

Climate change: the potential impact on occupational exposure to pesticides

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Abstract

Objective. This study investigates the possible influence of global climate change (GCC) on exposure to plant protection products (PPP) in the workplace.

Methods. The paper has evaluated the main potential relationships between GCC and occupational exposure to pesticides, by highlighting how global warming might affect their future use and by reviewing its possible consequence on workers' exposure.

Results. Global warming, influencing the spatial and temporal distribution and proliferation of weeds, the impact of already present insect pests and pathogens and the introduction of new infesting species, could cause a changed use of pesticides in terms of higher amounts, doses and types of products applied, so influencing the human exposure to them during agricultural activities. GCC, in particular heat waves, may also potentially have impact on workers' susceptibility to pesticides absorption.

Conclusions. Prevention policies of health in the workplace must be ready to address new risks from occupational exposure to pesticide, presumably different from current risks, since an increased use may be expected.

Key words

- climate change
- global warming
- pesticides
- occupational exposure

INTRODUCTION

Climate is defined as long-term averages and variations in weather measured over a period of several decades. The Earth's climate system includes the land surface, atmosphere, oceans, and ice. Many aspects of the global climate are changing rapidly, and the primary drivers of the change are human in origin. Despite the difficulty in predicting global warming effects because of the great complexity of the system, climate models developed by the Intergovernmental Panel on Climate Change (IPCC) argue an unequivocal increase of the average global temperature in ranges from 2.6-4.8 °C in the 21st century, if greenhouse gas emissions continue at the present rate [1]. In addition to the well-known direct effects to the detriment of the environment, including the melting of glaciers, the disintegration of the polar ice caps, rising sea levels, changes in the distribution of rainfall, increasing the frequency and intensity of natural events extremes and climate change, global warming is expected to causes many other indirect effects. In fact, temperature, light and water are the key elements that control the growth and development of organisms, therefore it is important taking into account global warming effects on changing of the nature and amount of pathogens and chemicals, as well as of their transport and fate in the environment. Climate change effects include, for example, significant changes in the

abundance and activity of seasonal pests such as insects, fungi, mites, mice, nematocides, unwanted plants [2-7]. Consequently, a conceivable future increase of the use of pesticides is expected. Pesticides may come into contact with the body passing through the skin (dermal route), by inhalation, or by swallowing (ingestion). In this paper, we analyze the likely influence of climate change on the occupational exposure to pesticides. The emphasis is on expected increase in the use of pesticides due to the global warming, by also including the employees' health consequences of changed exposure conditions to pesticides.

CLIMATE CHANGE AND THE FUTURE CROPS

Climate change is expected to have dissimilar effect in the various parts of the world. Some regions, such as North and South America, northern Europe, and northern and central Asia are projected to have increased precipitation, while others, including southern Africa and Asia and the Mediterranean, are expected to experience substantial droughts. There is concordance among scientists that climate change encompasses atmospheric carbon dioxide (CO₂) variations, altered worldwide temperatures and precipitation variation, alterations in arable land, crop yields, and changes in soil quality, nitrogen deposition and plant diversity [8, 9]. Besides,



changes in climate through this century will affect crops differently because individual species respond differently to warming. Plant response to climate change may be actually dictated by complex interactions among CO₂, temperature, solar radiation, and precipitation. Precipitation changes and temperature increases are the main pest infection determinants in terms of climate change [10]. About rainfall changes, the availability of water strongly influences any kind of agriculture: changes in total seasonal precipitation or in its pattern of variability are both important. Climate change will modify rainfall, evaporation, runoff, and soil moisture storage. Precipitation may influence variations in crop yields, yield quality and pests in both a positive and negative way: by increasing yields in greater precipitation during the growing season and by damaging crop productivity, especially for younger plants, during intense rainfall [11, 12]. Regarding temperature increases, higher temperatures and increased CO₂ concentrations, associated with a substantial change in photosynthetic activity, promote plant growth and expansion [13]. In contrast, a temperature variability increase can adversely affect crops growing at low or high mean temperatures due to diurnal and seasonal canopy temperature fluctuations that exceed the crop's optimum range. Each crop species has indeed a temperature range for growth, along with an optimum temperature. Plants have specific temperature tolerances: as temperatures increase over this century, crop production areas may shift to follow the temperature range for optimal growth and yield of grain or fruit. One critical period in which temperatures are a major factor is the pollination stage; pollen release is related to development of fruit, grain, or fiber. Exposure to high temperatures during this period can greatly reduce crop yields and increase the risk of total crop failure. Plants exposed to high nighttime temperatures during the grain, fiber, or fruit production period experience lower productivity and reduced quality.

Insect pests

Global warming improves overwintering, dispersal, migration and population characteristics such as reproduction and growth rates. Although insects flourish in all climates, research reports an earlier appearance and activity in warmer circumstances. Elevations in temperature, for example, may affect the rates of extrinsic incubation in insect vectors (*e.g.*, ticks and mosquitoes), extended vector transmission seasons and expanded distribution seasonally and spatially [14]. In addition, wet conditions may possibly bring on severe insect and plant pathogen infestations or effect a geographical shift of some pests. Insect profusion may be also determined by increases in CO₂ concentration, wind induced dispersal of pests, differences in soil nitrogen content and population density. Finally, extreme weather conditions seem to have divergent consequences on species' longevity reducing it in some species but not in others. In summary, climate change promotes distribution and abundance of pests due to migration and range shifts, increases pest outbreaks and alters the dissemination of vectors, all favoring pests compared to crops [10, 15].

Plant diseases

Plant diseases are mainly affected by temperature, rainfall, humidity, and radiation [16]. Different life stages may vary in their climatic susceptibilities but the direct effects on pathogens are likely to be strongest. Wet conditions promote the germination, the spread and activity of spores as well as the proliferation of fungi and bacteria. This is also the case for extreme events and rainfall in particular, which aid the dispersal of diseases. Climate warming may improve pathogen overwintering, development and dispersal, all resulting in an elevated disease severity and plant losses [17]. On the other hand, inverse correlations of pesticide use with arid and hot weather were recorded; in fact, warm and dry conditions can increase resistance to plant infections resulting in a reduced fungicide need, which is also the case with high atmospheric CO₂ concentrations. However, as we have found about local agriculture, increased temperatures will also affect plant productivity, giving rise to a potential increase in volume and array of pesticides used. Other climate effects are seen for pathogens that cause overwintering diseases. Due to milder winters and less snow cover, the importance of these pathogens can decrease. In contrast, for example, late blight incidence on potato is expected to increase in the case of warmer springs, summers and more humid conditions of the future [18]. In conclusion, it is difficult to seize completely the links between climate and disease processes, given the high degree of complexity in plant-pathogen systems and nonlinear thresholds in both. Nevertheless, an increased plant disease and physiological plant stress pressure is expected to increase host susceptibility and pesticide dependency.

Weeds

Climate change affects either crop or weed. A temperature increase appears to cause fundamentally altered weed communities and a geographic niche expansion of many species. Research also demonstrated that an increased atmospheric CO₂ concentration directly raises weeds' herbicide tolerance and severity because of the higher carbon dioxide fertilization effect and improved water use efficiency in comparison with agricultural crops [13]. Finally, increasing leaf thickness and the partial stomatal closure in this case, may reduce herbicide absorption and efficacy [19]. Weed resistance to herbicides and the decline in efficacy can influence the future total amounts use of herbicides.

PESTICIDE USE AND FATE UNDER GLOBAL WARMING CONDITIONS

Any significant change in climate on a global scale should influence local agriculture, and indirectly may affect the world's pesticide use. However, given the multivariate nature of climate change and nonlinear thresholds in natural processes, it is difficult to consider all the links between climate change and pesticide use. Nevertheless, as we have remarked above, there is agreement among scientists that climate change may increase pest populations, including weeds, invasive species, insects, and insect-borne diseases, which will likely lead to large increases in the use of pesticides (*Table 1*).



