

Review

Genetic Toxicology Research in Developing Countries: Challenges and Possibilities—Egypt as an Example

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Egypt, as many other developing countries, has several environmental exposure problems. There are exposures to chemical genotoxicants and to lifestyle factors that have been linked to increased risk for cancer. Infections can be associated with cancer development when the environmental factors interact with the infection and lead to the enhancement of the carcinogenic process. Currently, there is a growing interest to genetic toxicology research, the use of different biomarkers and genetic susceptibility testing, which can contribute effectively to risk assessment. Developing countries need to cooperate with developed countries to protect human health from disease determined or influenced by factors in the environment. The national and international research policies should highlight the need to mobilize resources for human resource development, networking, improving research culture, information sharing and pragmatic use of research findings. Exchanging of experience and training is the most vital issues in developing new cadres of people with skills in health research, information and communication, who are needed to address the challenges facing the development of genetic toxicology research and prevention programs. Organizing international meetings and training courses may enforce this field of research and help to develop cooperative research projects which deal with different exposure conditions.

Key words: genetic toxicology, developing countries, Egypt, gene environment interaction, capacity building, training, international conferences

Introduction

Environmental health and related genetic toxicology research are major areas of concern in most of the countries all over the world (1). Currently, there is an interest to the use of different biomarkers and genetic susceptibility testing, which can contribute effectively to risk assessment. Biomarkers can be used to detect the effects of environmental pollutants before adverse clinical health occurs.

Egypt, as an example of developing countries, shares most of the environmental problems of developing countries which resulted in the appearance and preva-

lence of non-communicable diseases. There are exposures to chemical genotoxicants (e.g., automobile exhaust, pesticides, metals and cytotoxic drugs) and to lifestyle factors (e.g., consumption of tobacco products) that have been linked to the expression of biological effects and to increased risk for cancer (2–10) (Table 1).

Industrial activities are one of the major sources of air pollution in Egypt. Eighty-three percent of the industries are located in Greater Cairo and Alexandria. Another important source of air pollution is motor vehicles. Forty five percent of the motor vehicles in Egypt are found in Cairo and 13% are in Alexandria. The greater Cairo has the worst air pollution in Egypt. Fumes from Cairo's 1–2 million vehicles, combined with suspended particulate matter (including lead) plus sand blown into urban areas from the neighboring Western Desert, create an almost permanent haze over the city. The level of air pollution in Cairo ranges from 10 to 100 times higher than the standards set by the World Health Organization (WHO) (11).

Total suspended particulate (TSP) collected from residential area surrounding tobacco manufacture factories proved to contain high concentrations of tar at the average $26.5 \mu\text{g}/\text{m}^3$, while, the concentration of tar in the TSP collected from residential area away from the factory was estimated to be $2 \mu\text{g}/\text{m}^3$ (12).

Persistent organic pollutants (POPs), including pesticides, resist degradation and accumulate in the food-chain. They can be transported over long distances in the atmosphere, resulting in widespread distribution across the earth, including regions where they have never been used. Over the past few decades enormous quantities of industrial and agricultural sources have been released into the environment, (water, soil and air) which cause severe problems with human health.

Egypt is a predominantly agricultural country; therefore pesticides have been used extensively. The amount

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Table 1. Examples of environmental pollutants in Egypt and their health effects

Environmental pollutant	Origin of pollutant	Impact on human health
Chemical genotoxicants		
Automobile exhaust	Higher exposures may occur in some occupations such as traffic policemen.	It has been shown to increase chromosomal damage (2).
Industrial chemicals	Enormous quantities of industrial sources have been released into the environment. 83% of the industries are located in Greater Cairo and Alexandria.	They cause severe environmental problems which affect the human health (3–10).
Persistent organic pollutants (POPs), including pesticides.	The use of pesticides in agriculture is the main source of exposure of the general public (16). Pollutants resist degradation and accumulate in the food-chain. They can be transported over long distances in the atmosphere. Pesticide use is doubled every ten years between 1952 and 1986, and up to 60,000 tons used annually in agriculture or for public health.	Agricultural workers exposed to pesticides showed increased incidence of chromosomal aberrations and sister chromatid exchanges (6). Significant increase in chromosome aberrations among pesticide applicators was reported (16). Exposures to organophosphorus and carbamate pesticides are additive risk factors to current hepatitis C virus (HCV) and hepatitis B virus (HBV) infection among rural males (41).
Lifestyle factors		
Tobacco products	It is more common in urban cities than rural villages.	Lung cancer is mostly related to air pollution and smoking. Heavy smoking is reported among 50% of HCC cases. It is considered a co-factor with HBV and HCV for hepatocarcinogenesis.
Biological effects		
Schistosoma heamatobium infection	Schistosoma heamatobium infection is one of the most common health problems in Egypt.	Development of urinary bladder carcinoma (21–23).
Chronic infection by HBV and HCV	Egypt suffers from high prevalence of hepatitis infections which are considered as the predominant risk factors for the development of liver cancer.	A substantial number of Egyptians are suffering from primary hepatocellular carcinoma (PHC) which is mainly preceded by chronic infection by HBV, HCV and long-term exposure to foodstuffs contaminated with aflatoxin.
Food toxins		
Aflatoxin (AFB1)	Due to lack of awareness of the dangers of improper grain storage. Approximately 36% of Egyptian lactating mothers (Breast milk samples) were positive for AFM1 (38).	Induction of hepatocellular carcinoma (28). The role of aflatoxins in carcinogenesis is complicated by HBV infection (5,7,29).

