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Workshop 5.1

Making decisions in the 21st century: Scientific data, weight of evidence, and the precautionary principle*

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Abstract: Traditionally, science has progressed by slow steps involving the accumulation of studies showing particular effects, leading eventually to a general consensus. However, with increasing development and industrialization, environmental problems have escalated faster than the ability to collect sufficient data to form clear consensus among scientists. Since managers require scientific information to make decisions about management, regulation, and public policy, the gap has been partially filled by two approaches: weight of evidence and the precautionary principle. I suggest that both are useful for making decisions about endocrine active substances, although few papers in the refereed literature link the precautionary principle with endocrine active substances. As with most public policy decisions, these involve an iterative process whereby scientific inquiry must continue to fill data gaps, and to determine if the decisions made by these processes are still appropriate and protective of human and ecological health. The precautionary principle is most useful when it continues to inform and help direct research to fill data gaps in our understanding of environmental problems, such as the effect of endocrine active substances on endocrine disruption.

INTRODUCTION

There is worldwide concern for global climate change, yet there are many global changes that involve increases in human populations, shifts in their distribution, concentration of people along coasts, shifts in land use, increases in the temporary movement of people, massive industrial and suburban development, and increases in technology with environmental consequences. Increasing industrialization, technology, and human populations clearly place people and their ecosystems at risk, particularly with respect to environmental degradation and contamination. Although the width of the dense population band along coasts may vary, increasing development places demands on fragile land–ocean margins and associated ecosystems, partly because it is in this region that transfer and transportation of products occur, allowing for the possibility of environmental contamination. In the coming years, the human dimensions of environmental health sciences, and conservation and protection of biodiversity will gain even more importance as global changes in population size and distribution, land use, and increased use of chemicals occur in many societal domains (agriculture, medicine, industry). While the intrinsic value

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of ecosystem protection and biodiversity are clear to some [1,2], the human health consequences of increased reliance on chemicals, petrochemicals, and pharmaceuticals are clear to all [3].

In the past, we have relied on sound scientific data to reach solutions for environmental problems, and to restore ecosystems. It is no longer enough to decry the continual loss and degradation of habitat and biodiversity. We must seek creative solutions that are advantageous both for protecting human health and the environment. However, the pace of technological development, the increase in the number and widespread use of chemicals, and the time required to adequately test these chemicals, petrochemicals, and pharmaceuticals increases, hence decisions must often be made before the data are all available. In the past, environmental agencies have relied on a cause–effect evidence, derived from evidence, hopefully leading to certainty. However, often this is no longer the case. Since managers require scientific information to make decisions about management, regulation, and public policy, the gap has been filled by two approaches: weight of evidence and precautionary principle. These two approaches should involve an iterative process whereby regulatory actions are taken, while scientific inquiry must continue to fill data gaps, and to determine if the decisions made by these processes are still appropriate and protective of human and ecological health.

In this paper, I explore weight of evidence and the precautionary principle as they are generally used, contrast them, and propose that both are useful for making decisions about endocrine active substances, with the caveat that scientific inquiry must continue, both to increase our knowledge base and to determine whether regulatory actions were protective of human and ecological health. Below, I will discuss briefly why making decisions about endocrine active substances requires these two approaches, define and describe some of the ways the two approaches have been used generally, and finally return to discuss briefly how they will be particularly useful for making decisions about endocrine active substances.

SPECIAL CASE OF ENDOCRINE ACTIVE SUBSTANCES

Governmental agencies, the private sector, and the public are increasingly interested in assessing the well-being of both humans, and other species within their ecosystems. Human health risk assessment and ecological risk assessment have emerged as separate paradigms embodying the disciplines of toxicology and exposure assessment [4,5]. In many cases, the two risk assessors either examine human health [6,7] or ecological health [8–14], although a few volumes have included both human and ecological risk assessment [15]. There have been some attempts to show the interconnections between human and ecosystem health [16,17], but these usually have not dealt with methodology. An important development, however, has been the development of conceptual models for exposure in food chains that include pathways for human exposure [18].

