Environmental Health Perspectives
Vol. 34, pp. 159-163, 1980

Aquatic Toxicology: Fact or Fiction?

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A brief history of the development of the field of aquatic toxicology is provided. In order to provide a perspective on the state-of-the-art in aquatic toxicology relative to classical toxicology, the two fields are compared from the standpoint of the type of scientist practicing each field, the respective objectives of each, the forces which drive the activity in each field, and the major advantages and disadvantages accruing to the practitioner of aquatic toxicology as a result of the differences in objectives and driving forces.

Introduction

In retrospect, it seems socially imprudent to raise the question posed in the title of this presentation in light of the dedicated efforts of the many talented and competent scientists which have been put forth to advance the field of aquatic toxicology during the last 10-15 years. Perhaps, many of my colleagues would take less offense if I had chosen "Aquatic Toxicology: Art or Science?" as a title. I suspect, however, that either title represents an appropriate expression of the real issue that I'd like to discuss, namely what we are doing under the guise of "aquatic toxicology," and how that activity compares to what is generally understood by the term "toxicology."

In order to put the field of aquatic toxicology into its proper perspective it is enlightening to consider its history. Therefore, I'd like to take you on a quick historical tour of the period 1930-1979, highlighting what was done, why it was done, and what it accomplished. Then I'd like to make some general comments regarding where I think we are now relative to classical toxicology, and where we can interface now with toxicologists concerned with human health considerations. Finally, I'd like to suggest some critical areas for future growth in aquatic toxicology. I will be happy to give you my own answer to the question of fact or fiction, art or science, but my objective here today is to provide you with sufficient perspective and understanding of aquatic toxicology to form your own judgments regarding this question.

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History

As early as the 1930's, acute toxicity tests were being conducted to establish cause/effect relationships between the presence of chemical contaminants in water and an observed effect on fish populations. During these early days such tests were usually conducted after the fact to confirm a suspicion regarding a causative agent. This type of toxicity testing occurred sporadically throughout the 40's.

Because of convenience, many early studies were conducted with the use of goldfish, until we discovered they were often significantly more resistant to chemical toxicity than many other fishes of social importance (e.g., trout). Subsequent to that discovery, we developed an acute case of the "goldfish allergy syndrome" and for therapeutic reasons began testing everything else that would fit in a jar. This response led to the development of a plethora of acute toxicity data on a wide variety of aquatic organisms which clearly demonstrated that differences in species susceptibility to acute exposure to chemicals were often very great.

In 1948, there occurred the first of a myriad of federal legislative actions which would key the rate and direction of growth in the field for the next 30 years. This first legislative act was the passage of the Federal Water Pollution Control Act of 1948, legislation with all kinds of good intentions but very little teeth. Thus, although it did stimulate some quantitative increase in amount of activity in the science, it had little impact on the type of activity. Except for stimulating the development of an awareness that there was a quantitative difference between acutely toxic thresholds and chronically toxic thresholds, we continued to suffer during the 1950's from "96-hour complacency."

It was not until the mid-1960's that two significant events occurred which produced the first quantum growth in the field of aquatic toxicology. The first event was the passage of the Water Quality Act with its attendant emphasis on water quality criteria designed to protect all species of aquatic organisms from continuous chronic exposure to chemical pollutants. Unfortunately, the response to concerns over chronic exposure was manifested in the use of arbitrary safety or application factors. The problems associated with selecting an appropriate safety factor resulted in a recognition that long-term toxicity studies were required to estimate quantitatively the chronic effects of chemicals on fish. The second significant event was the development of procedures allowing indigenous fish species (as opposed to aquarium species) to be cultured in laboratory test systems so that the effects of exposure to pollutants on growth and reproduction could be evaluated, at least empirically.

This latter development led to an intense period (1965-1975) of designing and constructing a variety of sophisticated laboratory life support systems, for deriving and conducting a myriad of empirical investigations of the subacute and chronic effects of pollutants on a wide variety of aquatic forms. Such studies classically involved empirically observing the effects of exposure to some concentration of a pollutant on survival, growth, number of eggs produced, hatchability of eggs, larval growth and development, and survival of F_1 generations. The major advantage of these activities was that they replaced the need for arbitrary safety factors by providing empirical data concerning the relationship between acutely toxic thresholds and chronically toxic thresholds. However, resources for these tests were limited, time and costs were extensive, and it was recognized very early that some short-cut methods to understanding or predicting the relationship between the acute and chronic toxicity of a chemical to aquatic organisms was essential.