of pesticide use is doubled every ten years between 1952 and 1986, and up to 60,000 tons used annually in agriculture or for public health. About 70% of pesticides are applied in cotton fields, where over 120,000 people work as sprayers every summer (May, July and September). There are many problems facing the Egyptian society when dealing with pesticides. They can be handled by inadequately informed or un-trained personnel, especially operators in small-scale enterprises. Effective mechanisms are lacking for coordination between those responsible for different aspects of pesticides safety. There is also a shortage of management skills needed to deal with the storage, transport, use or disposal of pesticides.

Pesticides include a wide range of compounds; differ greatly in their mode of action, metabolism and elimination from the body, and toxicity to humans. However, all of them are considered to be toxic chemicals that are frequently released into the environment. Therefore, it is necessary to be more serious in monitoring of pesticides for the safety of populations (10,13). The majority

of the pesticide toxicity studies have dealt with exposure of farmers to mixed pesticides, including OP/POP (organophosphates/parathion-type organophosphates) pesticides. The use of OP/POP pesticides has increased dramatically in the past 20 years, allowing them to replace organochlorines as one of the most commonly used agricultural insecticides around the world. With increased use of OP/POP around the world, especially in developing countries such as Egypt, it is important to understand the environmental and occupational health risk from the use of these pesticides (14). It is crucial to design effective prevention programs on environmental and occupational concerns.

The improper use of pesticides may endanger human health not only by the active ingredients and the associated impurities, but also by the solvents, carriers, emulsifiers and other constituents of the formulated products (15). Potential exposure from the environment can be estimated by environmental monitoring. Actual exposure (uptake) is measured by biological monitoring of human tissues and body fluids. Biomarkers are used to

detect the effects of pesticides before adverse clinical health occur (13). Agricultural workers exposed to pesticides showed increased incidence of chromosomal aberrations and sister chromatid exchanges (6).

In 1994, Amr *et al.* (16) reported that pesticides in agriculture were a main source of exposure of the general public to carcinogens in Egypt due to persistent pesticides residues. Analyses of blood cells from workers who formulated pesticides showed that neutrophils were abnormal based on peroxidase and alkaline phosphatase staining. In addition, the blood cells had increased chromosomal aberrations. However, the increases were irrespective of the duration of exposure, age and smoking habits. Chromosome aberrations among pesticide applicators significantly increased. These abnormalities were more frequently found among the younger workers.

Infections can be associated with cancer development when the environmental factors interact with the infection and lead to the enhancement of the carcinogenic process. Biological carcinogenic agents in the form of parasitic, viral, bacterial, and fungal agents can be associated with cancer development. The most common preventable biological carcinogenic agent in Egypt is schistosomiasis, followed by viral hepatitis and other oncogenic viruses (17–20).

Schistosoma heamatobium infection is one of the most common health problems in Egypt. It is strongly associated with the development of urinary bladder carcinoma (21–23).

Lung cancer, which is mostly related to air pollution and smoking, is more common in urban cities than rural villages. Higher exposures to engine exhausts may occur in some occupations such as traffic policemen. It has been shown to increase chromosomal damage which enhanced further by smoking (2).

Around the world, there is an emphasis on understanding genetic susceptibility to development of environmentally related cancers. An initial focus was on the inheritance of variant chemical metabolizing genes on the development of cancers (24–26). Egypt needs to develop international collaborative projects in these priority areas to address our environmental health concern.

Genetic Toxicology of Chemicals

Mutagenicity and carcinogenicity are highly regarded as important toxic effects of chemicals. The possible teratogenicity, immunotoxicity, or embryo-toxicity of a chemical should be considered when assessing overall hazard.

