ATHENS UNIVERSITY | SCHOOL OF MEDICINE

MASTER'S COURSE IN:
INTERNATIONAL MEDICINE-HEALTH CRISIS MANAGEMENT

"Possible cytotoxic effects due to extensive use of pesticides. Towards a green environment."

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ABSTRACT

The Food and Agricultural Organisation of the United Nations 2010 estimate, the most recent, says that 925 million people in the world are hungry. Regardless of the economic level of the countries, in order to solve this problem, food production must be increased. Agricultural yields per unit must be improved, crops and livestock must be better protected from attack by pests and the amount of land available for agricultural production must increase. Pesticides constitute a heterogeneous class of chemicals used worldwide to fight various pathogens and improve crop production. Few environmental issues have aroused widespread public concerns as much as pesticides since their release into the environment and, effects on human health are surrounded by controversy. In this review the publicly available scientific literature has been assessed in order to identify possible cytotoxic effects due to extensive use of pesticides. Specific aims of the review were to 1) identify the association between the extensive use of pesticides and health effects, 2) assess the effect of the extensive use of pesticides on the environment and, 3) propose alternatives to pesticides and measures leading to a green environment.

Keywords: Pesticides; Cytotoxic effects; Environment

ΠΕΡΙΛΗΨΗ

Η τελευταία εκτίμηση του Οργανισμού Τροφίμων και Γεωργίας των Ηνωμένων Εθνών, το 2010, αναφέρει ότι 925 εκατομμύρια άνθρωποι στον κόσμο πεινούν. Ανεξάρτητα από το οικονομικό επίπεδο των χωρών, προκειμένου αυτό το πρόβλημα να επιλυθεί, η παραγωγή τροφίμων πρέπει να αυξηθεί. Η γεωργική παραγωγή ανά μονάδα και η διαθέσιμη για γεωργική παραγωγή γη πρέπει να αυξηθεί, ενώ οι καλλιέργειες και τα ζώα θα πρέπει να προστατεύονται καλύτερα από τα παράσιτα. Τα φυτοφάρμακα συνιστούν μια ετερογενή κατηγορία χημικών ουσιών που χρησιμοποιούνται παγκοσμίως για την καταπολέμηση διαφόρων παθογόνων και τη βελτίωση της φυτικής παραγωγής. Περιβαλλοντικά ζητήματα για τα φυτοφάρμακα και την απελευθέρωσή τους στο περιβάλλον και τις επιπτώσεις στην ανθρώπινη υγεία, έχουν προκαλέσει εκτεταμένη δημόσια ανησυχία που περιβάλλεται από κοινωνικές διαμάχες. Στην παρούσα ανασκόπηση η διαθέσιμη επιστημονική βιβλιογραφία έχει αξιολογηθεί προκειμένου να εντοπιστούν πιθανές κυτταροτοξικές επιδράσεις που οφείλονται στην εκτεταμένη χρήση των φυτοφαρμάκων. Ειδικοί στόχοι της ανασκόπησης ήταν 1) να εντοπιστεί η σχέση μεταξύ της εκτεταμένης χρήσης των φυτοφαρμάκων και των επιπτώσεων στην υγεία, 2) η εκτίμηση της επίδρασης της εκτεταμένης χρήσης των φυτοφαρμάκων στο περιβάλλον και, 3) να προταθούν εναλλακτικές λύσεις για τα φυτοφάρμακα και μέτρα που οδηγούν σε ένα καθαρότερο περιβάλλον.

