HEALTH EFFECTS ASSOCIATED WITH ACUTE AND CHRONIC EXPOSURE TO PESTICIDES

ALINA FARCAS[1], ANDREEA VALCEANU MATEI[2], CRISTINA FLORIAN[1], MIHAELA BADEA[1] AND GHEORGHE COMAN[1]
[1] *Transilvania University of Brasov*
29 Eroilor Bdv., 500036 Brasov, Romania
[2] *Emergency County Hospital of Brasov*
25-27 Calea Bucuresti 500326 – Brasov, Romania

Correspondence Contct: gh.coman@unitbv.ro

Abstract. All living organisms are dynamic systems, functioning as a result of interdependent (bio) chemical reactions that are permanently maintained in an equilibrium state. Human exposure over a period of time to a complex mixture of pollutants at low level and consumption of polluted water and/or foods, is likely to significantly contribute to the human health status. Considering the time of exposure to toxicants, we can distinguish two different types of toxicity: acute toxicity (observed soon after short-time exposure to the pollutant) and chronic toxicity (resulted after long-term and/or repeated periods of exposure to lower doses of the chemical). Most of the acute effects are temporary, but may also cause coma and/or death. The chronic health effects have a latency period, which corresponds to the period of time between the first exposure and the development of the disorder. Most of the time, pesticide use involves their deliberate release into the environment for repelling, attracting, preventing, or killing any pests (target organisms) and may affect other organisms from the environment because they have relatively limited selectivity. Living organisms as well as humans are concurrently exposed to pesticides via the environment, which induces combined toxicological effects. The degree of health hazard depends on the quantity of pesticide and on the length of exposure (the dose of the pollutant). In this paper are presented general aspects on toxicology and clinical toxicology in view of the relationship exposure to pesticides – effects on human health.

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1. Introduction

All living organisms are dynamic systems, functioning as a result of interdependent (bio) chemical reactions that are permanently maintained in an equilibrium state. The presence of xenobiotic substances in a living system can easily disrupt this balance, by interacting with different components either through inhibition or activation (Biliet et al., 2004; Alcala et al., 2009).

Human health is a very complex mixture of elements such as hereditary factors, lifestyle choices (eating habits, exercise, smoking, alcohol, drugs), socio-economic status, access to medical services, and most certainly the environment.

Research has indicated that interaction between the environment and human health is far more complex than is commonly understood.

Pollution may be defined as an undesirable change in the physical, chemical or biological characteristics of air, water, soil or food that can adversely affect the health, survival and activities of humans or other living organism (Coman et al., 2006).

Human exposure over a period of time to a complex mixture of pollutants at low level and consumption of polluted water and/or foods, is likely to significantly contribute to the human health status (Reffstrup et al., 2010).

The role of toxicology and clinical toxicology is to study the toxic effects of chemical compounds on the human body, and recent developments in biochemistry, clinical biochemistry, biology and genetics can afford us the understanding of the processes at work in the human body in the presence of xenobiotics. In the human body, most of the biomolecules that interact with xenobiotics are proteins, which are structurally and functionally genetically conditioned (Dufol and Guillen, 2009).

Exposure to xenobiotic substances can produce toxicokinetic effects (enzymatic induction of metabolic pathway) and toxicodynamic effects (change in gene expression) in the human body.

It is useful to reconsider some commonly used definitions for toxic substances in order to facilitate the understanding of the processes, because these are often used interchangeably in literature. Therefore, a poison is legally, a substance that is fatal at a dose of less then 50 mg/kg body weight; a toxicant is a substance that may produce effects on plants, animals or humans; a toxin is a toxicant, produced during the metabolism of invading living organisms (microorganisms, plants, insects) which act on the host (in common usage, the word toxin is used as a synonym for toxicant – which is not correct); and a

xenobiotic is a chemical that is foreign (not synthesized) into the body of the animal which is exposed to it.

Apart from the expected contributions of lifestyle choices, dietary factors and genetic state, many xenobiotics increase the risk of appearance of some biological or health effects (Klaassen, 2001; Coman and Draghici, 2004).

There are several factors that govern the biological effects of the pollutants and their metabolites in any living organism (Coman et al., 2008). First, they need to enter the organism and be transported to the target sites where they need to bind to and interact with their biological receptors or be stored and resist the action of the degradative enzymes (biotransformation).