Human surveillance studies: A wide variety of techniques for monitoring genetic damage induced in humans by environmental chemicals or environment factors are now available. Rapid advances in improving the sensitivity of such techniques are being made, em-

phasis was placed on the proper use of these techniques, and the following points emerged:

- Populations selected for study should be influenced by a clear perception of the relative hazards in the given country or environment.
- Specific attention should be given to the experimental design of studies, in particular, the selection of appropriate and concurrent control groups, the choice of adequate group sizes, the elimination of confounding variables, the use of coded samples for analysis, and the selection of vigorous statistical methods for the evaluation of data.
- Attempts should be made, wherever possible, to include an intervention aspect to the study (e.g., the study of individuals before they enter the polluted environment, the follow-up of those who left it, and monitoring the effect of selective removal of a suspect genotoxin from the environment under study).
- The use of cytogenetic analysis in studies on human blood is strongly recommended. This will enable a common point of comparison between studies using other end points (e.g., hemoglobin adducts, *hprt* mutations, sister chromatid exchange) and between studies performed in different countries and in time.
- The current progress in human surveillance techniques suggests that refined methodologies will soon be available, and it will be important to reassess earlier studies using these new techniques. It is suggested that blood samples should be stored from all studies for further analysis.
- The possible role of lifestyle variables such as diet, food contaminants and infection in modulating genetic outcome from exposure to mutagens is of particular importance in developing countries.

Gene-environment interactions: A major barrier in promoting environmental health practices is the genetically heterogeneous individuals in human population who respond to environmental insult in significantly different manners. Advancement in the human genome program has provided valuable tools to evaluate genetic variations in human responses to environmental insult and thus to better explain health consequences.

In summary, when a major genetic hazard is recognized, it is important to monitor and quantify that hazard. Great care should be taken to optimize the derived data by adequately designing the studies. At present, human surveillance studies tend to be conducted on limited budgets and at the discretion of individual investigators.

Long-term follow-up of human studies: Attempts should be made to initiate appropriate long-term follow-up studies—specifically, to correlate the outcome of surveillance studies with eventual onset of disease.

Alternatively, in some cases where a population is identified as being exposed to a possible mutagen/car-

cinogen, blood samples could be stored for possible future use in the case of a subsequent epidemiological study which may reveal an increased cancer incidence in that population. In the absence of such follow-up studies, the present human surveillance will have limited values in that it simply provides samples for studies on long-term health effects. Ethical issues should be raised by the conduct of human surveillance studies. It is important to recognize and control human exposure to a potential human carcinogen/mutagen, actions should flow from the observation of a positive effect.

Hepatocellular carcinoma as an example of cancer related to exposure to biological and chemical agents: In recent years, the incidence of cancer in Egypt has increased. A substantial number of Egyptians are suffering from primary hepatocellular carcinoma (HCC) which is mainly preceded by hepatitis B virus (HBV) infection and or hepatitis C virus (HCV) infection. The carcinogenesis can be complicated by aflatoxin B1 (5,7,27), which has been classified by the International Agency of Research on Cancer (IARC) as a group I carcinogen. It has been suspected as a causal agent in the induction of HCC (27).

According to recent reports, the incidence of HCC has increased sharply in the last 5–10 years (29–31), with an especially high incidence in Egypt (32). The predominant risk factors for the development of liver cancer include chronic infection by HBV, HCV and long-term exposure to foodstuffs contaminated with aflatoxins. It has been well documented that Egypt has one of the highest prevalence rates of HCV infection in the world.

In Egypt, while HBV and HCV may account for the majority of HCC, there is suggestive evidence for an additional etiologic role of aflatoxin in hepatocarcinogenesis. Methods of grain storage are not controlled, and there is lack of awareness of the dangers of improper storage. A study was conducted in 2 districts in Upper Egypt to measure the presence of fungal population in silage. Aflatoxins showed the highest incidence rates of occurrence in 22.5% of all samples analyzed. Other mycotoxins were detected in all samples (33). A significant higher concentration of aflatoxins was detected in the serum of Egyptian patients with HCC compared to their controls; with two fold increased risk.

Aflatoxin B1 (AFB1): Many agricultural products are vulnerable to attack by a group of fungi that produce toxic metabolites called mycotoxins, which includes aflatoxins. Aflatoxins are toxic and carcinogenic metabolites of moulds, mainly *Aspergillus flavus* and parasiticum that contaminate a variety of agricultural commodities, particularly peanuts, maize and cottonseed, in countries with hot and humid climates.