Table 1
Main possible responses of crop, pests and weeds to climate change

Sources or contaminants	Potential effects of climate change	Class of phytosanitary products	References
<i>Insect pests</i>	Insect pests will generally become more abundant as temperatures increase, through a number of inter-related processes, as well as increased rates of population development, growth, and migration and over-wintering	Insecticides Repellents Fumigant	Delcour <i>et al.</i> , 2015 Bloomfield <i>et al.</i> , 2006 Miraglia <i>et al.</i> , 2009
<i>Plant diseases</i>	Increased use of PPP due to increased abundance and activity of plant diseases	Fungicides Bactericide Miticides (Acaricides) Nematicides	Patterson <i>et al.</i> , 1999 Harvell <i>et al.</i> , 2002 Roos <i>et al.</i> 2011
<i>Weeds</i>	Several weed species may benefit more than crops from higher temperatures and CO ₂ levels	Herbicides	Gutierrez <i>et al.</i> , 2008 Jackson <i>et al.</i> , 2011

The augmented quick pesticide resistance development under warm conditions might be insufficiently covered by current pest management strategies. Besides, in developing countries, easily available, biodegradable, low cost and low risk pesticides are needed for low-income peasant farmers and organic farmers. This is important since it is expected that these countries may suffer most from climate change. Some countries might even re-introduce or increase the use of banned or restricted pesticides.

Climate-induced changes may affect the amount of pesticides usage also by the acceleration of their dissipation and degradation. The conceivable increase of pesticides' leakage is due to a combination of improved volatilization and accelerated degradation and dissipation, strongly affected by higher amounts of precipitation, elevated temperatures and direct exposure to sunlight. Those last two elements also influence the chemical alteration of pesticides [12, 20].

In particular, regarding pesticides dissipation, volatilization and leaching are the main causes of pesticides in the environment; the first phenomenon takes place when a liquid or solid substance transfers to the gaseous phase, while the second is the downward movement through the soil, eventually reaching the groundwater. In climatic terms, rapid volatilization is mainly due to elevated temperatures, direct exposure to sunlight and a high soil moisture content [21]. In general, pesticide dissipation seems to be benefitted by higher amounts of precipitation in addition to temperature, degradation and sorption. Within leaves, the uptake and release equilibrium of semi-volatile pesticides is reached faster at higher temperatures and transport through the atmosphere, is predominantly impacted by local surroundings. Therefore, the timing and intensity of rainfall influence pesticide persistence and efficiency. In addition, temperature and light affect pesticide persistence through chemical alteration. About leaching, the transfer of pesticides to depth via leaching and to surface water via drainage was mostly influenced by interactions between climate and soil-pesticide combinations. Several studies reported an enhancing effect of precipitation volumes of variable duration, rainfall seasonality, intensity and timing in relation with pesticide applica-

tion. Temperature affects soil mineralogy and geochemistry and is consequently a main driver for leaching. In general, research describes a negative correlation with leaching, often caused by desorption. Pesticide dissipation is not only influenced by pesticide transport but also degradation. Degradation of pesticides in the soil or atmosphere is realized by phototransformation, chemical or microbial breakdown while, degradation on plant surfaces is caused by photodegradation, evaporation, rainfall wash off and growth dilution. Global warming is acknowledged to accelerate the degradation of chemical components due to accelerated microbial and chemical reaction rates and may reduce concentrations of pesticides in the environment. Elevated soil moisture contents and increased precipitation, also enhance pesticide degradation and accordingly persistence [22-24]. Furthermore, a higher relative humidity was proven to induce a faster environmental pesticide degradation, even though the more difficult initial degradation in this case [25]. In addition, a climate change consequence, in particular a temperature effect on phototransformation of pesticides can be expected with higher temperatures [12, 26]. Finally, the presence of soil microorganisms also plays an important role in pesticide dissipation and transformation. Biological and chemical reaction rates tend to rise at increased temperatures, which is also the case for microbial activity [22, 24, 27]. The soil moisture content enhances microbial activity, but in lesser extent than the temperature effect.

In general, a warmer climate may necessitate an increased pesticide usage. In fact, pesticide efficiency, represented by the initial deposit, pesticide fate and (eco-) toxicity, also has a major impact on pesticide use. Pesticide losses of mobile active substances are mainly influenced by the time gap between extreme weather events and pesticide application. In soil, transport of pesticides is thus mainly driven by rainfall seasonality, intensity and temperature increases but also land-use changes which indicates an indirect impact on the long term. The soil-biological microbial activity is affected by moisture content and soil temperature. Even though some reducing effects, increasing temperatures overall will result in higher volumes of pesticides that will have to be applied more often.

FOCUS ON OCCUPATIONAL EXPOSURE TO PESTICIDES

According to the Environmental Protection Agency (EPA), approximately five billion pounds of pesticide are consumed worldwide per annum [28]. The term “pesticide”, as defined by the US EPA, is used to mean a substance intended to repel, kill, or control any species designated as a “pest,” including weeds, insects, rodents, fungi, bacteria, or other organisms [29]. Historically, pesticides included heavy metals such as arsenic, lead and mercury and plant derivatives such as nicotine from tobacco leaves, pyrethrum from chrysanthemum flowers and rotenone from the derris root. Synthetic pesticides were developed in the 20th century, frequently for use in warfare. Conventional pesticides are chemicals or other substances developed and produced to kill organisms we consider undesirable. Pesticides include wood preservatives, chlorine/hypochlorite used in municipal water treatment, specialty biocides (such as water treatment chemicals for industrial and recreational purposes and disinfectants and sanitizers), and “other” pesticides (chemicals registered as pesticides but are produced and marketed mostly for other purposes such as sulfur, some petroleum products, salt, and sulfuric acid) [30, 31]. In this paper, we refer to pesticides used in agriculture or to any substances that characterize the agriculture-based industries, including herbicides, insecticides, rodenticides, plant growth regulators, miticides, nematocides, fungicides, fumigants, and antimicrobials. Occupational exposures to pesticides occur during the production, transportation, preparation and application of pesticides in the workplace [32].

Operators: individuals who are involved in activities relating to the application of a plant protection product (PPP); such activities include mixing/loading the product into the application machinery, operation of the application machinery, repair of the application machinery whilst it contains the PPP and emptying/cleaning the machinery/containers after use. Operators may be either professionals (e.g. farmers or contract applicators engaged in commercial crop production) or amateur users.

Workers: individuals who, as part of their employment, enter an area that has been treated previously with a PPP or who handle a crop that has been treated with a PPP.

Each group of workers has distinctive pesticide exposure profiles due to differences in the context and purpose of pesticide use. One of the major groups of pesticide-exposed are operators. The types of pesticide, frequency of use, and application method vary according to the task performed. Although agricultural activity accounts for the majority of occupational pesticide use, farm pesticide use is generally an intermittent, seasonal task and only one of the wide range of tasks undertaken by farm workers. Consequently, the exposure frequency and total exposure time among most farmworkers are typically lower than for pesticide applicators in other industries. Dedicated agricultural pesticide applicators have more frequent exposure than farm operators but may have fewer years of pesticide use. Many of the published cohort studies of pesticide exposure and health

effects have focused specifically on agricultural workers who are licensed pesticide users. However, there is evidence suggesting that pesticide exposure may not be universal among farm workers, and a large proportion of workers in the farming sector may not be exposed to pesticides directly. Dedicated nonagricultural pest control operators (structural or urban pest controllers) comprise a comparatively small fraction of the pesticide-exposed workforce, however, their exposure pattern is systematically different from that of agricultural pesticide applicators. These nonagricultural pest controllers are exposed on a more regular basis because the application of pesticides is a central task of their job [33-35].

