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Toxicology, environmental chemistry, ecotoxicology, and One Health: definitions and paths for future research

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The definitions of toxicology, environmental toxicology, environmental chemistry, environmental risk, and ecotoxicology are closely related and sometimes used as synonyms, whereas One Health is a more recent, complementary concept. This contribution examines the origins of the usages of these terms, explores their interchangeability (whether appropriate or not), and proposes some paths to better define each. The usage of these terms is evolving, and current research and paradigms are progressing toward the integration of broader, more integrative perspectives, such as the One Health approach. One Health is a holistic approach that helps link and integrate work on environmental and human health impacts. Definitions and research should not necessarily strive to segregate human vs. environmentally focused work, and most of the problems are complex and interconnected. Future research endeavors and funding programs must better reflect the multidisciplinary nature of environmental toxicology, and more broadly, One Health research and environmental research must recognize the interrelationships of human health, environmental health, ecotoxicology, and a multitude of geochemical, microbiological, and ecological processes.

KEYWORDS

environmental toxicology, ecotoxicology, One Health, definitions, research funding, environmental chemistry

Toxicology is the science of poisons

The simplest definition of toxicology is that it is "the science of poisons" and hence evolved from Paracelsus, assuming that too much of anything can kill. In essence, much of toxicology is focused on finding the dose–response, i.e., which quantity of a component will elicit a biological response, what concentration is without effects, when does it seem positive (whether through a hormesis effect or not), when could it be negative, and a wide range of sublethal responses that culminate in evaluating when does the exposure kill or affect the organism. We must also consider the need for more nuanced responses as we rarely get a binary biological response to a given challenge. Organisms or systems will be affected differently in different contexts, and it is critical to improve how we report environmental toxicology data to improve reproducibility, credibility, and transparency (Fleeger, 2020). This includes reporting the statistical significance of results, including error estimates of our toxicological assays and negative results (including a lack of toxic response), without limiting ourselves to testing for the significance of a null hypothesis

(Erickson and Rattner, 2020) and making sure to properly measure exposure and not presume that nominal additions represent actual concentrations.

Langman and Kapur have proposed that toxicology is multidisciplinary and developed into three specialized branches: environmental, clinical, and forensic (Langman and Kapur, 2006). This context seems anthropocentric, and environmental toxicology was initially concerned primarily with environmental exposure from chemicals in the air we breathe, the water we drink, or the food we eat. In this definition, some of the work in environmental chemistry would feed into a component of environmental toxicology. Clinical toxicology was focused on potential adverse effects of chemicals that are intentionally administered for therapeutic purposes. Forensic toxicology is looking into the medicolegal aspects of chemicals and poisons and understanding what has happened.

A simple yet very effective definition is that "toxicology is the study of the adverse effects of chemical, biological, or physical agents on living organisms" (Radenkova, 2008). This definition has a great advantage where it is not by itself anthropocentric and encompasses all living organisms and pretty much any form of agents that could potentially have negative biological impacts—thus going beyond the testing of the impact of a single chemical. Toxicology could then be divided into the toxicology of human health and environmental toxicology, encompassing all the organisms, entities, and systems that the environment is hosting. One must emphasize that in many ways, the toxicology of humans is easier to handle as it is focused on a single species and, for the most part, at the level of the individual, whereas environmental toxicology looks at the full breadth of biological organisms and must also consider ecotoxicological and ecological implications that move beyond the impacts on individuals and must integrate populational impacts (Belden, 2020).

We tend to have higher concerns for human health than environmental health, and we devote much more resources to protecting the former over the latter. However, the processes and research are similar in terms of what is needed to understand how toxicants affect the *homo sapiens* species relative to how toxicity would be expressed in some of the more than 6,000 recognized mammal species (considering many that are now extinct) (Burgin et al., 2018). Research needs to integrate greater complexity, such as mixtures of contaminants and how climate change may alter biological responses to exposures, and we must evaluate the impacts on different organisms, microbial processes, their interactions, or even on the integrity and balance of ecological systems.