Hifnawy *et al.* (2004) (34) suggested that the progressive nature of HCV-related liver diseases was influenced

by aflatoxin exposure.

Several studies were carried out to evaluate the level of aflatoxins in food products in different governorates in Egypt. From Qalubia and Kafr El-Sheikh Governorates, one hundred samples of imported and local wheat grains were collected (*Triticum sativum*) and examined for the natural occurrence of aflatoxins during 2000–2001. Results indicated that both local and imported samples were positive for AFB1 (17.5% and 20% respectively), and the concentration ranged from 3–25 µg/kg. The level of aflatoxins was dependent on the area of collection as well as the season of the year.

In a study to screen for biomarkers of aflatoxin exposure in Egypt, Polychronaki *et al.* (2006) (35) assessed the level and frequency of breast milk aflatoxin M1 (AFM1) as a biomarker of maternal exposure. Breast milk samples were collected from a selected group of 388 Egyptian lactating mothers of children attending the New El-Qalyub Hospital, Qalyubiyah governorate, Egypt, during May–September 2003. Approximately 36% of mothers tested were positive for AFM1. Various factors contribute to the occurrence of aflatoxin in breast milk. The factors may include non-working status, obesity, high corn oil consumption, number of children and early lactation stage (<1 month).

The same research group continued their study (36); fifty women who were AFM1 positive at baseline were followed up. They were revisited monthly for 12 months to assess the temporal variation in breast milk AFM1. In a multilevel regression model of the data; there was a highly significant ($p < 0.001$) effect of month of sampling on the frequency of AFM1 detection with summer months having the highest frequency (>80%) and winter months the lowest frequency (<20%) of detection. The duration of lactation and peanut consumption also contributed to the model. The identification and understanding of factors determining the presence of toxicants in human milk are important and may provide a knowledge driven basis for controlling the transfer of chemicals to infants.

In 2006, Hassan, *et al.* (37) assessed the presence of AFM1 in both mothers' milk and the infants' sera. Fifty healthy breast lactating mothers and their infants who were exclusively breast fed for at least 4 months were included. Twenty-four mothers (48%) and their infants had detectable levels of aflatoxin with the following mean contamination levels (ng/mL); mothers' serum of 8.9 ± 4.2 , mothers' milk of 1.9 ± 0.6 and infants' serum of 1.8 ± 0.9 .

Occupational exposure to pesticides may contribute to the etiology or progression of HCC. According to Ezzat *et al.* (38), a major segment of the Egyptian population is employed in agriculture and use pesticides routinely to control insects, weeds, rodents, and fungal infections of crops and livestock. This study therefore

suggested that exposures to organophosphorus and carbamate pesticides are additive risk factors to current HCV and HBV infection among rural males.

In 1999, Sylla *et al.* (39) expressed the importance of interactions between HBV infection and exposure to aflatoxins in the development of HCC. There is evidence from both epidemiological studies and animal models that the 2 factors can act synergistically to increase the risk of HCC (39). Alcohol may act as a co-carcinogen, and it has strong synergistic effects with other risk factors, including HBV, HCV, aflatoxins, vinyl chloride, obesity, and diabetes mellitus. Alcohol enhances the effects of environmental carcinogens directly; it also enhances them indirectly by contributing to nutritional deficiency and impairing immunological tumor surveillance. Acetaldehyde, the main metabolite of alcohol, causes hepatocellular injury and is an important factor in causing increased oxidant stress, which damages DNA (40). Heavy smoking is reported among 50% of HCC cases. Cigarette smoking is a major source to 4-aminobiphenyl—a hepatic carcinogen—which causes DNA damage and enhances cell proliferation. In addition, it induces P450 system which activates carcinogens and it is considered a co-factor with HBV and HCV for hepato-carcinogenesis.

Need for Training Programs

There is a critical demand of qualified scientists in these fields, and it is important to develop Training Programs. These programs can be implemented in collaboration with different collaborating centers, which will form a good partnership to provide short-term and long-term training opportunities. The training programs include laboratory work in molecular biology/genomics, cell biology, and proteins and bioinformatics. They are designed for the continuing education of research physicians and technicians in academic and industrial laboratories who want to enhance their knowledge and skills in the latest biotechnology areas. These programs could actively coordinate, strengthen, and encourage collaboration between the various disciplines. They give a chance for a wider understanding of biotechnology through the introduction of a seminar series, and postgraduate training opportunities. Developing country researchers who conduct health research in their countries need to learn current ethics rules and regulations. Training programs will bolster resources to provide the important bioethical perspective as well as increasing the awareness of investigators and institutions of the social, ethical, and legal aspects of modern genetics research, medical practice and in business management programs.