Another important difference is that nonagricultural pest controllers' work is predominantly associated with built environments and applying pesticides indoors, including restricted spaces [36]. Other occupational pesticide users include turf workers, such as greenkeepers and other sports facilities caretakers, ornamental gardeners, and park workers who may use weedicides, fungicides, and insecticides to maintain turf and gardens. Herbicide use is characteristic of workers involved in maintenance of public infrastructure and in particular clearance of vegetation from linear infrastructure corridors such as roads, railway lines, and overhead electrical distribution lines [37]. Line clearance and other vegetation control tasks using herbicides may also be common among forestry workers [38].

Toxicological properties

Health effects of pesticides depend on the type of pesticide. Many of them are persistent, they do not break down into safer constituent parts but rather remain intact over prolonged periods, and they are readily accessible to the human body. The combination of persistence and accessibility is dramatically illustrated by the fact that human biomonitoring studies indicate that most people in the United States have detectable levels of dichlorodiphenyltrichloroethane (DDT) in their bodies (CDC, 2005), despite the fact that DDT was banned from use in the United States in 1972 [39]. We can group pesticides into chemical families (Figure 1): compounds with similar chemical structures have similar characteristics and usually a similar mode of action. Insecticides include organophosphates, carbamates, pyrethroids. Typical chemical families of herbicides are phenoxy herbicides, benzoic acid herbicides, triazines, ureas. Substitution of chemical compounds is possible using so-called biopesticides. There are three major classes of biopesticides: microbial pesticides, plant-incorporated-protectants, biochemical pesticides. The active ingredients of pesticides are mixed with other compounds to improve their effectiveness, safety, handling and storage, such as solvents, mineral clays, stickers, wetting agents, or other adjuvant materials.

Some pesticides, such as organophosphates and carbamates, affect the nervous system. Others may irritate the skin or eyes. Some pesticides may be carcinogens. Others may affect the hormone or endocrine system in the body. Pesticides are for the most part toxic, persistent; bio-accumulative, that affect the physical and

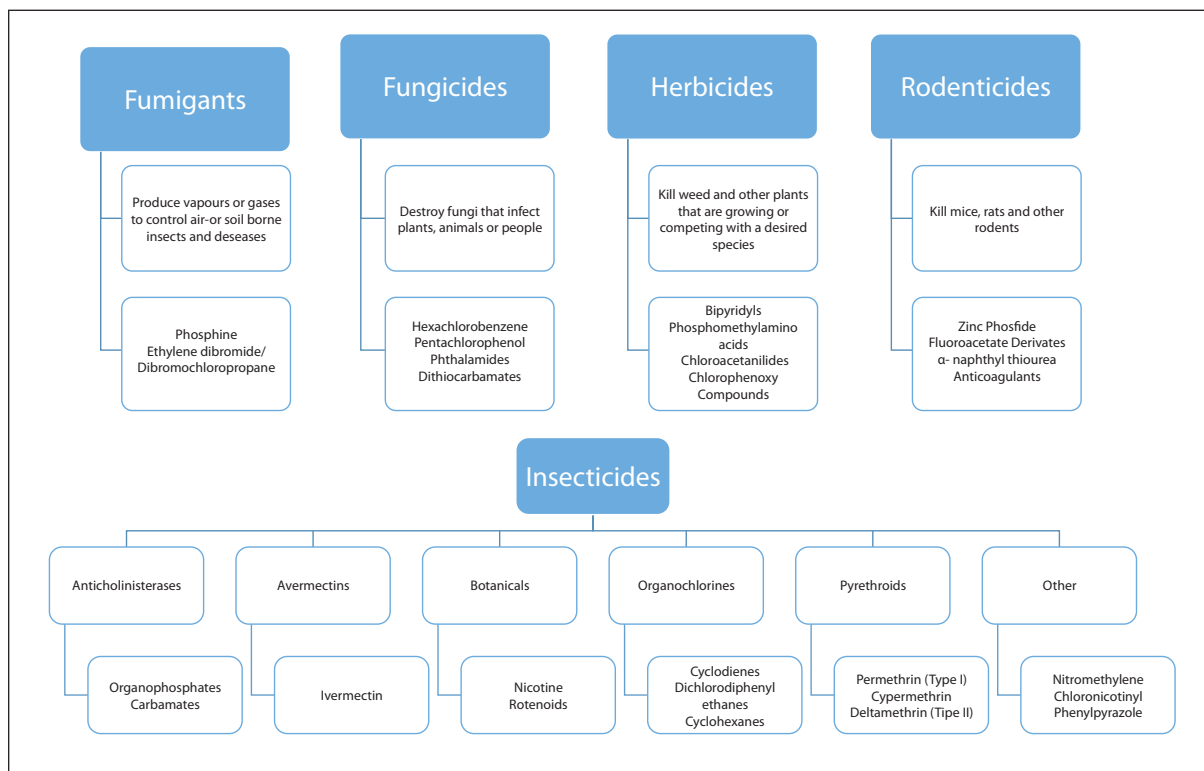


Figure 1
Classification of pesticides according to their target species and further subdivided based upon chemical structure.

chemical properties of soils and are often extremely harmful not only to human health, but also for the entire ecosystem and for any living organism. This section will briefly explore each adverse effect on human health due to exposure, both acute and chronic, to pesticides. Table 2 shows the WHO recommended classification of some widespread pesticides by hazard and Guidelines to classification: 2009.

Neurotoxicity

A main mode of action in controlling pests targets the nervous system, particularly for insecticides. For example, organophosphate insecticides like chlorpyrifos interfere with the enzyme that breaks down acetylcholine leading to a buildup of this key neurotransmitter [40]. Organophosphate poisoning produces an acute response, which includes symptoms of cognitive, motor, and sensory dysfunction [41, 42]. The effects of such poisoning may persist long after the immediate episode has resolved, suggesting permanent residual damage. Even less severe poisoning can have long-term effects. Many studies of moderate exposure have also found increases in neurologic symptoms representing a range of neurologic domains, including affect, cognition, and motor, sensory, and autonomic function [43-46].

Endocrine system

Several pesticides are known as endocrine-disrupting chemicals (EDC), a class of chemical agents that interfere with the production, release, transport, metabolism, action, or elimination of naturally occurring hor-

mones in the body that are part of the developmental regulation process [47]. They can affect the signaling of hormones, such as estrogens, thyroid, and androgens that are a vital component of normal embryonic development. They can also affect the neuroendocrine system, which plays a role in hemostasis and normal physiology processes. Examples of EDCs include bisphenol A, diethylstilbestrol (DES), and certain pesticides such as atrazine and vinclozolin. Exposure to a well-known EDC, DES, can result in a range of potential transgenerational, reproductive effects that stem from fetal exposure. Female offspring exposed to DES also have higher rates of preterm delivery, spontaneous delivery, and ectopic pregnancy [48]. The male offspring may be at increased risk of testicular and prostate cancer. Pesticides have also been implicated in altered thyroid function and decreased testosterone and estradiol possibly leading to infertility later in life, gestational diabetes, menstrual irregularities, and fetal death related to congenital birth defects [49, 50]. An epidemiological study of farm workers found that couples who conceived in the spring when herbicides are typically applied had infants with elevated birth defects, and exposure to fungicides resulted in less-than-expected number of male offspring [51].