INTRODUCTION

The Food and Agriculture Organisation (FAO) has defined the term of *pesticide* as: "any substance or mixture of substances intended for preventing, destroying or controlling any pest, including vectors of human or animal disease, unwanted species of plants or animals causing harm during or otherwise interfering with the production, processing, storage, transport or marketing of food, agricultural commodities, wood and wood products or animal feedstuffs, or substances which may be administered to animals for the control of insects, arachnids or other pests in or on their bodies. The term includes substances intended for use as a plant growth regulator, defoliant, desiccant or agent for thinning fruit or preventing the premature fall of fruit. Also used as substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport."[9]

Pesticides are categorized into four main substituent chemicals: herbicides; fungicides; insecticides and bactericides. Subclasses of pesticides include: herbicides, insecticides, fungicides, rodenticides, pediculicides, and biocides. Pesticides can be classified by target organism, chemical structure, and physical state.[53]

Many pesticides can be grouped into chemical families. The two largest classes of synthetic pesticides are insecticides, used to kill insects, and herbicides, used to kill plants. Insecticide chemical families include organochlorines (e.g. DDT), organophosphates, and carbamates) while herbicide chemical families include pheoxy and benzoic acid herbicides (e.g. 2,4-D), triazines (e.g. atrazine), ureas (e.g. diuron), and Chloroacetanilides (e.g. alachlor).

Pesticides can be also be classified based upon their biological mechanism function or application method. The biological activity of a pesticide, (chemical or biological in nature) is determined by its active ingredient (otherwise called active substance).

Pesticide products very rarely consist of pure technical material. The active ingredient is usually formulated with other materials and this is the product as sold, but it may be further diluted in use. Formulation improves the properties of a chemical for handling, storage, application and may substantially influence effectiveness and safety. The most frequently used products are formulations for mixing with water and then applying as sprays.

Pesticides are used to control organisms that are considered to be harmful.[38] For example, they are used to kill mosquitoes that can transmit potentially deadly diseases like West Nile virus, yellow fever, and malaria (e.g. DDT). They can also kill bees, wasps or ants that can cause allergic reactions. Insecticides can protect animals from illnesses that can be caused by parasites such as fleas.[38] Pesticides can prevent sickness in humans that could be caused by moldy food or diseased produce. Herbicides can be used to clear roadside weeds, trees and brush. They can also kill invasive weeds that may cause environmental damage. Herbicides are commonly applied in ponds and lakes to control algae and plants such as water grasses that can interfere with activities like swimming and fishing and cause the water to look or smell unpleasant.[17] Uncontrolled pests such as termites and mould can damage structures such as houses.[38] Pesticides are used in grocery stores and food storage facilities to manage rodents and insects that infest food such as grain. Each use of a

pesticide carries some associated risk. Proper pesticide use decreases these associated risks to a level deemed acceptable by pesticide regulatory agencies.

Pesticides can save farmers' money by preventing crop losses to insects and other pests. One study found that not using pesticides reduced crop yields by about 10%.[11]

Pesticide release into the environment and effects on human health have led to widespread public concerns and controversial disputes.[31]

HEALTH EFFECTS OF EXTENSIVE USE OF PESTICIDES

The three major routes in which pesticides may enter the human body are 1) through the skin, 2) through breathing 3) through the mouth.[53]

The toxicity of pesticides in human beings is influenced by various factors such as age, gender and health status of the individual in addition to the intensity and frequency of pesticide use.

Comparatively, children are at greater risk than adults.[23] Their internal organs are still developing and maturing and children eat and drink more than adults (in relation to their body weight) possibly increasing their exposure to pesticides in food and water. Also, the hand-to-mouth behaviour of children increases the chance of ingestion since they play on the ground outdoors and on the floor indoors.
Health condition deteriorates when the toxic level is increased beyond the capacity of the detoxification system.[57]

Humans are constantly exposed to a variety of pesticides as a consequence of their lifestyle. The food we eat, air we breathe, and the environments we live and work in, are contaminated with various chemicals. Humans are exposed to such chemicals while still in the womb of the mother. A number of studies have revealed the presence of pesticides in human milk, water, cow’s milk and dairy product samples.[30] One study found the presence of pesticides in sheep and goats.[50]

