ENVIRONMENTAL TOXICOLOGY AND HUMAN HEALTH

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Contents

Summary

Toxicology is the study of harmful effects of chemicals on biological systems. Humans, animals, and plants are increasingly being exposed to chemicals in the environment. The ever-increasing use of chemicals in industries has also resulted in further pollution of the environment. As toxic chemicals are widespread in the environment, there is a potential for these chemicals to cause significant damage and harmful effects on human health. In the past three decades, the environmental branch of toxicology has assumed a greater role in understanding the effects of the toxic chemicals on living organisms, especially human. Environmental toxic agents have caused many types of diseases, especially in high-risk population such as children, pregnant or lactating women,

geriatrics, and clinical patients. The environmental toxic agents are generally found in air, water, soil, and food. Upon exposure to a chemical, the first process is absorption of the chemical into the human body and distribution to reach the target organ where it can manifest its toxicity.

Once in the human body, the chemical can also be metabolized either to reduce or to further enhance its toxicity. Some chemicals can be stored for many years in the body, while others are eliminated via the excretion process. The various classes of toxic stressors found in the environment include metals, pesticides, aromatic and aliphatic hydrocarbons, volatile organic compounds, particulates, radiation, and biological agents such as mycotoxins and bacterial toxins.

In order to understand the myriad of public health issues related to chemicals in the environment, attempts to understand the acceptable levels of chemical exposure, and therefore its regulation, are crucial. Therefore, risk assessment must be carried out to determine the probability of adverse effects upon exposure to chemicals and how to manage this risk. In addition to risk assessment and risk management approaches, importance of risk communication should be emphasized. Integrated consideration rather than evaluation on individual items is important. Special consideration in evaluating chemical toxicity in the environment and the effects on health should be stressed.

1. Introduction

There is an ever-increasing use of chemicals and exposure to these chemicals and the resultant toxicity has long been a concern in humans. From a historical perspective, toxicology has always been associated with poisons. The word toxicology is derived from two Greek terms: *toxicon*—a poisonous substance into which arrowheads were dipped, and *toxicos*—a bow. A poison can be defined as any substance which has a harmful or deleterious effect on a living system. In this respect, Paracelsus (1493–1541), one of the most significant figures in the development of the science of toxicology, established the importance of the dose response relationship. He elegantly summarized this concept in his famous statement:

> All substances are poisons; there is none that is not a poison.
> The right dose differentiates a poison and a remedy.
>
> (Paracelsus)

The earliest poisons that were used for hunting, waging war, and official execution consisted of plant extracts, animal venoms, and minerals, including arsenic, lead, opium, and cyanogenic glycosides. It is inevitable today that poisons include both harmful naturally occurring substances, either from animals, plants, or microorganisms, and synthetic chemicals.

The former are generally termed toxins and the latter are better known as toxicants. The toxicants include synthetic chemicals/pharmaceuticals, which have economic benefits such as pesticides or drugs, and also those resulting from anthropogenic activities such as by-products of incomplete combustion.