Cancer

Research to date implicates pesticide exposures with leukemia, lymphoma, brain, kidney, breast, prostate, pancreas, liver, lung, and skin cancers [52, 53]. Occupational exposure to pesticides and/or residential pesti-



Table 2
The WHO recommended classification of pesticides by hazard and guidelines to classification, 2009

Chemical group – biological activity	Products name	WHO Class	LD ₅₀ for the rat (mg/kg body weight)		
			Oral	Dermal	
Organophosphorus					
<i>Insecticides</i>	<i>Acephate</i>	III	Slightly hazardous	Over 2000	Over 2000
	<i>Chlorpyrifos</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Dichlorvos</i>	Ib	Highly hazardous	5-50	50-200
	<i>Dimethoate</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Ethion</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Malathion</i>	III	Slightly hazardous	Over 2000	Over 2000
	<i>Monocrotophos</i>	Ib	Highly hazardous	5-50	50-200
	<i>Novaluron</i>	U	Unlikely to present acute hazard	5000 or higher	
	<i>Parathion</i>	Ia	Extremely hazardous	< 5	< 50
	<i>Profenofos</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Spinosad</i>	III	Slightly hazardous	Over 2000	Over 2000
	<i>Triazophos</i>	Ib	Highly hazardous	5-50	50-200
<i>Herbicides</i>	<i>Acetamiprid</i>	II	Moderately hazardous	50-2000	200-2000
<i>Nicotinoids insecticides</i>					
Chlorinated Hydrocarbons					
<i>Insecticides</i>	<i>Endosulfan</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Lindane</i>	II	Moderately hazardous	50-2000	200-2000
Carbamates					
<i>Insecticides</i>	<i>Carbaryl</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Carbofuron</i>	Ib	Highly hazardous	5-50	50-200
<i>Acricides</i>	<i>Indoxacarb</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Methomyl</i>	Ib	Highly hazardous	5-50	50-200
	<i>Propargite</i>	III	Slightly hazardous	Over 2000	Over 2000
<i>Alphamethrin</i>	II	Moderately hazardous	50-2000	200-2000	
Pyrethroids					
<i>Insecticides</i>	<i>Deltamethrin</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Fenvalerate</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Quinalphos</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Cypermethrin</i>	II	Moderately hazardous	50-2000	200-2000
Dithiocarbamates					
<i>Fungicides</i>	<i>Mancozeb</i>	U	Unlikely to present acute hazard	5000 or higher	
Anilide	<i>Carboxin</i>	III	Slightly hazardous	Over 2000	Over 2000
Copper	<i>Copper sulphate</i>	II	Moderately hazardous	50-2000	200-2000
Benzimidazole					
<i>Fungicides</i>	<i>Benzimidazole</i>	U	Unlikely to present acute hazard	5000 or higher	
Dinitroaniline					
<i>Phenoxyacetic</i>	<i>Pendimethalin</i>	III	Slightly hazardous	Over 2000	Over 2000
	<i>2,4-D</i>	II	Moderately hazardous	50-2000	200-2000
	<i>Bentazon</i>	III	Slightly hazardous	Over 2000	Over 2000
<i>Glyphosate</i>	II	Moderately hazardous	50-2000	200-2000	

cide use appear to be cancer risk factors for fetus [54]; during pregnancy, pesticide exposures increased risk for acute lymphocytic leukemia, Wilms' tumor, and brain cancer [55].

Other health effects

There is evidence that a wide variety of pesticides can affect immune system [56]. Furthermore, prenatal exposures to pesticides have been linked with otitis media, respiratory distress, asthma, decreased fetal growth and length of gestation, and certain birth defects [57]. Finally, some pesticides, including organophosphate

pesticides (OPs) and Pyrethroids, are suspected to be toxic agents for human auditory system [58].

Routes of exposure to pesticides

Workers are exposed to pesticides through three main pathways of dermal exposure (absorption through the skin or eyes), respiratory (inhalation), or oral exposure (swallowing).

Dermal exposure

Skin absorption is the most common route of operator poisoning from pesticides. The process will continue as

long as the chemical remains in contact with the skin. Skin contamination may occur due to a splash, spill or drift when mixing, loading or applying a pesticide and contact with residue on application equipment, protective clothing or treated surfaces. Besides, it is very easy to transfer pesticides residues from one part of the body to another. Liquid pesticides are absorbed more readily than powders, dusts or granules formulations. Each part of the body has different rate of dermal absorption. Absorption through wounded skin is particularly hazardous; furthermore, as we shall see in more detail below, particularly vulnerable to absorption is sweating skin.

Inhalation exposure

Inhaled pesticides may cause serious damage to nose, throat and lung tissues or be transferred through the lungs into the bloodstream. Absorption of PPPs through lung tissues is very rapid and complete therefore hazard of poisoning from respiratory exposure is considerable. Respiratory tract may be exposed to pesticides by inhalation of powders, airborne droplets or vapors, namely:

- the powder may be inhaled during opening containers, weighing and mixing operations;
- inhalation of spray droplets during use of low pressure application equipment is fairly low because most droplets are too large to remain airborne. However, when high pressures or fogging equipment is used, the droplets are in the mist or fog size-range and can be carried on air currents for a large distance thus considerably increasing the potential for respiratory exposure;
- use of fumigants due to effectiveness of their toxic vapors for a pest control also has the highest hazard with respect to worker exposure to vapors. Some non-fumigant PPPs may also produce vapors being toxic to applicators or bystanders. The hazard is much higher in enclosed spaces with limited air movement (e.g. unventilated storage areas, greenhouses, etc.). Increasing temperature causes higher vapor levels therefore; it is recommended that PPPs should not be applied when air temperatures are above 30 °C.

Oral exposure

Pesticides can be swallowed and entered into the digestive track where can be absorbed directly or transformed and then absorbed into the blood stream. The ingestion may be accidental or intentional. The most frequent accidental oral exposure is related to the keeping pesticides in an unlabeled bottle or food container instead of its original labelled container. People may be poisoned when drinking pesticides from such bottle or by drinking water stored in contaminated container. Workers handling pesticides or application equipment can consume pesticides residues from unwashed hands during eating or smoking. Pesticides may enter applicators mouth when trying to clear a spray line or nozzle by blowing [59]. Oral exposure may be controlled by hygiene practices normally established in workplaces.

Factors involved in occupational exposures to chemicals usually include application intensity, frequency, duration and method, safety behaviors (e.g., use of personal protective equipment – PPE), as well as the physiochemical and toxicological profiles of the chemi-

cal agents in use. Factors which most of all may affect exposure during working with pesticides are following:

- the form of formulation. Liquids may splash and spill resulting in direct skin contact or indirect skin contact through clothing contamination. Solids may generate dust during loading product into the application equipment, resulting in the face and the eyes exposure and respiratory hazards;
- depending on the type and size of packaging in combination with the pesticide formulation opening the bags can result in some kind of exposure (splash of liquids or spread of dust);
- the application modality (manual or tractor assisted), which also influences the physical activity and the consequent absorption capacity of the inhaled dose.

HOW GLOBAL CHANGES COULD AFFECT OCCUPATIONAL EXPOSURE TO PESTICIDES

According to climate projections, extreme heat episodes and heat waves will increase in frequency and severity in the future. An intensification of the frequency of heat waves during climate change could be associated with a shift of the mean temperature or an increase of temperature variability or both (Figure 2).

These weather conditions may considerably affect occupational exposure. For example, high temperature cause more rapid evaporation of spray droplets between the spray nozzle and the target and this vapor may reach the operator. Warm weather conditions also influence the perspiration rate of the human body

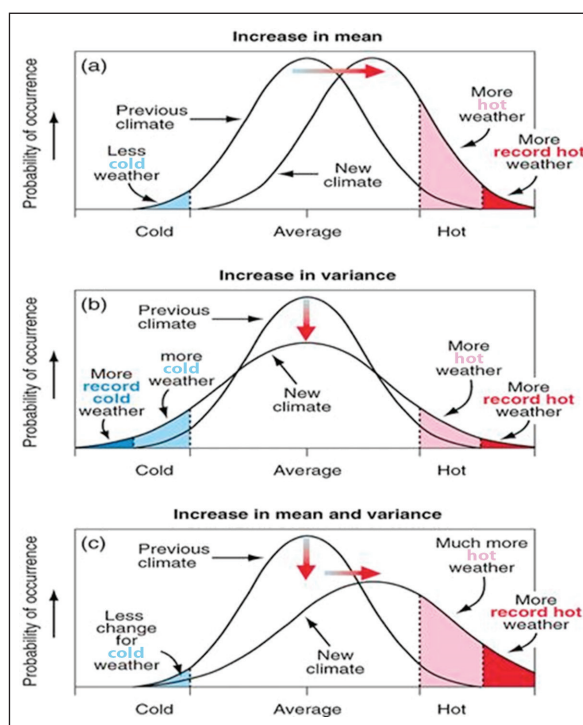


Figure 2

Climate change-induced shifts in hot days and extreme heat events. Graphics reproduced with kind permission from the Intergovernmental Panel on Climate Change (IPCC). Source: IPCC Third Assessment Report. Synthesis Report, 2001.

influencing the dermal absorption ability and increasing the discomfort in using PPE. Besides temperature, wind increases spray drifts resulting in operators extra exposure to pesticide and in contamination of areas near the treated field. During pesticide application, a large amount of spraying liquid ends up on the soil, depending on drop size, crop density and maturity. In the case of increasing precipitation, rain-fastness will be an important characteristic.