Since world demand for pesticides is projected to increase 2,9 percent though 2014 [11], the use of pesticides to which humans are exposed, is expected to increase in the near future.[51] The World Health Organization and the UN Environment Programme estimate that each year, 3 million workers in agriculture in the developing world experience severe poisoning from pesticides, about 18,000 of whom die.[33] According to one study, as many as 25 million workers in developing countries may suffer mild pesticide poisoning yearly.[21] Misuse of highly toxic pesticides, coupled with a weak or a totally absent legislative framework in the use of pesticides, is one of the major reasons for the high incidence of pesticide poisoning in developing countries.[25] Low education levels of the rural population, lack of information and training on pesticide safety, poor spraying technology, and inadequate personal protection during pesticide use have been reported to play a major role in the intoxication scenario.[19] One study found pesticide self-poisoning the method of

choice in one third of suicides worldwide, and recommended, among other things, more restrictions on the types of pesticides that are most harmful to humans.[13]

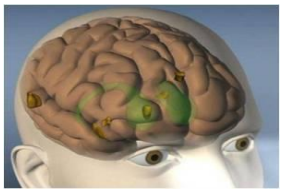
The World Health Organization has classified pesticides into classes by hazard to human health as extremely hazardous (class Ia), highly hazardous (class Ib), moderately hazardous (class II), slightly hazardous (class III) and unlikely to present acute hazard (class IV).[55]

Pesticides may cause acute and delayed health effects in those who are exposed.[33] Pesticide exposure can cause a variety of adverse health effects. These effects can range from simple irritation of the skin and eyes to more severe effects such as those affecting the nervous system[59], mimicking hormones causing reproductive problems[12][27], and also causing cancer.[41]

A 2007 systematic review provides evidence from research on humans that consistently points to positive associations between pesticide exposure and three chronic non-cancer health effects, namely neurologic, reproductive and genotoxic effects. This same systematic review indicates that results of dermatologic studies are less consistent and of poorer quality and indicates the need for a primary care prevalence study of pesticide-related skin conditions.[41]

The large amount of evidence found in another systematic review indicates a positive relationship between exposure to pesticides and development of some cancers, particularly brain, prostate and kidney cancers as well as non-Hodgkin lymphoma and leukemia.[2] Other epidemiological studies have implicated pesticides as causative agents in human cancer [50][60][47]

There is substantial experimental and epidemiological evidence that many pesticides in widespread use around the world are immunosuppressive. This poses potentially serious health risks in populations highly exposed to infectious and parasitic diseases that are subject to malnutrition and inadequately served by health programmes.[57]



Parkinson's disease is the most common neuro-degenerative disorder. It is now proposed that environmental factors in conjunction with genetic susceptibility may form the underlying molecular basis for idiopathic Parkinson's disease.[48][50]

Evidence indicating that prolonged exposure to multiple pesticides affect the liver and kidney exists.[1] One study found an increase in the prevalence of liver disorders among Ranch Hand workers in high exposure category's [32], while another indicated that liver enzymes may be used to detect the effect of pesticides before adverse clinical health effects occur.[6]

Some pesticides may mimic or block hormones or may trigger inappropriate hormone activity. One study has identified 127 pesticides as suspected of having endocrine disrupting effects.[29]

- **Methods used for detection of health risks to pesticides**

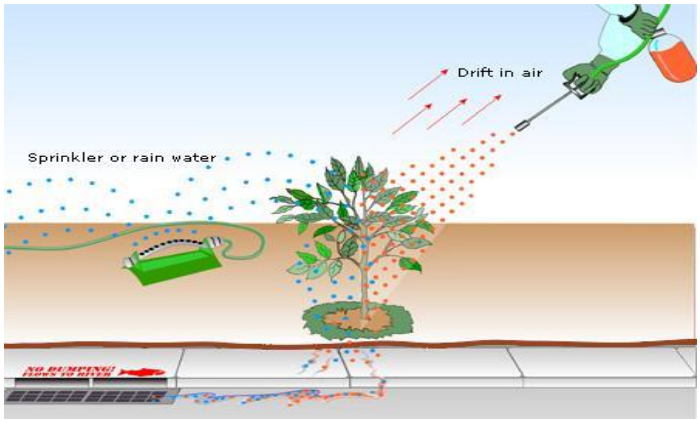
One study found that excessive exposure to pesticides caused cytotoxic changes in the hepatic and renal biochemical markers which were positively correlated with pesticide residues and further concluded that biomarkers might be used for monitoring of adverse effects of pesticides on the health of farm workers.[24]