Solubility is a major determinant for the penetration of pollutants through cell membranes. Water and other biological media solubility influences the mobility of toxins, as blood and lymph serve as pollutants means of transport and liver, fat tissues, kidney and bone serve as pollutants storage.

2. Relationship Exposure to Pesticides – Effects on Human Health

Exposure to a pollutant is the presence of a certain concentration of pollutant material in the air, water or soil to which an animal is exposed in contrast with the dose received by an organism where we need to take into account the time of exposure and the quantity of pesticide (Costa, 2006). Doses are often expressed in weight or molecular units per kilogram of body weight or per square meter of body surface area while exposure is a concentration of the compound in the air, water or soil to which an animal is exposed.

Considering the time of exposure to toxicants, we can distinguish two different types of toxicity:

- acute toxicity – observed soon after a short-time or one-time exposure to the chemical;

- chronic toxicity – resulted after long-term and/or repeated periods of exposure to lower doses of the chemical.

Pesticides are environmental pollutants (Carrillo et al., 2004; Beard, 2006) and may be described as any physical, chemical, or biological agent developed to control or kill certain organisms (undesirable plants, animals or microorganisms). As a consequence, they have the potential to cause adverse effects to non-target organisms (associations with health effects with different latency periods for the different pesticide classes). Pesticide (Kiss and Virag, 2009; Chen et al., 2012) is the generic name for a substance or a mixture of substances classified on the basis of the organism killed (pest control) and the pattern of use (Stamati, 2007): insecticides, herbicides, fungicides, rodenticides, acaricides, molluscides, larvacides, scabicides, miticides, pediculicides,

defoliants, repellants, desiccants, plant growth regulators, attractants (pheromones).

Plant extracts containing pyrethrin or nicotine and secondary plant metabolites such as phenols, terpenes, alkaloids, tannins, sterols, gums, and sugars were used in agriculture before the discovery of synthetic pesticides, as plant defenses against microbial pathogens or invertebrate pests (Rattan, 2010).

Most of the pesticides are hydrophobic compounds and therefore tend to accumulate in human (mammalian) fatty tissue and induce many pathologic states (Garry, 2004; Kanthasamy et al., 2005; Slotkin, 2004).

For humans exposure to pesticide or pesticide residues can follow one or more of a number of pathways: through consumption of contaminated foods or drinking contaminated water, through residential application of pesticides, and in the course of occupational handling of pesticides.

Routes of exposure to pesticides can be oral, inhalation and dermal, depending on pollutants physical and chemical properties (Mckinlay et al., 2008). The sources of pesticide exposure for humans and their pathways are shown in Figure 1.

In the EU there is a significant presence of pesticides or pesticide residues in foods and consumers are exposed to more than one pesticide at the same time or in a short span of time (Boobis et al., 2008; Hernandez et al, 2012):

- in 53-64% of foods pesticides were not detectable;
- 32-42% of foods contained detectable pesticide levels (below the maximum residue levels-MRL);
- 3-5,5% of foods contained levels above the MRL;
- 14-23% of foods contained more than one pesticide;
- more than 50% of streams contained five or more pesticides.

Most of the time, pesticide use involves their deliberate release into the environment for repelling, attracting, preventing, or killing any pests (target organisms) and may affect other organisms from the environment because they have relatively limited selectivity (Moretto and Colosio, 2011; Hillocks, 2012).

Pesticides are known to be a major environmental hazard because only 5% of the used pesticides reach the targeted pests, while more than 95% of the used pesticides dispersed in the environment reach non-target organisms.

Because the use of pesticides induces environmental pollution, depollution strategies are necessary at the local level: chemical oxidation, photodegradation and phytoremediation (Coman et al., 2008; Bai et al., 2010).

Living organisms in general, as well as humans in particular are concurrently exposed to two or more pesticides in their environment, situation that leads to the development of combined toxicological effects (Reffstrup et al., 2010). These emerging effects are:

- simple effect or independent action of the individual pesticide where the effect of one pesticide is the same whether the other one is present or not and the combined effects will be the sum of the individual effects.