The link with extreme events additionally influences the timing of pesticide applications [60]. For example, predicted higher soil moisture deficits in autumn can limit fieldwork or move it to an earlier date than now, while high soil moisture in humid areas can also hinder field operations. This can oblige farmers to apply autumn herbicide treatments earlier resulting in a more difficult winter weed control [61].

One of the consequence of climate change and global warming is, therefore, that more workers will be exposed to heat stress. In fact, the human body has relatively efficient methods for maintaining a core temperature of 37 °C, but when pushed to its limit, the immediate consequences of heat exposure can range from heat stress, to heat syncope and heat stroke [62-64]. The ability of populations to tolerate elevated temperatures may be impaired with toxicant co-exposures. Alterations in climate change parameters, predominantly temperature, will act as co-stressors with chemical toxicants, thereby affecting physiological processes and the ability of wildlife to maintain homeostasis [65]. In humans, the exposure to high ambient temperatures causes an increase in body temperature, which translates into cutaneous vascular dilation, sweating, and increased heart rate. A hot day is only one challenge to the body's ability to maintain its core temperature. Since systems of the body require energy to function, they produce heat. When there is a high physical demand, excess heat must be shed by the body to avoid increased core body temperature and negative health outcomes [66]. Heat exposure may also cause an increased risk of physical injury, due to fatigue and reduced vigilance. In fact, the dehydration caused by exposure to a hot environment also seems to have effects on cognitive performance,

visual motor capacities, short-term memory, and vigilance. Moreover, several factors can intensify the effects of heat exposure on workers. Heat tolerance levels seem to diminish in people over 45 years of age because physical activity is more physiologically demanding on them. They sweat more readily and their metabolism takes longer to return to normal [67].

In addition, workers with health problems (such as heart disease, hypertension, or blood circulation problems), workers who are overweight, and those on sodium restricted diets or who take certain medications are more likely to have problems following excessive heat exposure. Lastly, pregnant women, who have a higher metabolic rate, are also more vulnerable. The physical discomfort associated with an increase in body temperature can also alter the worker's emotional state (e.g. irritability or anger), leading to negligence regarding safety procedures and reducing vigilance during the performance of dangerous tasks. Exposure to extreme heat can also cause decreased productivity [68-71].

Location, season, and type of activity are other factors that can exacerbate the effects of heat exposure. In working populations, the dissipation of this "extra" heat may be complicated by factors such as poor hydration, poorly acclimatized workers, lack of rest periods, and lack of food breaks. Furthermore, wearing PPE can aggravate the effect of high temperature, increasing heat and/or decreasing the efficiency of sweat evaporation [63, 72].

Climate factors such as high humidity and temperature, in fact, make the use of PPE very uncomfortable, especially respirators, facemasks and overalls. *Table 3* shows the recommendations to alter the work/rest schedule to permit more rest time for workers wearing chemical-resistant suits with the aim to control the daily length of time and temperature to which a worker is exposed in heat stress conditions.

It is obvious that high humidity and temperatures are not favorable working conditions but in combination, these factors affect the attitude and behavior among agricultural workers resulting in reduced PPE use. Consequentially, many workers in thermally stressful occupations give up wearing their protective equipment

Table 3

Work/rest schedules for workers wearing chemical-resistant suits*. Adapted from US EPA/OSHA [1993]

Air Temp (°F)	Light work			Moderate work			Heavy work		
	Full sun	Partly cloudy	No sun ^a	Full sun	Partly cloudy	No sun ^a	Full sun	Partly cloudy	No sun ^a
75	Normal	Normal	Normal	Normal	Normal	Normal	35/25 ^b	Normal	Normal
80	30/30	Normal	Normal	20/40	Normal	Normal	10/50	40/20	Normal
85	15/45	40/20	Normal	10/50	25/35	Normal	Caution ^c	15/45	40/20
90	Caution ^c	15/45	40/20	Caution ^c	Caution ^c	25/35	Stop work	Caution ^c	15/45
95	Stop work	Stop work	15/45	Stop work	Stop work	Stop work	Stop work	Stop work	Stop work

*Workers are/are wearing: heat-acclimatized, under the age of 40, physically fit, well rested, and fully hydrated; Tyvek coveralls, gloves, boots, and a respirator. Cooling vests may enable workers to work for longer periods. Adjustments must be made when additional protective gear is worn.

^aNo shadows are visible or work is in the shade or at night.

^b35 minutes work and 25 minutes rest each hour.

^cHigh levels of heat stress, consider rescheduling activities.

because of their discomfort, which can promote the absorption of chemicals. In addition, this equipment can impede heat loss and lead to marked hyperthermia when worn in the summer months, situation that is likely to be encountered more often in the context of climate change.

Additionally, exposure to chemicals can affect the thermoregulatory mechanisms in humans, thereby reducing workers' capacity to adapt to heat stress. The amounts of xenobiotics absorbed through the lungs and the skin during work in a hot environment can be increased significantly due to higher pulmonary ventilation and cutaneous blood flow. Therefore, the overall impact of heat exposure translates, in most cases, into an increased concentration of xenobiotics in the biological fluids [72]. *Figure 3* summarizes some of the main consequences of climate change on environmental and occupational exposure to pesticides. Since the "internal dose" of contaminant is increased, workers may report more health effects. Studies have shown that temperature, humidity and occlusion all have an influence on the extent of skin hydration and permeability [73-75]. Vanakoski *et al.* (1996) suggested that high temperature increased skin absorption through enhanced skin blood flow [76].

Schafer *et al.* (2002) studied the effects of occlusion and environmental conditions on the forearms of volunteers. Lower temperatures and humidity (20 °C and 30%, respectively) had little impact on skin surface water loss or the relative humidity in the microclimate between the skin and the occlusive article but did reduce skin hydration [77]. Higher temperatures and humidity (30 °C and 75%, respectively) increased both the relative humidity of the microclimate and skin hydration.

Studies in the pharmacology sector show an increase in the absorption and effects of certain drugs when they are administered simultaneously to heat exposure. Regarding the occupational exposure to pesticides, workers in agriculture, including pesticide applicators and aerial spraying pilots, have potential increased exposure to organophosphate insecticides and reductions in cholinesterase activity when they are heat stressed. Chemical toxicant exposures may also affect homeostatic temperature regulation in humans and other endotherms. Organophosphate and carbamate insecticides are known to elicit a fever in humans. Conversely, acute exposures in the rat lead to an acute reduction in core temperature followed by a delayed elevation in the core temperature [78].

In additional experiments, rats have been chronically exposed to dietary chlorpyrifos, and then subsequently challenged with a larger dose of chlorpyrifos [79]. The ensuing hypothermic response was observed to be greater than for a normal acute dose, indicating that chronic exposure may sensitize the thermoregulatory response. Intoxication by these classes of pesticides may make it even more difficult for humans (and other endotherms) to maintain normal core temperatures, especially during times of thermal stress, such as heat waves. In vitro and in vivo studies have suggested that heat stress, with or without exercise, will activate thermoeffectors (*e.g.*, skin blood flow, sweating, respiration) that will, in turn,

accelerate pesticide absorption in humans [80-82].