The term biomarker includes almost any measurement reflecting an interaction between a biological system and an environmental agent (chemical, physical, or biological). Biomarkers can be used to identify causal associations and to make better quantitative estimates of those associations at relevant levels of exposure.[54] They may also make it possible to identify susceptible groups or individuals who are at risk of exposure to certain types of environmental and occupational agents. The advances in molecular genetics have led to an increase in trust in most susceptibility factors and identification of polymorphism of various enzymes has become possible [49]. Biomarkers include detection of the environmental substance itself or its metabolites in urine or blood, changes in genetic material, and cell death. The biological events detected can represent variation in the number, structure, or function of cellular or biochemical components. Recent advances in molecular and cellular biology allow for measurement of biological events or substances that may provide markers of exposure, effect, or susceptibility in humans. Two kinds of measurement have been used for assessing the exposure to pesticides, enzymes activity and pesticides residue in the blood.

Cytogenetic markers such as chromosomal aberrations (CA), sister chromatid exchange (SCE), micronuclei (MN) and single cell gel electrophoresis (SCGE) have been extensively used for detection of early biological effects of DNA-damaging agents.[36][5]

Pesticides residual analysis is mainly done with High Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC).

ENVIRONMENTAL EFFECTS OF EXTENSIVE USE OF PESTICIDES



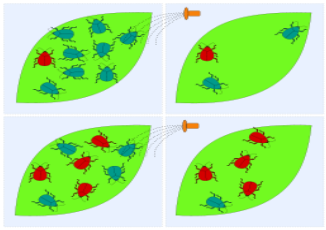
Pesticide use raises a number of environmental concerns. Over 98% of sprayed insecticides and 95% of herbicides reach a destination other than their target species, including non-target species, air, water and soil.[18]

Pesticide drift occurs when pesticides suspended in the air as particles are carried by wind to other areas, potentially contaminating them.

Pesticides are one of the causes of water pollution, and some pesticides are persistent organic pollutants and contribute to soil contamination. Wild animals and domestic livestock also ingest pesticides by drinking contaminated water or by eating smaller animals and vegetation in which toxic chemicals exist.[31]

In addition, pesticide use reduces biodiversity, reduces nitrogen fixation,[40] contributes to pollinator decline,[14][52][15][16] destroys habitat (especially for birds),[35] and threatens endangered species.[33]

Pests can develop a resistance to the pesticide (pesticide resistance), necessitating a new pesticide. Alternatively a greater dose of the pesticide can be used to counteract the resistance, although this will cause a worsening of the ambient pollution problem.



Depiction of pest resistance

Assessing the toxic effects of pesticides on ecosystems is difficult, because so many species and processes are interacting. Furthermore, observations made in one location may not apply to other sites because of variation among ecosystems. Finally, highly managed ecosystems may be more or less sensitive to a pesticide than a more natural community. It is to humans' benefit to consider all uses and risks of pesticides to ensure preservation of critical systems in the environment.[58]

TOWARDS A GREEN ENVIRONMENT

- **Alternatives to pesticides**

Alternatives to pesticides are available and include methods of cultivation, use of biological pest controls (such as pheromones and microbial pesticides), genetic engineering, and methods of interfering with insect breeding.[33] Application of composted yard waste has also been used as a way of controlling pests.[30] These methods are becoming increasingly popular and often are safer than traditional chemical pesticides. In addition, EPA is registering reduced-risk conventional pesticides in increasing numbers.