- dose addition effect or agonist effect, which refers to mixtures of individual pesticides with the same mode of action and the same toxicological effects , which differ only in their potencies.

- interaction effect which is referred to as the joint action, where the combined effects of more pesticides may be greater (synergistic) or less (antagonistic) than the predicted effects.

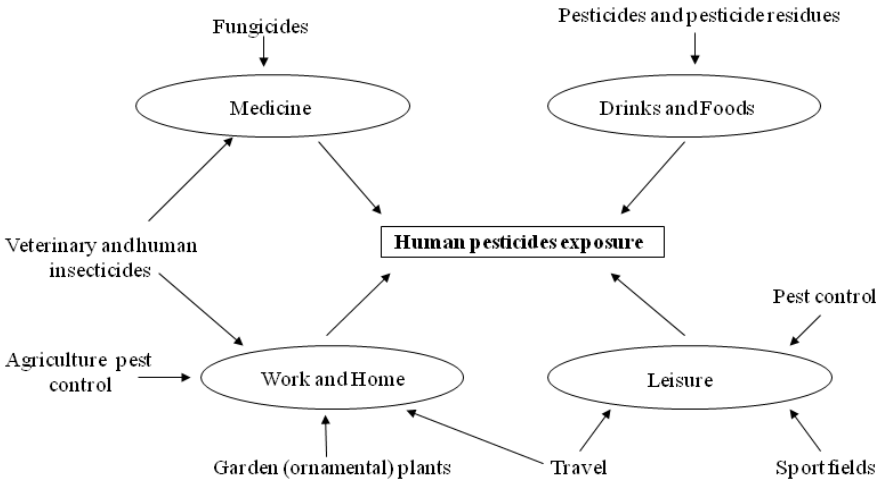

Figure 1. Human sources and pathways of pesticides exposure

Most of the pesticides are hydrophobic compounds and tend to accumulate in human (mammalian) fatty tissue and may induce many pathologic states (Coman and Draghici, 2004; Landau et al., 2009).

The degree of health hazard depends on the quantity of the pesticide and on the length of exposure (the dose of the pollutant).

In the dose–response relationship it is important for the response (effect) to be readily quantified in a reproducible way, relevant to the toxic processes.

The estimation of the dose–effect or concentration–effect relationship for pollutants (pesticides) is using some expressions: LD_{50} – lethal dose; LC_{50} – lethal concentration and IC_{50} – inhibited concentration.

LD_{50} is the dose which corresponds to a 50% mortality of the exposed organisms and it is a measure for acute toxicity.

LC_{50} is the concentration in air or water which corresponds to a 50% mortality of the exposed organisms, in a given amount of time.

IC_{50} is the concentration which corresponds to a 50% inhibition of growth or activity.

Low toxicant concentrations may produce no observable effects, but as the concentration increases towards the critical level, symptoms will appear that will range from the lowest observable effect to severe affectation and even death.

Figure 2 shows the cumulative dose-response relationship as a sigmoid curve, where the no observable effect concentrations (NOEC) and lowest observable effect concentrations (LOEC) are represented alongside LC_{50} (LD_{50}).

Acceptable limits of pesticides or pesticide residues in foods or in the environment are designed based on this dose-response relationship curve , and the usage of pesticides requires authorization (World Health Organization, 2004).

The degree of health hazard depends on the quantity of the pesticide used and on the length of exposure (the dose of the pollutant).

Most of the acute effects are temporary, but may also cause coma and even death (Mansour, 2004).

The chronic health effects (Ostrea et al., 2009) have a latency period which corresponds to the period of time between the first exposure and the development of the disorder: leukemia, cancer, cirrhosis, lung diseases and asthma, obesity and diabetes, kidney and urinary tract diseases, cardiovascular and hematologic diseases, gastrointestinal disorders, genetic alterations, and pathologic states of the bone marrow, the central nervous system, the blood cells (Garg et al., 2004; Rahimi and Abdollahi, 2007; Carozza et al., 2009; Franco et al., 2010.

Today, in our society, the debate over pesticide use is a social issue and continues at all levels, the controversy resting in the opposition between the rationale for pesticides and the need to minimize the health risks.