Epidemiological studies on the impact of simultaneous exposure to heat stress and air pollution also have revealed a significant effect on mortality rate. Extrapolating these population data to workplace gives cause to believe that concomitant exposure to heat stress and chemicals is likely to increase the potential risk for workers' health. Meuling *et al.* (1997) studied the dermal absorption of the propoxur, a carbamate insecticide, at 30 °C under various humidities (50, 70 or 90%). A linear relationship between the environmental relative humidity and the level of skin moisture was observed, indicating that skin moisture is important in dermal absorption of propoxur. The study concluded that, by assessing health risks of workers in agriculture exposed dermally to pesticides and *e.g.* in testing the efficiency of protective clothing under realistic conditions, the influence of the level of skin moisture on absorption of substances may be considerable and has to be taken into account [83]. To summarize, as meteorological conditions such as high ambient temperature and humidity can promote the absorption of chemicals, more workers may experience chemical intolerance or toxicity in the context of global warming. Because of varying individual susceptibility (such as age, physical fitness, acclimatization) and environmental factors (such as air movement, radiant heat, etc.), it is currently difficult to accurately predict the impact of climate change on workers' health. However, individuals working in hot environment and ex-

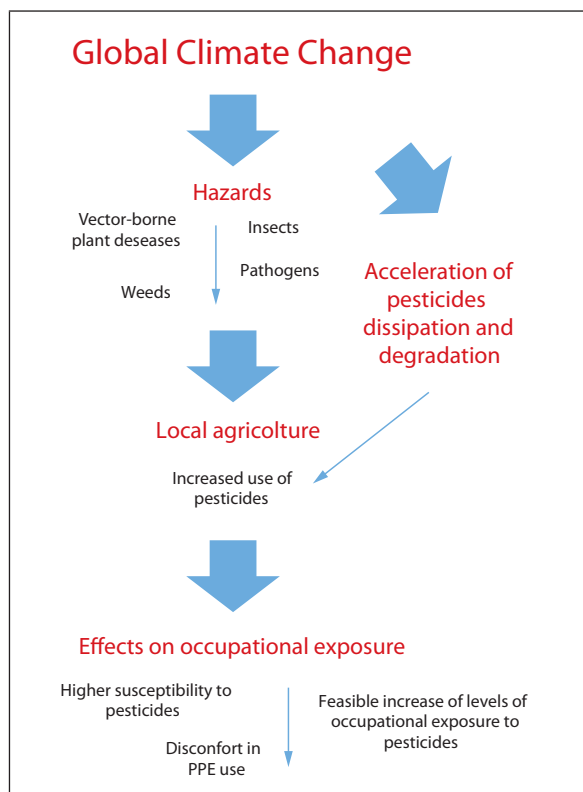


Figure 3 Climate change effects on environmental alterations and their feasible consequences on pesticides' exposure and adsorption at work.

posed to a significant level of chemical or workers with pre-existing illness may be more at risk.

CONCLUSIONS

Climate change is real and the consequences could not be ignored. Regional changes in climate, particularly increases in temperature, may have substantial ramifications on weeds, invasive species, insects, and plant diseases. Consequently, it is likely an increase of the use of pesticides as well as pesticide efficiency, represented by the initial deposit, pesticide fate and (eco-) toxicity, also has a major impact on pesticide use. In general, pesticide losses of mobile active substances are mainly influenced by the time gap between extreme weather events and pesticide application. Since increasing temperatures overall will result in higher amounts doses, frequencies and different varieties of pesticides, consequently, GCC may likely affect occupational exposure to pesticides. Alongside changes in exposure, alterations in the sensitivity of humans to chemical exposure are expected due to factors such as increases in the levels of heat stress, psychosocial factors and variations in pesticide absorption because of changes in skin blood flow, sweating, respiration. Furthermore, many workers who labour in thermally stressful occupations give up wearing their PPE because of their discomfort, which can further promote the pesticides absorption. As the current links between agricultural exposure and human health are unclear, because of varying individual susceptibility and environmental factors, it is difficult to predict accurately the impact of GCC on workers' health. It is essential, anyway, to manage many of these risk increases through better regulation, monitoring, and the development of a long-term research program. In order to more accurately portray the consequences of

climate change on occupational exposure to pesticides and support better-informed adaptation strategies, future research efforts should focus on:

- identifying early effects of changing weather patterns on climate-sensitive outcomes;
- updating and revising some of the scenarios and models currently used in health risk assessment of pesticides exposure in order to reflect some of the future changes described earlier;
- generating experimental data sets for exposure pathways to improve the understanding of the uncertainties and limitations of climate scenario data for future agricultural contaminant fate;
- promoting analyses of the response of human and natural systems to multiple climate and non-climate stressors;
- refining regulatory procedures in light of new knowledge and existing risk assessments.

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Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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REFERENCES

1. Symon C. Climate change: Action, trends and implications for business. The IPCC's Fifth Assessment Report; 2013.
2. Bloomfield JP, Williams RJ, Goody DC, Cape JN, Guha P. Impacts of climate change on the fate and behaviour of pesticides in surface and groundwater—a UK perspective. *Sci Total Environ* 2006;369:163-77. DOI: 10.1016/j.scitotenv.2006.05.019
3. Cannon RJC. The implications for predicted climate change on insect pests in the UK, with emphasis on non-indigenous species. *Glob Chang Biol* 1998;4:785-96. DOI: 10.1046/j.1365-2486.1998.00190.x
4. Food and Agriculture Organization. climate related transboundary pests and diseases. Rome: FAO; 2008.
5. Gale P, Adkin A, Snary E, Cheung S, Wooldridge M. *Climate change and animal health. Veterinary Laboratory Agency, Final Report to DEFRA*. London: DEFRA; 2007.
6. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. *CMAJ* 2000;163(6):729-34.
7. Patterson DT. Weeds in a changing climate. *Weed Sci* 1995;43:685-701.
8. Fontaine JJ, Decker KL, Skagen SK. Spatial and temporal variation in climate change: A bird's eye view. *Clim Change* 2009;97(1-2):305-11. DOI: 10.1007/s10584-009-9644-9
9. Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS, et al. Climate warming and disease risks for terrestrial and marine biota. *Science* 2002;296(5576):2158-62. DOI: 10.1126/science.1063699
10. Delcour I, Spanoghe P, Uyttendaele M. Literature review: Impact of climate change on pesticide use. *Food Res Int* 2015;68:7-15. DOI: 10.1016/j.foodres.2014.09.030
11. Gadgil S, Rao PRS, Rao KN. Use of climate information for farm-level decision making Rainfed groundnut in southern India. *Agric Syst* 2002;74(3):431-57. DOI: 10.1016/S0308-521X(02)00049-5
12. Rosenzweig C, Iglesias A, Yang X, Epstein PR, Chivian E. Climate change and extreme weather events; implications for food production, plant diseases, and pests. *Global Change and Human Health* 2001;2(2):90-104. DOI: 10.1023/A:1015086831467
13. Gutierrez AP, Ponti L, d'Oultremont T, Ellis C. Climate change effects on poikilotherm tritrophic interactions. *Clim Change* 2008;87(1):167-92. DOI: 10.1007/s10584-007-9379-4
14. Nolan BT, Dubus IG, Surdyk N, Fowler HJ, Burton A, Hollis JM, Reichenberger S, Jarvis NJ. Identification of key climatic factors regulating the transport of pesticides in leaching and to tile drains. *Pest Manag Sci* 2008;64(9):933-44. DOI: 10.1002/ps.1587