Cultivation practices include polyculture (growing multiple types of plants), crop rotation, planting crops in areas where the pests that damage them do not live, timing planting according to when pests will be least problematic, and use of trap crops that attract pests away from the real crop. In the U.S., farmers have had success controlling insects by spraying with hot water at a cost that is about the same as pesticide spraying.[33]

Release of other organisms that fight the pest is another example of an alternative to pesticide use. These organisms can include natural predators or parasites of the pests. Biological pesticides based on entomopathogenic fungi, bacteria and viruses that cause disease in the pest species can also be used.[33]

Interfering with insects' reproduction can be accomplished by sterilizing males of the target species and releasing them, so that they mate with females but do not produce offspring.[33] This technique was first used on the screwworm fly in 1958 and has since been used with the medfly, the tsetse fly, and the gypsy moth. However, this can be a costly, time consuming approach that only works on some types of insects.[44]

Another alternative to pesticides is the thermal treatment of soil through steam. Soil steaming kills pest and increases soil health.[43]

In India, traditional pest control methods include using Panchakavya, the "mixture of five products." The method has recently experienced a resurgence in popularity due in part to use by the organic farming community.[37]

Some evidence shows that alternatives to pesticides can be equally effective as the use of chemicals. For example, Sweden has halved its use of pesticides with hardly any reduction in crops. In Indonesia, farmers have reduced pesticide use on rice fields by 65% and experienced a 15% crop increase.[26][33] A study of Maize fields in northern Florida found that the application of composted yard waste with high carbon to nitrogen ratio to agricultural fields was highly effective at reducing the population of plant-parasitic nematodes and increasing crop yield, with yield increases ranging from 10% to 212%; the observed effects were long-term, often not appearing until the third season of the study.[22]

- **Integrated Pest Management**

Integrated Pest Management (IPM) is a strategy that contributes to pesticide risk reduction by: reducing reliance on chemical pesticides and encouraging the use of non-chemical alternatives, encouraging the use of reduced-risk pesticides when pesticide treatment is necessary, preventing pest problems through better crop management and maintenance of natural resources, and by increasing farmer knowledge about agricultural pests and ecosystems.[53]

Integrated pest management, the use of multiple approaches to control pests, is becoming widespread and has been used with success in countries such as Indonesia, China, Bangladesh, the U.S., Australia, and Mexico.[33] IPM attempts to recognize the more widespread impacts of an action on an ecosystem, so that natural balances are not upset.[4] New pesticides are being developed, including biological and botanical derivatives and alternatives that are thought to reduce health and environmental risks. In addition, applicators are being encouraged to consider alternative controls and adopt methods that reduce the use of chemical pesticides.

- **Pesticides of Botanical Origin**

Pesticides can be created that are targeted to a specific pest's life cycle, which can be environmentally more friendly. For example, potato cyst nematodes emerge from their protective cysts in response to a chemical excreted by potatoes; they feed on the potatoes and damage the crop. A similar chemical can be applied to fields early, before the potatoes are planted, causing the nematodes to emerge early and starve in the absence of potatoes.[42]

Botanical pesticides presently play only a minor role in crop protection since stringent regulatory requirements have prevented all but a handful of botanical products from reaching the marketplace in the past 20 years.[20]
One review concludes that the regulation of natural products as crop-protection agents may have to undergo the same procedure as for a conventional chemical product.[34]

- **Monitoring**

Pesticide monitoring is performed by National and private laboratories, operating in each European country. National laboratories monitor pesticides and inform the European Union in order to publish specific pesticide reports. Private laboratories in each country perform routine analysis for major pesticide categories, with agricultural samples originating from independent farmers, farmer groups, supermarkets.

A risk assessment study suggests that a wide spectrum of pesticides be included in monitoring programs in order to eliminate the possibility of contaminated samples reaching the markets stores.[46]

- **Safety Education**

Pesticide safety education and pesticide applicator regulations are designed to protect the public from pesticide misuse, but do not eliminate all misuse. Reducing the use of pesticides and choosing less toxic pesticides may reduce risks placed on society and the environment from pesticide use.[18] Fortunately, many farmers have expressed the need for information and training programs on pesticide safety, and therefore are likely to be responsive to such programs.[45]