The next quantum step in the growth of aquatic toxicology occurred during the 1970's when investigators in the field of aquatic toxicology turned their concerns and emphasis from whole organism responses to the effect of chemicals at the cellular or organ systems levels, and the effects of the biological systems on the chemical. This has led to a proliferation of efforts and information relating to classical clinical toxicological approaches utilizing hematology, histology (oncology), histochemistry, metabolism, pharmacokinetics, and physiological or biochemical effects as measures of toxicity. Simultaneous to that activity was the development of an interest in very sophisticated behavioral studies, often conducted in specialized test apparati which have been automated through the use of television and minicomputer technology. The major shortcoming of the past (and current) uses of such data is that the producers (i.e., scientists) and the users (i.e., regulatory agencies) of the data have made little, if any, effort to make the classical toxicological distinction between "physiological response" and "pathological effect." Furthermore, we have only begun to address an even finer, but necessary, toxicological distinction, namely, that between "pathological effect" and "significant ecological effect."

Finally, during the 1970's an area of aquatic toxicology evolved which provided the first interface with classical toxicology as it relates to human health concerns. This interface was concerned with the question of measuring and/or predicting the occurrence of potentially toxic chemical residues in components of aquatic food chains which also represented components of the human diet. Perhaps because this particular area was related to human health, represented an activity routinely performed in animal toxicology, and utilized procedures and pharmacokinetic models already available from animal toxicology studies, this area of aquatic toxicology matured much more rapidly than any other area.

To summarize, we can consider the brief history of aquatic toxicology analogous to the physical development of an embryo. From 1930 to 1960's we went through a period of cell division, in the mid-1960's we began to specialize and differentiate into tissues, and during the early 1970's we are beginning a variety of more complicated developmental activities intended to prepare us for coordinated and integrated efforts.

Current Status

In order to understand where the field of aquatic toxicology is today, I believe it is necessary to enumerate what I perceive to be some very significant differences between aquatic toxicology and classical toxicology. These differences relate to the characteristics of the aquatic toxicologist, the objectives of his efforts, the forces which drive the direction of those efforts, and the major advantages and disadvantages that exist for the aquatic toxicologist relative to his counterpart in classical toxicology.

Concerning the differences between the aquatic toxicologist and the classical toxicologist, clearly there is a significant difference between the academic preparation of each for his respective science. In the case of the classical toxicologist, the breadth of available formal academic training related to his chosen profession is extensive, both qualitatively and quantitatively. The pursuit of one or more academic endeavors such as medicine, veterinary pathology, toxicology, pharmacology, comparative physiology, etc. are routinely required to pursue a career in classical toxicology. As I look around the aquatic toxicology community, I can count on one hand the number of scientists who have the luxury of any such training. Most of us here gravitated, often serendipitously, to the field from some other discipline. Thus, our progress is mediated for the most part through the trial-and-error method which frequently results in reinventing the toxicological wheel, or butting our heads against stone walls which have long ago disappeared for the classical toxicologist.

Concerning objectives, the ultimate objective is the same in both fields, namely, to minimize harm and maximize safety, while providing for the beneficial use of chemicals. However, there are some obvious — and some not so obvious — differences in the immediate objectives of the two fields. Our immediate objectives are not concerned with human safety; rather we are concerned with assessing the effects of chemicals on an indeterminate number of aquatic species. Underlying this obvious difference in objectives between the two fields, is a more fundamental nuance which often is not perceived by the regulatory users of aquatic toxicology data. I believe that, in reality, that classical toxicology is focused ultimately on providing data to protect the integrity of each and every individual human being. I believe that in aquatic toxicology we cannot, need not, and should not have our efforts focused on providing data to protect individual organisms. Rather, clearly we should be addressing data that relates, at a minimum, to populations of a species, and realistically to functional types of communities and ecosystems.

Concerning the forces which drive the field, I believe that because of the relative maturity of the two fields, classical toxicology is currently more concerned with understanding mechanisms than measuring effects. There is clearly a wealth of "basic research" being conducted towards addressing a variety of questions which exist as a result of a healthy scientific curiosity to know "why." On the other hand, aquatic toxicology (at least to date) has been driven solely by a regulatory pressure to measure effects. Thus there is currently little, if any, basic research being conducted in aquatic toxicology, and most, if not all, of the activity is directed towards answering questions related to regulatory needs for information concerning potential effects.

To the extent that the above differences in the scientist, his objectives, and the forces which drive his activities obviously exist, it is clear that certain advantages and disadvantages accrue to the aquatic toxicologist (Table 1). The major advantages appear to be twofold in nature. First, in the use of aquatic toxicity data the margin for error can and should be significantly lower, since the potential effect of being wrong does not have the social significance or implications of an error in human health applications. Secondly, we have no ethical limitations on experimenting directly on the species of interest. Thus, we can at least make empirical observations on toxicity assuming the organism of interest can be successfully handled in the laboratory.