15. Miraglia M, Marvin HJP, Kleter GA, Battilani P, Brera C, Coni E, *et al*. Climate change and food safety: An emerging issue with special focus on Europe. *Food Chem Toxicol* 2009;47(5):1009-21. DOI: 10.1016/j.fct.2009.02.005
16. Patterson DT, Westbrook JK, Joyce RJV, Lingren PD, Rogasik J. Weeds, insects, and diseases. *Clim Change* 1999;43(4):711-27. DOI: 10.1023/A:1005549400875
17. Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS, *et al*. Climate warming and disease risks for terrestrial and marine biota. *Science* 2002;296(5576):2158-62. DOI: 10.1126/science.1063699
18. Roos J, Hopkins R, Kvarnheden A, Dixelius C. The impact of global warming on plant diseases and insect vectors in Sweden. *Eur J Plant Pathol* 2011;129(1):9-19. DOI: 10.1007/s10658-010-9692-z
19. Jackson L, Wheeler S, Hollander A, O'Geen A, Orlove B, Six J, *et al*. Case study on potential agricultural responses to climate change in a California landscape. *Clim Change* 2011;109(1):407-27. DOI: 10.1007/s10584-011-0306-3
20. Munkvold GP, Yang XB. 1995. Crop damage and epidemics associated with 1993 floods in Iowa. *Plant Disease* 1995;79:95-101. DOI: 10.1094/PD-79-0095
21. Otieno PO, Owuor PO, Lalah JO, Pfister G, Schramm KW. Impacts of climate-induced changes on the distribution of pesticides residues in water and sediment of Lake Naivasha, Kenya. *Environ Monit Assess* 2013;185(3):2723-33. DOI: 10.1007/s10661-012-2743-5
22. Caceres TC, Megharaj M, Naidu R. Degradation of fenamiphos in soils collected from different geographical regions: The influence of soil properties and climatic conditions. *J Environ Sci Health B* 2008;43(4):314-22. DOI: 10.1080/03601230801941659
23. Noyes PD, McElwee MK, Miller HD, Clark BW, Van Tiem LA, Walcott KC, *et al*. The toxicology of climate change: Environmental contaminants in a warming world. *Environ Int* 2009;35(6):971-86. DOI: 10.1016/j.envint.2009.02.006
24. Wang YS, Huang YJ, Chen WC, Yen JH. Effect of carbendazim and pencycuron on soil bacterial community. *J Hazard Mater* 2009;172(1):84-91. DOI: 10.1016/j.jhazmat.2009.06.142
25. Athanasopoulos PE, Kyriakidis NV, Stavropoulos P. A study on the environmental degradation of pesticides azinphos methyl and parathion methyl. *J Environ Sci Health B* 2004;39(2):297-309. DOI: 10.1081/PFC-120030243
26. Rosenzweig C, Iglesias A, Yang X, Epstein PR, Chivian E. Climate change and extreme weather events; implications for food production, plant diseases, and pests. *Global Change & Human Health* 2001;2(2):90-104. DOI: 10.1023/A:1015086831467
27. Kookana R, Holz G, Barnes C, Bubbs K, Fremlin R, Boardman B. Impact of climatic and soil conditions on environmental fate of atrazine used under plantation forestry in Australia. *J Environ Manage* 2010;91(12):2649-56. DOI: 10.1016/j.jenvman.2010.07.037
28. US Environmental Protection Agency. *Pesticide market estimates: 2006-2007*. EPA. Available from: www.epa.gov/pesticides/pestsales/07pestsales/table_of_contents2007.htm
29. US Environmental Protection Agency. *What is a pesticide?* Available from: www.epa.gov/pesticides/about/index.htm.
30. Grube A, Donaldson D, Kiely T, Wu L. *Pesticide industry sales and usage 2006 and 2007 market estimates*. Washington, DC: US EPA; 2011.
31. Langley RL, Mort SA. Human exposures to pesticides in the United States. *J Agromedicine* 2012;17(3):300-15. DOI: 10.1080/1059924X.2012.688467
32. Maroni M, Fanetti AC, Metruccio F. Risk assessment and management of occupational exposure to pesticides in agriculture. *Med Lav* 2006;97:430-7.
33. MacFarlane E, Carey R, Keegel T, El-Zaemay S, Fritsch L. Dermal exposure associated with occupational end use of pesticides and the role of protective measures. *Saf Health Work* 2013;4(3):136-41. DOI: 10.1016/j.shaw.2013.07.004
34. Curwin B, Hein M, Sanderson W, Barr DB, Heederik D, Reynolds SJ, Ward EM, Alavanja MC. Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa. *J Expo Sci Environ Epidemiol* 2005;15:500-8. DOI: 10.1038/sj.jea.7500428
35. Sperati A, Rapiti E, Settimi L, Quercia A, Terenzoni B, Forastiere F. Mortality among male licensed pesticide users and their wives. *Am J Ind Med* 1999;36(1):142-6.
36. Cattani M, Cena K, Edwards J, Pisaniello D. Potential dermal and inhalation exposure to chlorpyrifos in Australian pesticide workers. *Ann Occup Hyg* 2001;45:299-308. DOI: 10.1093/annhyg/45.4.299
37. MacFarlane E, Benke G, Del Monaco A, Sim MR. Causes of death and incidence of cancer in a cohort of Australian pesticide-exposed workers. *Ann Epidemiol* 2010;20:273-80. DOI: 10.1016/j.annepidem.2010.01.004
38. Green LM. A cohort mortality study of forestry workers exposed to phenoxy acid herbicides. *Br J Ind Med* 1991;48:234-8. DOI: 10.1136/oem.48.4.234
39. Centers for Disease Control and Prevention. *Third national report on human exposure to environmental chemicals*. Atlanta, GA: CDC; 2005.
40. Gilden RC, Huffling K, Sattler B. Pesticides and health risks. *J Obstet Gynecol Neonatal Nurs* 2010;39(1):103-10. DOI: 10.1111/j.1552-6909.2009.01092.x
41. Ecobichon DJ. Toxic effects of pesticides. In: Klaassen DC, Amdur MO, Doull J (Ed). *Casarett and Doull's toxicology: the basic science of poisons*. New York: McGraw-Hill; 1996.
42. Keifer M, Mahurin R. Chronic neurologic effects of pesticide overexposure. *Occup Med* 1997;12:291-304.
43. Kamel F, Engel LS, Gladen BC, Hoppin JA, Alavanja MCR, Sandler DP. Neurologic symptoms in licensed pesticide applicators in the Agricultural Health Study. *Hum Exp Toxicol* 2007;26:243-50. DOI: 10.1177/0960327107070582
44. London L, Nell V, Thompson M, Myers J. Effects of long-term organophosphate exposures on neurological symptoms, vibration sense and tremor among South African farm workers. *Scand J Work Environ Health* 1998;24:18-29. DOI: 10.5271/sjweh.274
45. Hatcher JM, Pennell KD, Miller GW. Parkinson's disease and pesticides: a toxicological perspective. *Trends Pharmacol Sci* 2008;29(6):322-9. DOI: 10.1016/j.tips.2008.03.007
46. Bazylewicz-Walczak B, Majczakowa W, Szymczak M. Behavioral effects of occupational exposure to organophosphorous pesticides in female greenhouse planting workers. *Neurotoxicology* 1999;20:819-26.
47. Woodruff T, Carlson A, Schwartz J, Giudice L. Proceedings of the summit on environmental challenges to reproductive health and fertility: Executive summary. *Fertil Steril* 2008;89(Suppl. 1):e1-20. DOI: 10.1016/j.fertnstert.2008.01.065
48. Kaufman RH, Adam E, Hatch E, Noller K, Herbst AL, Palmer JR, *et al*. Continued follow-up of pregnancy outcomes in diethylstilbestrol-exposed offspring. *Obstet Gynecol* 2000;98(4):483-9. DOI: 10.1016/S0029-7844(00)00959-5
49. Meeker JD, Ryan L, Barr DB, Hauser R. Exposure to nonpersistent insecticides and male reproductive hor-