- **Regulation**

In Europe, recent EU legislation has been approved banning the use of highly toxic pesticides including those that are carcinogenic, mutagenic or toxic to reproduction, those that are endocrine-disrupting, and those that are persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB).[7] Measures were approved to improve the general safety of pesticides across all EU member states.[8]
Though pesticide regulations differ from country to country, pesticides and products on which they were used are traded across international borders. To deal with inconsistencies in regulations among countries, delegates to a conference of the United Nations Food and Agriculture Organization adopted an International Code of Conduct on the Distribution and Use of Pesticides in 1985 to create voluntary standards of pesticide regulation for different countries.[56] The Code was updated in 1998 and 2002.[10] The FAO claims that the code has raised awareness about pesticide hazards and decreased the number of countries without restrictions on pesticide use.[9]

Three other efforts to improve regulation of international pesticide trade are the United Nations London Guidelines for the Exchange of Information on Chemicals in International Trade [28] and the United Nations Codex Alimentarius Commission.[40] The former seeks to implement procedures for ensuring that prior informed consent exists between countries buying and selling pesticides, while the

latter seeks to create uniform standards for maximum levels of pesticide residues among participating countries.[39] Both initiatives operate on a voluntary basis.[39]

CONCLUSIONS

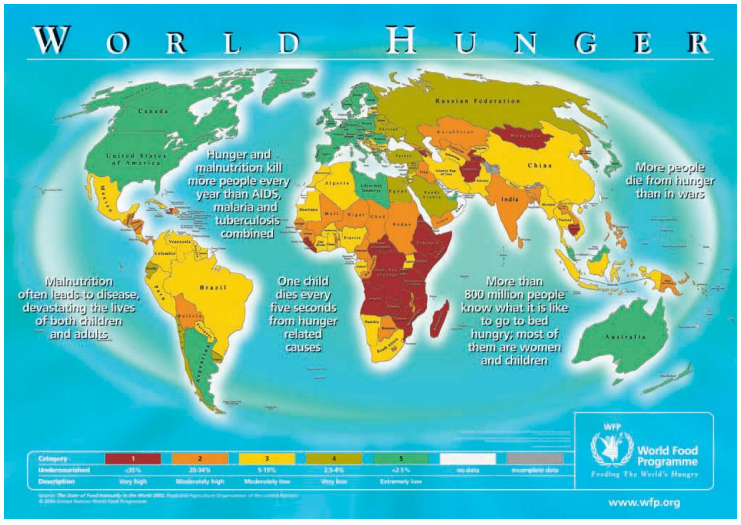
The Chinese in 2,000 B.C. recommended the burning of “brimstone” (sulfur) to control pests. Ancient Greeks recommended gall from the green lizard to protect apples from worms to rot. Using chemicals to control pests is not a new idea, only the types of chemicals used today are new.

The use of these chemicals is necessary to produce food and fibre needed to feed, clothe and house the ever-expanding world population. These chemicals, pesticides, function to protect the crop while it grows. Pesticides are expensive and all farmers would like to reduce their use of them, but there is a level below which they cannot reduce treatments and still produce a profitable crop.[61]

The American Medical Association recommends limiting exposure to pesticides and using safer alternatives: "Particular uncertainty exists regarding the long-term effects of low-dose pesticide exposures. Current surveillance systems are inadequate to characterize potential exposure problems related either to pesticide usage or pesticide-related illnesses…Considering these data gaps, it is prudent…to limit pesticide exposures…and to use the least toxic chemical pesticide or non-chemical alternative."[3]

The aim of this review was to assess the publicly available scientific literature and it is clear that positive association exists between the extensive use of pesticides and health effects. The environment is indeed effected by the extensive use of pesticides. Although alternatives to pesticide use exist, in many cases these have a high cost and when implemented they may or may not be unsuccessful.

Pesticide use presents real problems which must be addressed. Pesticides are toxic, but faced with world hunger increasing, their use cannot be eliminated. Attempts must be made by mankind to use them safely thereby minimizing health effects to humans or to the environment and ultimately leading towards a green environment.



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