Ecotoxicology, environmental toxicology, and environmental chemistry are intertwined

The concept of ecotoxicology has evolved from an early concept of the study of exposure pathways, uptake, and effects of chemicals on organisms, populations, communities, and ecosystems (Connell et al., 1999). Vasseur et al. proposed an interesting storyline for the evolution of the concept of ecotoxicology (Vasseur et al., 2021), with the initial use of the term "ecotoxicology" attributed to Jouany (1971) and phrased as "the study of the influence of nuisances on the relationship between an individual [species] and his [its] environment could simply be termed ecotoxicology" with "nuisances" defined as "harmful and inimical factors induced by humans" (translated from French) (Vasseur et al., 2021).

This was paraphrased as "toxicology in an ecological perspective," aiming to study the deleterious effects of chemical, physical, and biological agents on living organisms and the interrelations within communities and their interaction with the environment (Vasseur et al., 2021). This vision is similar to Hodgson's definition: "*Environmental toxicology* is concerned with the movement of toxicants and their metabolites and degradation products in the environment and in food chains and with the effect of such contaminants on individuals and, especially, populations" (Hodgson and Hodgson, 2004).

Leblanc has further defined *environmental toxicology* as the study of the fate and effects of chemicals in the environment (encompassing both naturally found chemicals (venoms or natural toxins) and those of anthropogenic origin) (Leblanc and Hodgson, 2004). He also divided environmental toxicology into *environmental health toxicology* and *ecotoxicology*. Environmental health toxicology focuses on the adverse effects of environmental chemicals on human health, while ecotoxicology involves the study of the adverse effects of toxicants on a myriad of organisms that compose ecosystems, ranging from microorganisms to top predators (Leblanc and Hodgson, 2004).

Early vocabulary for environmental toxicology and ecotoxicology could be considered synonymous or closely related, but they have a distinct difference from "toxicology," which solely focuses on human health, while environmental toxicology and ecotoxicology deal with the effects on the environment and all of the species and ecosystems that could be impacted.

Moriarty mentioned that "ecotoxicology is concerned ultimately with the effects of pollutants on populations not individuals. Sublethal effects, and changes to the environment, can have a greater impact on population size than does acute toxicity" (Moriarty, 1988), thus hinting at a more ecologically oriented definition of ecotoxicology. Chapman further emphasized that ecotoxicology stems from "ecological toxicology" and integrates ecology and toxicology. As such, it should be inspired from ecological risk assessment (Chapman, 2002). He further emphasized that ecotoxicology's "objective is to understand and predict effects of chemicals on natural communities under realistic exposure conditions" (Chapman, 2002). Much of toxicological research work is focused on testing specific chemicals individually, while multiple contaminants are generally simultaneously present in the environment. Furthermore, critical ecological impacts are not always linked to exposure to a single toxic chemical as they are related to habitat loss, introduced species, nutrient enrichment, and global climate change (Chapman, 2002).

Environmental impacts are multifaceted and difficult to assess in simple metrics. The tendency to recalculate everything in equivalence of tons of carbon dioxide is a good example of the weakness, albeit this is useful to compare the potential warming impacts of releases of methane relative to carbon dioxide or other gases. Using carbon dioxide equivalence is hardly appropriate to assess the endocrine disruption potential of pharmaceuticals, the problems caused by tons of plastic pieces affecting marine fauna, and the various toxicological effects caused by emerging contaminants in the environment. Ecotoxicology should be viewed as the portion of environmental toxicology that takes a holistic perspective to look at potential impacts, with special considerations to ecological impacts and disruptions of ecosystems, and "ecotoxicology" should not be focused on single-species testing of single toxicants (albeit such testing is certainly useful, they should be viewed as environmental toxicology work, not specifically ecotoxicological).

For a long time, toxicology focused on human health, with environmental toxicology work being segregated into other venues and endeavors. Nevertheless, this is evolving, and many of the impacts on human health can be traced back to a broader environmental issue having effects on other species or environmental processes. We must recognize that the environment as a whole, including humans, is a complex multi-component system and that *Homo sapiens* is but one of the many species that need to be protected.