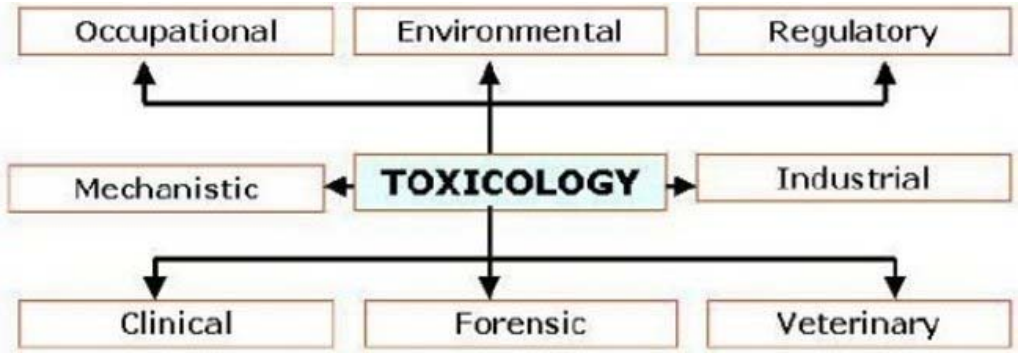

Figure 1. The multidisciplinary branches of toxicology

In a broader sense, toxicology may involve activities such as the study of the detection, occurrence, properties, effects, and regulation of toxic substances. Hence, toxicology, like medicine, is a multi-disciplinary subject covering many sub-disciplines including environmental toxicology (Figure 1). However, overlapping of the different branches of toxicology is common, especially in the fields of occupational, environmental, and regulatory toxicology.

Environmental toxicology is concerned primarily with the movement and impact of toxicants and their metabolites in the environment, in food chains, and upon the structure and function of biological systems. The biological systems include any living systems such as human and other mammals, plants, other organisms, and their habitats. One of the major problems arising from the environmental threat is the loss of biodiversity. Biodiversity, coined from *bio*logical *diversity*, is a term relating to species, genes and habitats. The diversity occurs in species from the plant and animal kingdoms, fungi, bacteria, protozoa, and viruses, as well as the ecological complex such as the rain forest, tundra, and coral reefs. For the purpose of this theme, the emphasis will be on the harmful effects of environmental toxicants on human health, rather than ecological changes in the environment itself. In this respect, another relatively new and related field called environmental health plays a major role in contributing knowledge on the adverse health effects of environmental stressors.

In a meeting of WHO European member states in 1993, a definition for environmental health was proposed:

Environmental health comprises of those aspects of human health, including quality of life, that are determined by physical, biological, social and psychosocial factors in the environment. It also refers to the theory and practice of assessing, correcting and preventing those factors in the environment that can potentially affect adversely the health of present and future generations.

(CIEH, 1995)

Environmental toxicology is a relatively new field and perhaps its rapid expansion and progress is attributed to Rachel Carson (1962), who wrote *Silent Spring*. Carson's emphasis then was to stop the wide and indiscriminate use of pesticides and other chemicals. This had the impact of awakening the public to the dangers of polluting the environment with chemicals. In a nutshell, she delivered her high impact message: For

as long as man has dwelt on this planet, spring has been the season of rebirth, and the singing of birds. Now in some parts of America spring is strangely silent, for many of the birds are dead—incidental victims of our reckless attempt to control our environment by the use of chemicals that poison not only the insects against which they are directed but the birds in the air, the fish in the rivers, the earth which supplies our food, and, inevitably (to what degree is still unknown), man himself.

(Carson, 1962)

This led to the establishment, from 1970 onwards, of many regulatory laws to protect human health and the environment by the US Environmental Protection Agency. The awakening of environmental awareness in industry has led to the development of yet another important field called occupational medicine. This field involves understanding of the diseases which occur as a result of human exposure, and which are occupational or industrial in origin, as well as ways to regulate and prevent the diseases. Indeed, in the last few centuries, toxicologic plagues and disaster have become increasingly common events either accidental or incidental in nature (Table 1).

Year	**Place**	**Toxicologic problems**
79 AD	Pompeii	Volcanic gas especially oxides of nitrogen and sulfur from the eruption of Mount Vesuvius, leading to thousands of deaths.
1700s	England	High incidence of scrotal cancer in chimney sweeps as a result of exposure to polycyclic aromatic hydrocarbons—the first description of occupation-related cancer.
1800s	New Jersey	Outbreak of mercurialism in the hatters working in the felting process of the hatting industry.
1900s	Worldwide	Increased incidence of bladder cancer in dye industry workers as a result of ß-naphthylamine exposure.
1920s–present	Worldwide	Millions at risk of asbestos exposure resulting in marked increase in asbestos-related disease and cancer.
1930	Meuse Valley, Belgium	Smog caused illness and 64 deaths.
1939–1954	Japan	Cadmium contaminated water resulted in Itai-Itai disease.
1948	Donora, Pennsylvania	Smog caused 20 deaths and thousands were ill due to polluted air.
1950	Minamata Bay, Japan	Organic mercury poisoning from the consumption of fish.
1952	London, England	Photochemical smog resulted in 4 000 deaths.
1971	Iraq	Methylmercury contaminated grain resulted in 459 deaths.
1970s	California	1,2 dibromo-3-chloropropane DBCP, a nematocide, resulted in infertility among pesticide workers.
1976	Seveso, Italy	Increased incidence of chloracne after accidental release of