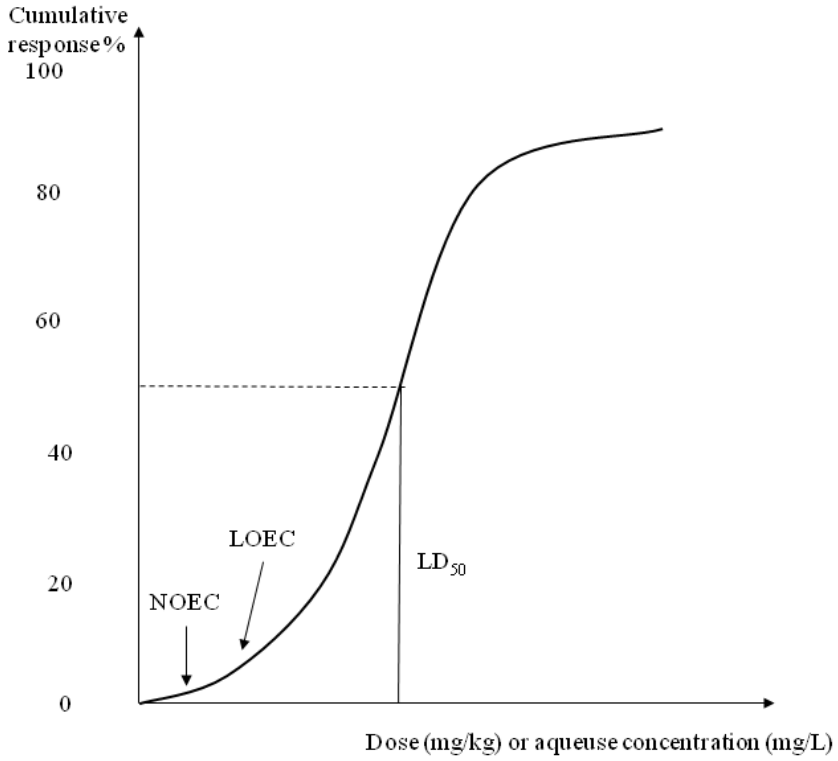

Figure 2. Cumulative dose-response curve

3. Conclusion

The human body can be intermittently or continuously exposed to the environmental pesticides, which can easily enter it using various routes. The presence of certain pesticides in the human body can induce combined toxicological effects (altered cell function) and can lead to various diseases.

Our review presented general aspects on toxicology and clinical toxicology, through the point of view of the relationship between the exposure to pesticides and its effects on human health.

Today the purpose of a pest management system is to discourage the excessive proliferation of pests as well as to switch toward using the newest and least damaging pesticides in the attempt to maintain the agricultural productivity and the level of control over vectors of disease while decreasing the impact on health and the environment.

References

L.Q. Alcala, A.D. Alkon, W.T. Boyce, S. Lippert, N. Davis, A. Bradman. D. Barr, B. Eskenazi, 2009, Maternal prenatal and child organophosphate pesticide exposures and childrens autonomic function, Neuro Toxicology, 32, 646-655;

I.Bai, J.Chen, Y.Yang, L.Guo, C.Zhang, 2010, Degradation of organophosphorus pesticide induced by oxygen plasma, Chemosphere, 81, 408-414;

J. Beard, 2006, DDT and human health, Science of the Total Environment, 355, 78-89;

H. Biliet, C. Draghici, Gh. Coman, Analitical biotechnology. Principles and applications, 2004, Transilvania University Press, Brasov;

A.R. Boobis, B.C. Ossendorp, U. Banasiak, P.Y. Hamey, 2008, Cumulative risk assessment of pesticide residues in food, Toxicology Letters, 180, 137-150;

S.E.Carozza, B.Li, Q.Wang, S.Horel, S.Cooper, 2009, Agricultural pesticides and risk of childhood cancers, Int.J.Hyg.Health, 212, 186-195;

M.L. Carrillo, D. Amato, P. Wegman, C.G. Horta, Y. Corona, L.H. Sanin, 2004, Relation between pesticide exposure and intrauterine growth retardation, Chemosphere, 55, 1421-1427;

K. Chen, J. C.Mackie, E.M. Kennedy, B.Z. Dlugogorski, 2012, Determination of toxic products released in combustion of pesticides, Progress in Energy and Combustion Science, xxx, 1-19;