Need for International Coordination

The collaboration between universities and different

research institutions, at the national and international level, is necessary and consistent with fulfilling the priority for inter-sectorial cooperation for achieving significant improvement in environmental health and disease prevention.

The scientific community plays a crucial role in understanding the environmental causes of human health problems, and in collaborating with communities, industries and government agencies in resolving health problems.

Examples of Efforts to Enhance International Cooperation

International Conferences on Environmental Mutagens (ICEM): The field of environmental mutagenesis has been gaining international recognition for many years. The well-recognized pioneers who had promoted this field, particularly at the international level, are the late Dr. Alexander Hollaender and the late Dr. Frederick Sobel. Through their independent efforts, they have organized workshops and conferences in countries where Environmental Mutagen Society had not been established. From these activities, many scientists in these countries have received education and training to initiate their careers and scientific societies that are committed to the field of environmental mutagenesis. With dedicated effort from many scientists, the initiatives from the late Hollaender and the late Sobel continued to flourish and became sustainable programs. Many of these programs are promoted by the EMS-Hollaender Fund for International Programs and the International Association for Environmental Mutagen Societies (IAEMS). One sustainable program is the series of conferences known as the International Conference on Environmental Mutagens in Human Populations (ICEMHP).

During 1987 and 1988, Dr. Wagida Anwar from Egypt was a visiting scientist in the University of Texas Medical Branch, Galveston, Texas, USA to conduct research studies in collaboration with Dr. William Au. They also considered opportunities in organizing outreach activities such as conferences. There was a lack of such conferences that are held in developing countries. They also recognized that many scientists from developing countries would not have the opportunity to travel to other countries to attend international conferences. Therefore, they decided to organize a series of conferences that would be held in countries where the field of environmental mutagenesis is in the developmental stages and where environmental health is of major concern locally and regionally. The overall objectives are to enhance the awareness of and to identify solutions to human environmental health problems, to facilitate interactions and to foster international collaborations.

Dr. Au and Dr. Anwar planned to have the first con-

ference in Cairo, Egypt. With the help of Dr. Sobel, the conference received support from many sponsors, notably from the EMS-Hollaender Fund for International Programs and the IAEMS. In collaborating with several scientific societies and government agencies *the 1st ICEMHP was held in Cairo, Egypt, January 19–24, 1992* (41,42). The meeting sparked the interest in addressing environmental health concerns among scientists in the African Continent and stimulated the organization of the Pan African Environmental Mutagen Society (PAEMS). Subsequent meetings were organized in Czech Republic (1995), Thailand (1998), Brazil (2003), and Turkey (2007) and next one will be organized in Qatar in 2012. All previous conferences were tremendously successful and they generated numerous new collaborations and sustainable programs.

ICEMHP: *The 1st ICEMHP was held in Cairo, Egypt, 1992.* The objective of the conference was focused on the state of knowledge on environmental, biological, genetic and reproductive problems affecting humans from exposure to environmental mutagens. The conference attracted over 200 participants from 31 countries. More than half of the participants were from the Middle East and Africa. The conference monograph was published in *Environmental Health Perspectives* (41). These accomplishments certainly justify the value of hosting the meeting in countries where the field of environmental mutagenesis is in the developmental stages.

The conference sparked the activities of the PAEMS. Since then, the society has organized several scientific conferences throughout Africa approximately every two years: Cairo, Egypt, 1993; Cape Town, South Africa, 1996; Harare, Zimbabwe, 1999; Cairo, Egypt, 2003, Fes, Morocco, 2005 and South Africa, 2008. Many international collaborative projects were initiated based on interactions in the 1st ICEMHP. The success of the 1st ICEMHP and the PAEMS conferences has attracted the attention and long-term support from several external sources, particularly from the National Institute of Environmental Health Sciences (NIEHS), USA.

The 2nd ICEMHP was held in Prague, Czech Republic, 1995. A total of 220 scientists from 30 countries attended this conference. The high scientific level of all presentations and the enthusiasm among the participants provided strong endorsement for continued organization of the conferences in the 4-year period. Another positive characteristic was that the monograph from the conference was published in *Environmental Health Perspectives* within 9 months (43).

The conference definitely highlighted the serious and potentially overlooked environmental pollution and health problems in the former Soviet countries. More importantly, the conference gathered a critical mass of scientists and provided the opportunity to develop collaborations to address the problems. In addition, the

collaboration developed during the meeting was timely for these scientists to respond to the new research funding mechanism from the European Union. The emphasis was to award grants for collaborations between member and non-member States.