Year	Place	Toxicologic problems
		dioxin into the environment.
1978	Love Canal, New York	Toxic wastes caused great public concern.
1982	Iraq and Iran	Mustard gas used in chemical warfare caused hundreds of casualties.
1984	Bhopal, India	Industrial release of methyl isocyanate vapor resulted in 3 000 deaths and 200 000 injuries.
1986	Chernobyl, Soviet Union	Ionizing radiation from the nuclear power plant resulted in 32 immediate deaths and affected 5 million people.
1990	Bronx, New York	Toxic smoke including carbon monoxide and cyanide resulted in 87 deaths at the Happy Land Social Club.

Table 1. Selected episodes of environmental, occupational, and industrial toxicologic disasters

Many chemicals are encountered by humans, either incidentally because they are in the atmosphere, or by contact during occupational or recreational activities, or by ingestion of food additives. When atmospheric pollution is the source of chemicals, it is obvious that all exposures are incidental, whereas exposure to chemicals used in industry is limited by industrial hygiene and occupational safety and the health regulations and practices of that particular industry. It is conceivable that some chemicals may be inadvertently released into the environment and therefore be hazardous to human health. With the increasing rate of production and the growing use of industrial chemicals, it seems that no occupation is entirely free of exposure to a variety of chemicals capable of producing undesirable effects on biologic tissues.

At the present time, more than 10,000 chemical entities contribute to some 500,000 products that are used in industries to produce many durable and non-durable products. Some toxicity data are available on many of these chemicals and a majority of chemical manufacturers find it necessary to obtain at least a minimal amount of toxicity information on each and every compound they use.

Chemicals added to the feed of animals may be drugs intended for therapeutic purposes, or pesticides and insecticides. Limitations have been placed on the amounts that may be used, and on the time in which such additives must be withdrawn, if the animals are to be used for human food. The use of pesticides and insecticides in agriculture has enabled the farmer to produce more and better products, but present the possibility of residues of these chemicals being present when the food is consumed. The addition of chemical preservatives to processed foods has made possible the existence and prolonged life of certain food preparations. The study of the limitations that must be observed with regards to food additives, and the evaluation of safety from the harmful effects of such chemicals is the concern of environmental toxicologists.

A continuing trend toward urbanization of human populations has accompanied the industrialization of the world. In the United States, more than half the population lives

on less than 5 percent of the total land space. Pollution of water by products of industry and improper sewage disposal, as well as pollution of the atmosphere by industry and by automobiles in the areas of concentrated populations, has created a distinct public health hazard. Although humanity has depended upon the enormous volume of atmosphere to dilute the pollutant concentrations to below effective levels, it is now apparent that atmospheric dilution is not unlimited, but rather is dependent upon weather conditions and the amount and extent of pollution that is created.

The pollution varies from gases to aerosols to dusts, and from carbon monoxide to alkalis and acids. Such pollution of the air and water is not only aesthetically undesirable, but exposes large populations to an unlimited variety of potentially harmful chemicals capable of producing known acute harmful effects and possible chronic debilitating illness in humans.

Environmental toxicology is therefore that branch of toxicology dealing with incidental exposure of biologic tissue, and more specifically human tissue, to chemicals that are basically contaminants to environment, food, or water. It is the study of the causes, conditions, effects, and limits of safety of such exposure to chemicals.