One Health offers a holistic perspective

This is where the "*One Health*" approach, which recognizes that "the health of humans, domestic and wild animals, plants, and the wider environment are closely linked and interdependent," shows that it is somewhat futile to deal separately with problems related to human health or to environmental health and that ultimately, all biological organisms are somewhat interdependent and interconnected (Larsson et al., 2023). There is a plethora of definitions, but this version was proposed by the One Health High-Level Expert Panel (WHO, 2023) from a quadripartite initiative of international agencies that adopted it: the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the UN Environment Program (UNEP), and the World Health Organization (WHO). The current definition is as follows:

"One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines, and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems while addressing the collective need for clean water, energy, and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development."

This highlights that even from an anthropocentric point of view, we should put a lot of research efforts and corrective actions focused on the environment as it has significant impacts on humans and their health (however, we should not forget that the environment fully deserves to be protected for itself).

Moving forward for environmental toxicology research

Toxicology research must better integrate the One Health approach and realize that humans, farm animals, and wildlife are interconnected and further dependent on invisible microbiological organisms and complex ecosystem interactions. Albeit specific studies need a clear focus, the complexity, interdependence, and potential transferability of results must be considered when designing new experiments. This type of research also needs better recognition and better support by granting agencies—environmental toxicology and even more so "One Health" projects are, by definition, multidisciplinary and are often at the uncomfortable interface of sections, divisions, and sectors and, as a result, often more difficult to evaluate and fund through usual granting programs. In addition to being multidisciplinary and at the crossroads of different disciplines, it is also at the interface of fundamental and applied research and too often left aside—if the data are needed for regulatory agencies, granting agencies will be reluctant to fund the research, and if the data are deemed research-oriented, regulatory agencies then would want research granting agencies to fund it. One would think that being at the interface would prove easier to get the research funded, but in reality, it is often more difficult.

There should be more funding and professional support dedicated specifically to aid interdisciplinary research at the interface of disciplines and that focus on One Health—we need work that combines concepts and expertise in toxicology and chemistry to connect seemingly traditionally disparate research topics and draw conclusions on broader environmental and human health concerns and integrating risk assessment.

Funds for environmental toxicology research should be increased to better match the efforts dedicated toward human health because our lack of understanding of other environmental issues, whether from contamination or management problems, will ultimately come back to haunt the health of human populations. We must rethink how we design environmental research and make sure that toxicological work, whether focused on humans or other biological organisms, integrates the "One Health" approach and the complexity of the interactions among biological organisms and a very wide range of processes, whether microbial, biochemical, within the environment, or through an organism's internal metabolic pathways, ecological interactions, and many others.

We must do a better job to assess the toxicological impacts of the combinations of chemical toxicants—both in developing better testing systems and better accounting for potential interactions and finding ways to integrate toxicant interactions into environmental quality guidelines. It will be even more complicated to model or account for interactions of chemical toxicity with other "non-chemical" challenges (pathogens, invasive species, global warming, eutrophication, rising sea levels, shorter snow/ice cover, loss of habitat, etc.).

Even privately funded toxicological research is problematic as companies are reluctant to publish or release information that could potentially reduce the competitiveness of the products they commercialize. Even when they do release some information, the capacity to selectively pick and choose what they release and what information they retain greatly reduces the trust we can give to such partial results (Sauvé, 2019). Health and environmental agencies should refuse to use any data that are not peer-reviewed and not available for outside experts to use and criticize. Companies seeking approbation for new chemicals (or legacy products seeking reapproval or derogatory measures) should provide data based on impartial work that must be peer-reviewed and publicly available (this research could still be funded by private interest but at arm's length and without any say on how the studies are designed, how the results are interpreted, and whether or not the data should be published).

Finally, we must further improve how we perform toxicological testing, integrate more chronic exposure and nonlethal effects, and further develop our tools to test for endocrine disruption; there is certainly a lot of work left on how to best correlate environmental concentrations, chemical speciation, body burdens, and actual toxicological effects.

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