The 3rd ICEMHP was held in Bangkok/Khao Yai, Thailand, 1998. The meeting convened in Bangkok for two days and in Khao Yai, which created tremendous opportunity for the participants to interact with each other for three days. By organizing the meeting in Thailand, scientists from many countries in the surrounding region were able to attend an international conference. Notably are scientists from countries like Laos, Sri Lanka and Vietnam that had no scientific programs in the field of environmental mutagenesis.

The theme was “Understanding gene and environmental interactions for disease prevention”. The theme was addressed in the following 9 important topics: 1) Mechanisms of mutagenesis and carcinogenesis, 2) Methods to detect exposure and Effects of genotoxic agents, 3) Metabolic influences on cancer susceptibility, 4) Genetic susceptibility influencing disease outcome, 5) Prospects for cancer prevention, 6) Influences of environmental mutagens in different countries, 7) Germinal and reproductive effects of environmental mutagens, 8) forum on Issues in safety and health assessment and 9) forum on Developing sustainable studies on environmental health. Manuscripts from presentations in the conference were published in *Mutation Research* (25).

With the organization of three highly successful international conferences, IAEMS has officially adopted the series into its portfolio of activities. With this recognition, the series of conferences received support from the EMS-Hollaender Fund for International Programs, the NIEHS, the Environmental Protection Agency (EPA) and the IAEMS.

The 4th ICEMHP was held in Brazil in 2003. The conference followed the similar structure and pattern already seen in the previous conferences in the sense; it was also designed to identify solutions for human environmental health problems and to facilitate the establishment of sustainable collaborative programs in the region and around the world. The conference focused on environmental exposure, genetic effect, health impact of environmental pollutants and individual susceptibility. It also focused on themes such as the identification of genes involved with environmental diseases, use of genomics in understanding toxicological responses and the functional evaluation of polymorphic genes for susceptibility. Specific symposium topics were: 1) Mechanisms of mutagenesis and carcinogenesis, 2) Biomarkers for mutagen exposure and for prediction of health risk, 3) Health impact of environmental pollutants, 4) Genetic and acquired susceptibility to environmental disease, 5) Genome-based technology for

toxicology and health, 6) Health impact of food-borne mutagens and antimutagens and 7) Unique concerns for environmental health in Latin America.

The 5th ICEMHP was held in Turkey in 2007. Dr. Semra Sardas, Dr. Ali Karakaya and Dr. William Au were co-chairpersons in the conference. The theme of the conference was "Identification of environmental hazards and promotion of health". The conference was held in the beautiful and historical Mediterranean city, Antalya, Turkey, May 20–23, 2007. Different symposia discussed the different topics included 1) Mechanisms of mutagenesis and carcinogenesis, 2) Children environmental health, 3) Human monitoring for health risk evaluation and disease prevention, 4) Gene-environmental interactions on health; new technologies and frontiers in environmental health, 5) Unique environmental health concerns and environmental disasters, 6) Trans-placental and trans-generational exposures and health consequences, 7) Translation of scientific knowledge into public health practices and 8) Building environmental health infrastructure through science, education and outreach effort.

The next 6th ICEMHP will be organized in Qatar Doha in March 2012 as a continuation of these series of conferences.

The Pan African Environmental Mutagen Society (PAEMS): Realizing the importance of research on the relation between environmental pollutant exposures and their genetic effect, PAEMS has been established in 1983 to encourage research on environmental mutagenesis. Its headquarters was located in Nairobi, Kenya. However, during the 1st ICEMHP, which was organized in Cairo in 1992, a PAEMS meeting took place to reactivate the society. The meeting recommended the transfer of headquarter of the society from Nairobi, Kenya to Cairo, Egypt.

The main goals of the PAEMS are to spread new information and technologies concerning environmental mutagens and carcinogens and to stimulate cooperation and to present training programs between countries in Africa and countries abroad.

The main objectives of the PAEMS are:

1. To help African scientists to recognize and control their own problems.
2. To encourage the study of mutagens, carcinogens and substances of related biological activity in the human environment, particularly those of public health importance in Africa.
3. To facilitate the spread of information and technology concerning environmental mutagens and carcinogens.
4. To promote cooperation and training between different African countries with leading laboratories and international agencies around the world. The PAEMS plans to organize regular scientific meetings

in different African countries to discuss health problems of special importance to the African countries. This will help to disseminate the information to African countries.