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Biographical Sketches

Tetsuo Satoh, Ph.D., Director, Biomedical Research Institute, Chiba, Japan; Professor Emeritus, Chiba University, Chiba, Japan.

Dr Satoh's major research areas include disposition and metabolism of drugs, pesticides, and environmental pollutants; role of biotransformation in chemical-induced tissue injury; and pharmacogenetics, with a focus on genetic polymorphisms of enzymes that catalyze the hydrolysis of drugs and other xenobiotics. He has published more than 250 scientific papers, invited reviews, and book chapters. His review article entitled "The Mammalian Carboxylesterases: From Molecules to Functions" was published in the Annual Review of Pharmacology and Toxicology in 1998.

Dr Satoh is a member of numerous national and international scientific organizations including the Japanese Society of Toxicology, Pharmacological Society of Japan, Japanese Society of Clinical Pharmacology, Society of Toxicology (USA), American Society of Pharmacology and Experimental Therapeutics (ASPET), American Society of Clinical Pharmacology and Therapeutics (ASPET), and International Society for Study of Xenobiotics (ISSX). He has served on numerous committees of the scientific organizations. He has a number of awards, including the 1st Visiting Professor Award of the American Society of Toxicology in 1996, Education Award of the Pharmaceutical Society of Japan, and the Merit Award of the Japanese Society for Study of Xenobiotics. He was elected as the Founding Secretary-General of the Asian Society of Toxicology(ASIATOX) in 1994, and in 1995 he was appointed

the Vice President of the International Union of Toxicology(IUTOX). He was a member of the Scientific Program Committee for the 8th and 9th International Congresses of Toxicology in 1998 and 2001, respectively. He has served as a member of editorial boards and review committees for a variety of international and national journals including *Toxicological Sciences* (Society of Toxicology, USA) and (as Associate Editor) *Regulatory Pharmacology and Toxicology* (USA).

Salmaan H. Inayat-Hussain was born in Kuala Terengganu, Malaysia and grew up in Dungun, Terengganu, where he attended primary and secondary education. He attained a Bachelor's degree in Pharmacology with honours in 1991 from Universiti Kebangsaan Malaysia. He then worked for Pfizer (Malaysia) Pte Ltd until the end of 1992 prior to joining Universiti Kebangsaan Malaysia. In 1993, he went to the MRC Toxicology Unit, Leicester, UK and obtained his Ph.D. in Biochemical Toxicology in 1997. He is currently a faculty member of the Department of Biomedical Science, Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia. He also spent a year (1999–2000) as a Visiting Research Associate at the Molecular Toxicology and Environmental Health Program, University of Colorado Health Sciences Center in Denver, Colorado, USA, under the supervision of Professor David Ross.

Dr Inayat-Hussain's main research interest is understanding the molecular mechanisms of apoptosis induced by various toxicants including benzene metabolites especially hydroquinone and the anti-psychotic remoxipride. He has also developed an interest in the mechanisms of plant natural products induced apoptosis as potential anti-cancer lead compounds, as well as safety evaluation of commercialized plant extracts. In addition to research, Dr Inayat-Hussain has also been involved in teaching toxicology to the Biomedical Science, Occupational and Environmental Health and Pharmacy undergraduate programs as well as the postgraduate program in Occupational Health. He has been appointed as a consultant to carry out toxicological assessment of chemicals, as required in the Environmental Impact Assessment exercise.

He has been awarded numerous fellowships including ones from the Wellcome Trust, Nippon Trust, and UNESCO, and has been involved in editorial and review work for toxicology journals such as *Chemical Research in Toxicology*. Currently he is an editorial member of *Chemico-Biological Interactions* and an Associate Editor of *Journal of Toxicological Science* (The Japanese Society of Toxicology). Dr Inayat-Hussain is also a full member of the British Toxicology Society and Malaysian Society of Pharmacology and Physiology.