breathing. Nausea. Unconsciousness. Vomiting. Pupillary constriction muscle cramp excessive salivation. Pain. Pupillary constriction. Redness. Pain. Abdominal cramps. Diarrhoea. Nausea. Vomiting. Pupillary constriction muscle cramps excessive salivation.	Fresh air rest. Refer for medical attention. Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention. First rinse with plenty of water for several minutes (remove contact lenses if easily possible) then take to a doctor. Rinse mouth. Induce vomiting

			(ONLY IN CONSCIOUS PERSONS!). Give plenty of water to drink. Refer for medical attention.
	Carbofuran	nausea, vomiting, abdominal cramps, sweating, diarrhea, excessive salivation, weakness, imbalance, blurring of vision, breathing difficulty, increased blood pressure, and incontinence.	
	Propoxure	Dizziness. Headache. Sweating. Laboured breathing. Nausea. Unconsciousness. Vomiting. Pupillary constriction muscle cramp excessive salivation. Pupillary constriction. Blurred vision. Abdominal cramps. Convulsions. Diarrhoea. Weakness. Muscle twitching.	Fresh air rest. Half-upright position. Refer for medical attention. First rinse with plenty of water for several minutes (remove contact lenses if easily possible) then take to a doctor.

			Give a slurry of activated charcoal in water to drink. Induce vomiting (ONLY IN CONSCIOUS PERSONS!). Rest. Refer for medical attention.
Organochlorine	DDT	hyperaesthesia of the mouth and lower part of the face. Dizziness, an objective disturbance of equilibrium, paraesthesia and tremor of the extremities, confusion, malaise, headache, fatigue, and delayed vomiting (probably centrally mediated).	Contaminated clothing and contact lenses should be removed to prevent further absorption. In the case of skin contact, affected area should be washed carefully with soap and water. Wash eyes for 10 to 15 minutes with clean running water. First aid personnel should wear rubber or plastic gloves

			and avoid contamination. Ingestions of small amounts of DDT do not constitute a Significant risk, and may be managed by dilution with water.
	DDE	Hypersensitive to stimulation, sensation of prickling, tingling or creeping on skin. Headache, dizziness, nausea, vomiting, incoordination, tremor, mental confusion, hyperexcitable state. In severe cases: convulsions, seizures, coma and respiratory depression.	
	Aldrin	Convulsions. Dizziness. Headache. Nausea. Vomiting. Muscle twitching.	Fresh air rest. Refer for medical attention. Remove contaminated

			clothes. Rinse and then wash skin with water and soap. Refer for medical attention. First rinse with plenty of water for several minutes (remove contact lenses if easily possible) then take to a doctor. Give a slurry of activated charcoal in water to drink. Do NOT induce vomiting. Rest. Refer for medical attention.
	Dieldrin	Convulsions. Dizziness. Headache. Nausea. Vomiting. Muscle twitching.	Give slurry of activated charcoal in water to drink. Do NOT induce vomiting. Rest. Refer for medical

			attention.
	Endrin	Convulsions. Dizziness. Headache. Nausea. Vomiting. Weakness.	Give a slurry of activated charcoal in water to drink. Rest. Refer for medical attention.
	Hexachlorocyclohexane	Confusion. Dizziness. Headache. Vomiting. Weakness. Redness. Convulsions. Diarrhoea. Dizziness. Drowsiness. Laboured breathing. Vomiting. Tremors. Muscles spasms. Depression.	Rinse mouth. Induce vomiting (ONLY IN CONSCIOUS PERSONS!). Rest. Refer for medical attention. Fresh air rest. Refer for medical attention
	Lindane	Convulsions. Cough. Dizziness. Headache. Nausea. Weakness. Tremors. Paresthesias. Symptoms may be delayed. Abdominal pain. Diarrhoea.	Rinse mouth. Give a slurry of activated charcoal in water to drink. Do NOT induce vomiting. Give plenty of water to drink. Rest. Refer for medical attention.

			Fresh air rest. Artificial respiration if indicated. Refer for medical attention.
--	--	--	---