The first activity of PAEMS was a two-day meeting on "mycotoxins as mutagens and carcinogens: possibilities for disease prevention" from 23–25 January, 1993. The meeting discussed the possible exposure conditions, monitoring methods, hazards of mycotoxins as mutagens and carcinogens, interactions between mycotoxins and viral infections, and different intervention strategies. It was held in Cairo, Egypt in collaboration with IARC, WHO, Lyon, France (7).

The 2nd PAEMS Conference was held in Cape Town, South Africa 23–25 January 1996. It had the following theme "Risk Assessment of Environmental Mutagens and Carcinogens". Dr. WFO N. Marasas and his colleagues at the Medical Research Council in South Africa organized the conference under the auspices of the South Medical Research Council (MRC).

The 3rd Conference of the PAEMS was held in Harare, Zimbabwe 1–5 March 1999. The theme of the meeting was "Susceptibility to environmental mutagens: molecular, epidemiological and public health aspects". The meeting was held at the University of Zimbabwe and was organized by PAEMS President-Elect, Dr. Julia Hasler and Dr. Y. S Naik.

The 4th Conference of the PAEMS was held in Cairo, Egypt, 2–7 March 2003 at Ain Shams University. The theme of the meeting was "Child health and environmental mutagenesis". Since the PAEMS is encouraging young scientists to be attracted to this important field, the PAEMS officers decided to announce the creation of PAEMS Award for young scientists for excellence in environmental mutagenesis research.

The objective of the conferences was focused on child health and environmental mutagens as an African agenda for preventive research. Children, who are uniquely vulnerable to toxicants because of their delicate developmental metabolic processes and inherent disproportionately heavy exposure, are more endangered from a polluted environment than adults. Also diseases that are triggered by mutagens require decades to develop and accordingly future generations are in real danger.

The attendance of scientists from different parts of Africa was a reflection to the importance of protecting children against environmental toxicant, which recently became a major challenge to modern societies. At the conference 150 scientists from different continents in the world were gathered. African scientists were mainly from Egypt, South Africa, Sudan, Zimbabwe, Kenya, Mauritius, Morocco, Cameroon, Burkina Faso, Nigeria, Tanzania and Gambia. Scientists from outside Africa were from United Kingdom, Denmark, Greece,

Poland, Bulgaria, Japan, Siberia, Portugal, Spain, Armenia, Lithuania, Yugoslavia, South Korea, France, Italy, Russia, USA, Germany, Brazil, Australia, Sweden and Kazakhstan. Non African scientists attended to share their ideas and exchange their knowledge in the field of genetic toxicology.

Training and Practical Demonstration courses were also organized to provide the latest practical information for upgrading technical skills of molecular biology scientists in Egypt and African countries in the field of PCR, site directed mutagenesis, recombinant plasmid DNA and bioinformatics. Practical workshops were distributed over several laboratories within Ain Shams

University in order to be able to allow the largest number of participants to benefit from the courses.

The 5th conference of PAEMS was held in Fès, Morocco, 24–26 November 2005. The coordinator was Pr. Fatima-Zahra SQUALI. The meeting offered a forum to exchange information, ideas and knowledge on the environmental issues, and to develop new ideas and initiate regional and international collaborative programs in the field of environmental mutagenesis. The scientific program featured internationally recognized experts who participated in plenary lectures, symposia, workshops, continuing education sessions and debates. Alexander Hollander training courses and study groups.