Gh. Coman, C. Draghici, 2004, Pollutants and their impact on human body, Transilvania University Press, Brasov;

Gh. Coman, C. Draghici, E. Chirila, M. Sica, 2006, Pollutants effects on human body, in L.Simeonov, E.Chirila (eds.) Chemical as international and accidental global environmental threats, Springer, 255-266;

Gh. Coman, C. Draghici, C. Vrabie, 2008, Accumulatin and transformation processes of pollutants in soil, in L.Simeonov, V.Sargsyan (eds.), Soil Chemical pollution, risk assessment, remediatin and security, Springer Science, 349-357;

L.G. Costa, 2006, Current issues in organophosphate toxicity, Clinica Chimica Acta, 366, 1-13;

A.F.Dufol, S.M. Guillen, 2009, Toxicogenomics and clinical toxicology, Toxicology Letters, 186, 2-8;

R. Franco, S. Li, H. Rodriguez, M. Burns, M. Panayiotidis, 2010, Molecular mechanisms of pesticide neurotoxicity, Chemico-Biological Interactions, 188, 289-300;

U.K.Garg, A.K.Pal, G.J.Jha, S.B.Jadhao, 2004, Haemato-biochemical and immuno-pathophysiological effects of chronic toxicity with synthetic pyrethroid, organophosphate and chlorinated pesticides, International Immunopharmacology, 4, 1709-1722;

V.F. Garry, 2004, Pesticides and children, Toxicology and Applied Pharmacology, 152-163;

A.F.Hernandez, T.Parron, A.M. Tsatsakis, M.Requena, R. Alarcon, 2012, Toxic effects of pesticides mixtures at a molecular level, Toxicology, in press;

R.J. Hillocks, Farming with fewer pesticides, 2012, Crop Protection, 31, 85-93;

A.G. Kanthasamy, M. Kitazava, A. Kanthasamy, V. Anantharam, 2005, Dieldrin-Induced Neurotoxicity, NeuroToxicology, 26, 701-719;

A. Kiss, D. Virag, 2009, Interpretation and modeling of environmental behaviour of diverse pesticides by revealing photodecomposition mechanisms, Microchemical journal, 92, 119-122;

C.D. Klaassen, 2001, Toxicology. The basic science of poisons, McGraw-Hill Professional;

M.Landau, N.Rabia, J.Pelage, L.Marquet, 2009, Why pesticides could be a common cause of prostate and breast cancers in the French Caribbean Island, Biomedicine & Pharmacotherapy, 63, 383-395;

S.A. Mansour, 2004, Pesticide exposure, Toxicology, 198, 91-115;
R.McKinlay, J.A.Plant, J.N.B.Bell, N.Voulvoulis, 2008, Calculating human exposure to endocrine disruption pesticides via agricultural and non-agricultural exposure routes, Science of the Total Environment, 398, 1-12 ;
A. Moretto, C. Colosio, 2011, Biochemical and toxicological evidence of neurological effects of pesticides, NeuroToxicology, 32, 383-391;
E.M. Ostrea, D. M.Bielwski, N.C. Posecion, M. Corrion, 2009, Combined analysis of prenatal and neonatal matrices to detect fetal exposure to environmental pesticides, Environmental Research, 116-122;
R. Rahimi, M. Abdollahi, 2007, A rewiew on the mechanisms involved in hyperglycemia induced by organophosphorus pesticides, Pesticide Biochemistry and physiology, 88, 115-121;
R.S.Rattan, 2010, Mechanism of action of insecticidal secondary metabolites of plant origin, Crop Protection, 29, 913-920;
T.K. Reffstrup, J.C. Larsen, O. Meyer, 2010, Risk assessment of mixtures of pesticides, Regulatory Toxicology and Pharmacology, 56, 174-192;
T.A. Slotkin, 2004, Guidelines for developmental neurotoxicity and their impact on Organophosphate pesticides, NeuroToxicology, 25, 631-640;
P.N. Stamati, L. Hens, C.V. Howard, 2007Congenital diseases and the environment, Springer,;
**** World Health Organisation, 2004, Neuroscience of psychoactive substance use and dependence, Geneva;