- mones. *Epidemiology* 2006;17(1):61-8. DOI: 10.1097/01.ede.0000190602.14691.70
50. Saldana TM, Basso O, Hoppin JA, Baird DD, Knott C, Blair A, et al. Pesticide exposure and self-reported gestational diabetes mellitus in the Agricultural Health Study. *Diabetes Care* 2007;30(3):529-34. DOI: 10.2337/dc06-1832
 51. Garry V, Harkins M, Erickson L, Long-Simpson L, Holland S, Burroughs B. Birth defects, season of conception and sex of children born to pesticide applicators living the Red River Valley of Minnesota, USA. *Environ Health Perspect* 2002;110(Suppl. 3):441-9.
 52. Clark HA, Snedeker SM. Critical evaluation of the cancer risk of dibromochloropropane (DBCP). *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev* 2005;23(2):215-60. DOI: 10.1080/10590500500234996
 53. Dharmani C, Jaga K. Epidemiology of acute organophosphate poisoning in hospital emergency room patients. *Rev Environ Health* 2005;20(3):215-32. DOI: 10.1515/REVEH.2005.20.3.215
 54. Zahm SH, Ward MH. Pesticides and childhood cancer. *Environ Health Perspect* 1998;106(3):893-908.
 55. Infante-Rivard C, Weichenthal S. Pesticides and childhood cancer: An update of Zahm and Ward's 1998 review. *J Toxicol Environ Health B Crit Rev* 2007;10(1/2):81-99. DOI: 10.1080/10937400601034589
 56. Caress SM, Steinemann AC. A review of a two-phase population study of multiple chemical sensitivities. *Environ Health Perspect* 2003;111(12):1490-7.
 57. Weselak M, Arbuckle TE, Wigle DT, Krewski D. In utero pesticide exposure and childhood morbidity. *Environ Res* 2007;103(1):79-86. DOI: 10.1016/j.envres.2006.09.001
 58. Gatto MP, Fioretti M, Fabrizi G, Gherardi M, Strafella E, Santarelli L. Effects of potential neurotoxic pesticides on hearing loss: a review. *Neurotoxicology* 2014;42:24-32. DOI: 10.1016/j.neuro.2014.03.009
 59. European Agency for Safety and Health at Work (EU-OSHA). Agriculture - Use of pesticides/plant protection products. Available from: https://oshwiki.eu/wiki/Agriculture_-_Use_of_pesticides/plant_protection_products.
 60. Otieno PO, Owuor PO, Lalah JO, Pfister G, Schramm KW. Impacts of climate-induced changes on the distribution of pesticides residues in water and sediment of Lake Naivasha, Kenya. *Environ Monit Assess* 2013;185(3):2723-33. DOI: 10.1007/s10661-012-2743-5
 61. Bailey SW. Climate change and decreasing herbicide persistence. *Pest Manag Sci* 2003;60:158-62. DOI: 10.1002/ps.785
 62. Hancock PA. Heat stress impairment of mental performance: a revision of tolerance limits. *Aviat Space Environ Med* 1981;52(3):177-80.
 63. National Institute for Occupational Safety and Health. *Occupational exposure to hot environments*. Washington DC, USA: DHHS, NIOSH; 1986.
 64. Parsons KC. *Human thermal control: The effects of hot, moderate, and cold environments on human health, comfort, and performance*. London: Taylor and Francis; 2003.
 65. Broomhall SD. Egg temperature modifies predator avoidance and the effects of the insecticide endosulfan on tadpoles of an Australian frog. *J Appl Ecol* 2004;41:105-13. DOI: 10.1111/j.1365-2664.2004.00883.x
 66. Adam-Poupard A, Labreche F, Smargiassi A, Duguay P, Busque MA, Gagne C, Rintamaki H, Kjellstrom T, Zayed J. Climate change and occupational health and safety in a temperate climate: potential impacts and research priorities in Quebec, Canada. *Ind Health* 2013;51:68-78. DOI: 10.2486/indhealth.2012-0100
 67. Marszałek A, Konarska M, Bugajska J. Assessment of work ability in a hot environment of workers of different ages. *Int Congress Ser* 2005;1280:208-13. DOI: 10.1016/j.ics.2005.02.092
 68. National Oceanic and Atmospheric Administration. *Heat waves. A major summer killer*. Available from: www.nws.noaa.gov/om/brochures/heatwave.pdf.
 69. Intergovernmental Panel on Climate Change. *Human Health*. In: Intergovernmental Panel on Climate Change. *Climate Change 2007: Working Group II: Impacts, Adaptation and Vulnerability*. IPCC; 2007. Available from: www.ipcc.ch/ipccreports/ar4-wg2.htm.
 70. Tawatsupa B, et al. The association between overall health, psychological distress, and occupational heat stress among a large national cohort of 40, 913 Thai workers. *Glob Health Action* 2010;3:10-20. DOI: 10.3402/gha.v3i0.5034
 71. Kjellstrom T, Gabrysich S, Lemke B, Dear K. The "Hotthaps" programme for assessing climate change impacts on occupational health and productivity: an invitation to carry out field studies. *Glob Health Action* 2009a. DOI: 10.3402/gha.v2i0.2082
 72. Occupational safety & health administration. *Heat stress. OSHA technical manual*. Washington, DC, USA: Department of Labor, OSHA; 1999.
 73. Jones K, Cocker J, Doddand LJ, Fraser I. Factors affecting the extent of dermal absorption of solvent vapours: A human volunteer study. *Ann Occup Hyg* 2003;47(2):145-50. DOI: 10.1093/annhyg/meg016
 74. Wiechers JW. The barrier function of the skin in relation to percutaneous absorption of drugs. *Pharm Weekbl Sci* 1989;11:185-98. DOI: 10.1007/BF01959410
 75. Boman A, Maibach HI. Percutaneous absorption of organic solvents. *Int J Occup Environ Health* 2000;6:93-5. DOI: <http://dx.doi.org/10.1179/oeh.2000.6.2.93>
 76. Vanakoski J, Seppala T, Sievi E, Lunell E. Exposure to high ambient temperature increases absorption and plasma concentrations of transdermal nicotine. *Clin Pharmacol Ther* 1996;60:308-15.
 77. Schafer P, Bewick-Sonntag C, Capri MG, Berardesca E. Physiological changes in skin barrier function in relation to occlusion level, exposure time and climatic conditions. *Skin Pharmacol Appl Skin Physiol* 2002;15:7-19. DOI: 10.1159/000049384
 78. Noyes PD, McElwee MK, Miller HD, Clark BW, Van Tiem LA, Walcott KC, Erwin KN, Edward D, Levin ED. The toxicology of climate change: Environmental contaminants in a warming world. *Environ Int* 2009;35:971-86. DOI: 10.1016/j.envint.2009.02.006
 79. Gordon CJ. Behavioral thermoregulatory response to chlorpyrifos in the rat. *Toxicology* 1997;124(3):165-71. DOI: 10.1016/S0300-483X(97)00147-9
 80. Watkinson WP, Campen MJ, Wichers LB, Nolan JP, Costa DL. Cardiac and thermoregulatory responses to inhaled pollutants in healthy and compromised rodents: modulation via interaction with environmental factors. *Environ Res* 2003;92(1):35-47. DOI: 10.1016/S0013-9351(02)00023-3
 81. Gordon CJ, Padnos BK. Dietary exposure to chlorpyrifos alters core temperature in the rat. *Toxicology* 2002;177(2-3):215-26. DOI: 10.1016/S0300-483X(02)00227-5
 82. Gordon CJ, Leon LR. Thermal stress and the physiological response to environmental toxicants. *Rev Environ Health* 2005;20(4):235-63. DOI: 10.1515/REVEH.2005.20.4.235
 83. Meuling WJ, Franssen AC, Brouwer DH, van Hemmen JJ. The influence of skin moisture on the dermal absorption of propoxur in human volunteers: a consideration for biological monitoring practices. *Sci Total Environ* 1997;199:165-72. DOI: 10.1016/S0048-9697(97)05492-2