Table 2. Challenges and possible actions

Challenges/difficulties	Possible actions/solutions
1-Insufficient resources in genetic toxicology research.	The scientific community can play a crucial role in understanding the environmental causes of human health problems, and in collaborating with communities, industries and government agencies in resolving health problems. Adequate expertise and resources should be available to investigate and respond to such problems.
2-Availability of good biomarkers	Encouragement of the use of different biomarkers and genetic susceptibility testing, which can contribute effectively in risk assessment.
3-Insufficient Training Programs.	<ul style="list-style-type: none"> -Exchanging of experience and training are the most vital issues in developing new cadres of people with skills in health research, information and communication, who are needed to address the challenges facing the development of genetic toxicology research and prevention programs. -Training programs can be implemented in collaboration with different collaborating centers, which will form a good partnership to provide short-term and long-term training opportunities. -The training programs include laboratory work in molecular biology/genomics, cell biology, and proteins and bioinformatics. They are designed for the continuing education of research physicians and technicians in academic and industrial laboratories.
4-Lack of implementation of national regulations:	The responsibility of the regulatory authorities is to monitor the safety of imported or domestic chemicals such as pesticides and herbicides. Ensuring that laws, regulations, and practices protect the public and the environment from hazardous agents; Further, there is an evident role for international coordination of information on the major chemicals of commerce, including agrochemicals, pesticides, and herbicides. Decisions to use a particular chemical will vary depending on local needs, but the toxicological profile of such chemicals should be internationally available as a primary input to such decisions.
5-Insufficient information about current ethics rules and regulations.	Training programs will provide the important bioethical perspective as well as increasing the awareness of investigators and institutions of the social, ethical, and legal aspects of modern genetics research.
6-Need for International Cooperation	-Developing countries need to cooperate with developed countries, to protect human health from disease determined or influenced by factors in the environment. Organizing international meetings may enforce this field of research and help to develop cooperative research projects which deal with different exposure conditions.
7-Actions for environmental protection.	-Preventing environmental health problems requires collaboration between universities and different research institutions in various disciplines at the national and international level. There is a need for a standards and internationally available toxicological profile through seminars and training opportunities.
8-Need for national and international coordination of human surveillance studies	<ul style="list-style-type: none"> -Monitoring the population and its environment to detect hazards and to provide early warning signals for health problems. -Development of methods to measure environmental hazards in people will permit more careful assessments of exposures and health effects. -Coordinating the efforts of all government and non-governmental groups responsible for environmental health.
9-Lack of understandable and useful information on hazards and health effects.	Monitoring the population and its environment to assess the effectiveness of prevention programs; The national and international research policies should highlight the need to mobilize resources for human resource development, networking, improving research culture, information sharing and use of research findings.
10-Lack of financial resources	Providing adequate resources to accomplish these tasks.

The focus areas were: 1) Environment and nutritional status, 2) Environment and childhood cancer, 3) Environment and congenital malformation, 4) Smoking and drug addiction in children, 5) Pharmaceuticals and childhood cancer, 6) National preventive program.

The 6th Conference of PAEMS was held in Cape Town, South Africa 3–5 November 2008. Prof. Hester Vismer was the Chairperson of the Organizing Committee. More than one hundred delegates from 21 countries attended. Ten countries from Africa were represented, including Egypt, Tunisia, Cameroon, Nigeria, Morocco, Zimbabwe, Lesotho, Botswana, South Africa and Mauritius. The other countries that were represented were Croatia, Slovakia, Poland, Russia, Switzerland, India, France, Germany, Italy, United Kingdom and USA.

Eminent scientists from all over the world were invited as plenary and invited speakers, including Prof. W Anwar (Egypt); Prof. T Bahorun (Mauritius); Dr. D DeMarini (US EPA and President of IAEMS); Prof. W Gelderblom (South Africa); Prof. MGulumian (South Africa); Prof. M Kew (South Africa); Prof. Vr Mersch-Sundermann (Germany); Prof. I Parker (South Africa) and Prof. C Wild (Director-elect of the IARC). These and other speakers set the scene for the topics that were discussed during nine sessions of the conference, i.e., air-, water-, food-borne and occupational mutagens and carcinogens, antimutagenesis, chemoprevention, cancer, DNA repair, genomics, genotoxic risk factors, micro-organisms as mutagens and carcinogens, molecular mechanisms of mutagenesis and carcinogenesis, radiation as a mutagen and carcinogen, risk assessment and intervention strategies. Sessions were generally well attended.

The 7th Conference is planned to be in Cairo during 2012. The theme will be about nutrition, diet and cancer.

Future Prospects

Prevention of environmental health problems requires: (1) Having adequate expertise and resources to investigate and respond to such diseases and injuries; (2) Monitoring the population and its environment to detect hazards and to provide early warning signals for health problems; (3) Monitoring the population and its environment to assess the effectiveness of prevention programs; (4) Educating the public and select populations on the relationship between health and the environment; (5) Ensuring that laws, regulations, and practices protect the public and the environment from hazardous agents; (6) Providing public access to understandable and useful information on hazards and their sources, distribution, and health effects; (7) Coordinating the efforts of all government agencies and non-governmental groups that are responsible for environ-

mental health; (8) Providing adequate resources to accomplish these tasks; and (9) Development of additional methods to measure environmental hazards in people will permit more careful assessments of exposures and health effects (Table 2).

Conclusion

Despite the great efforts made to improve the situation, currently several actions are still required for environmental protection. There is a need for a standard and internationally available toxicological profile on all major man-made environmental chemicals. There is an equal need for both national and international coordination of human surveillance studies in cases where people are exposed to a known carcinogen or mutagen at levels considered likely to induce significant genetic effects. Finally, at the national level, it is necessary to consider the relative importance to human health of discrete chemical mutagen and carcinogens.

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