The major disadvantages accruing to aquatic toxicologists due to the above differences in objectives are basically three. First, frequently we are unable to even identify, let alone test, all of the vast number of species of concern and to that extent the degree of

Table 1. Differences between aquatic toxicology and classical toxicology.

Aquatic toxicology	Mammalian toxicology
Aquatic toxicologist usually has little relevant formal academic training	Classical toxicologist always has the benefit of formal relevant academic training
Objective: protection of populations of many diverse species	Objective: the protection of individuals of one species (man)
There has been essentially no "basic" research conducted; emphasis has been on measuring effects	There has been extensive "basic" research conducted; emphasis has been on understanding mechanisms
The margin for error is not significant since the result of being wrong does not have severe social implications	The margin for error must be significant as the result of error is socially unacceptable
Ability to test species of concern	Ethical problems with human experimentation; animal models must be used
Inability to identify and test all species of concern; degree of extrapolation uncertain	Species of interest (man) known, degree of extrapolation certain
Test systems and their environments relatively unstable (poikilothermic), thus toxicity may not be sufficiently predictable	Test systems and their environments are relatively stable (homothermic), toxicity predictable
Tools are relatively primitive, their utility uncertain	Tools are well developed, their utility and limitations are well understood

extrapolation in the application of aquatic toxicity data is frequently uncertain, probably unquantifiable, but certainly greater than that associated with human health hazard assessments. Secondly, our test systems are relatively unstable. By that I mean that since our test organisms are poikilothermic; they of themselves are subject to random changes in temperature. Furthermore, these organisms exist in an environment (water) which can have a wide variety of physical and chemical characteristics, many of which affect the dose-response relationship. Thus, our ability to predict toxicity may be severely restricted relative to that in the field of mammalian toxicology. Finally, there exists a major disadvantage to the aquatic toxicologist which is the result of the relative age of the two fields of endeavor. Obviously, our tools are primitive, and their applicability is uncertain and must be verified. To illustrate, let me point out that only recently have we become concerned with understanding what might be described as the effective dose. From the very beginning aquatic toxicologists have only crudely measured "dose" as a function of concentration in water and duration of exposure (e.g., 96-hr LC50).

To sum up, then, where we are now: we are beginning to understand what it is we should be trying to accomplish (objectives), we are aware of the major obstacles (problems) which we must overcome, we have some basic tests we know are reproducible (tools), and we have some ideas on how the tools can be used (hypothesis) to overcome the problems and accomplish our goals. We must now get about the job of documenting (verification) that these ideas are scientifically valid and of social utility.

Future Developments

If the present legislation (Toxic Substances Control Act) is vigorously pursued, there is little doubt that the need for, and the use of, aquatic toxicity data will increase exponentially. Using the presently available empirical approaches, there is now more work to be done than there are qualified poeple, established laboratory facilities, and dollars to do the work. Clearly, the single most significant area of progress must be in the realm of predictive aquatic toxicology. That developments in this area have not been forthcoming yet should not be surprising. We have only recently developed the empirical data base on chronic toxicity of chemicals to a variety of aquatic forms against which to measure predictive capabilities of short-term tests, or the extrapolability of chronic data from one aquatic species to another.

In my opinion, another area for future development is cooperative efforts between aquatic toxicologists and classical toxicologists, to evaluate the potential for aquatic systems (organisms) to be used as tools in human health evaluations. Given the fundamental similarities at the cellular, tissue, and organ levels, and the advantages that accrue from the smaller size of aquatic organisms, their availability in large numbers, and their relatively short generation times, it appears to me that they offer significant potential for use as *in vivo* and *in vitro* systems for evaluating such sensitive areas as oncogenicity, teratogenicity, mutagenicity, modes of action, target organs, etc.

Lastly, I see a major difference, in the future, in the type of scientist practicing aquatic toxicology. I believe he will be formally trained in toxicology and related fields and this can only accelerate the rate of development of the field of aquatic toxicology, increase the interaction that is just beginning to occur between aquatic toxicologists and their counterparts in classical toxicology, and end forever any debate that may exist regarding the question of fact or fiction, art or science.

Summary

To sum up my thoughts I would like to construct an analogy to the human reproductive cycle. I should point out that, although valid in the qualitative sense, the analogy falls to pieces (in the quantitative sense) when one considers the time frames. That is, I believe the time frames for the various periods in the development of the field of aquatic toxicology are inversely proportional to the time frames for the various periods in the development of a mature human being. The science of aquatic toxicology has just completed embryogenesis and parturition, is suffering from the characteristic hypertrophy of a new born fetus (in that we can generate data faster than we know how to use it), and can now be expected to undergo a significant period of rapid growth and development leading to the formation of a mature science.