Endocrine active substances provide an excellent example of an environmental issue that has important consequences for both human and ecological health. The question of whether environmental contaminants are inducing adverse health effects in humans and wildlife because of disruptions to the endocrine system is one of the more important questions of our age, and is, for example, one of the highest research priorities of the U.S. Environmental Protection Agency [19]. Endpoints for assessment of the effects of endocrine active substances include multigenerational measures. Endocrine active substances in the broadest sense include not only man-made chemicals, but natural agents that occur in the diet [20,21], however, it is often interpreted as referring only to man-made chemicals. A major concern is that persistent bioaccumulating chemicals affect fetal development by acting like estrogens or antiestrogens [22].

Initially, concerns arose because of the observation that some synthetic chemicals in the environment were associated with adverse developmental and reproductive effects in wildlife [23]. The effects of exposure (in utero) to the potent estrogen diethylstilbestrol (DES) in children of treated women (and later tests with treated mice) further led to concern. The pesticide DDT interfered with female reproduction in birds. There is information on associations between synthetic chemical and adverse biological outcomes that are normally mediated by the endocrine system [23], although the mechanisms are not always clear [21]. While it is always difficult, costly, and time-consuming to determine the cause and effect of a chemical in the environment, the task for endocrine active substances is made more difficult by the mixture of chemicals humans and wildlife are normally exposed to [21]. It is not the purpose of this paper to discuss the scientific data, but to examine the current state of our knowledge and the consequences of the state of the science.

The main difficulty is the conflict between the need on the part of governmental agencies and the public for concrete data demonstrating the links between specific chemicals and outcomes and the state of our knowledge regarding endocrine active substances. We need or want to know more than science seems able to produce. However, the potential consequences of waiting to make a decision until every aspect is scientifically proven beyond a shadow of doubt may be severe if endocrine disruption is occurring in humans and wildlife, and if the effects are intergenerational. Thus, there is a need to adopt methods that will allow reasonable decisions in the face of uncertainties and knowledge gaps.

Below, I discuss two methods of dealing with knowledge gaps and uncertainties regarding the effects, mechanisms, and magnitude of effects of chemicals that act as endocrine active substances to cause endocrine disruption. While quantitative risk assessment provides another approach [24], often the data necessary for such assessments are not available.

WEIGHT OF EVIDENCE

The phrase "weight of evidence" is fashionable, ambiguous, and difficult to define. It suggests a quantitative ranking of evidence, or the qualitative appraisal of many different forms of evidence to arrive at a conclusion [25]. Sometimes, much of the evidence is qualitative or otherwise not suitable for statistical treatment. Evidence derives from epidemiological and clinical studies, long-term laboratory assays, and predictive short-term tests, the latter two with animal models [25–27]. Epidemiology can provide useful information on human populations, but it has the disadvantages of lacking rigorous controls, has difficulties determining exposure, and is usually reactive, rather than preventive [27]. A preponderance of data used in weight-of-evidence approaches are derived from animals tests, often with mammals.

Weight-of-evidence approaches to consensus often comes from scientific committees that are empowered by organizations such as the United Nations, International Agency for Research on Cancer, International Program on Chemical Safety, International Labor Organization, World Health Organization, and the Scientific Committee for Problems of the Environment, among others. Within countries, such committees are organized by academies of science, such as the U.S. National Academy of Sciences [5,9,21]. Such committees function by convening a diverse group of scientists to evaluate the evidence and reach consensus views—they weigh the evidence [27].

In the case of endocrine disruption, much of the weight of evidence comes from epidemiology studies of wildlife in nature [23]. While such studies can provide epidemiological evidence, they do not shed light on the mechanisms [21]; this must await controlled laboratory experiments. Further, a weight-of-evidence approach, with endocrine active chemicals or any other, can only be used when there is evidence or studies to consider. Where such evidence exists, scientific committees can pull the data together to support a weight-of-evidence conclusion, which can be used for regulatory purposes [28].

PRECAUTIONARY PRINCIPLE

"In order to protect the environment, the precautionary approach shall be widely applied by states according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." (Rio Declaration of the United Nations Conference on Environmental Development, 1992, see Applegate [29]).

This definition partly reflected an articulation by Bergen [30]. The precautionary principle is invoked when there is reason to assume that chemicals or technology introduced into the environment may create hazards, either directly or indirectly, to humans or other receptors. There does not have to be evidence of a causal relationship [31]. The hazard has to be more than plausible and usually severe and irreversible. The precautionary principle is a way of dealing with uncertainties or where there is a clear knowledge deficit [32–35]. It deals with uncertainty by "staying on the safe side" [36].

The precautionary principle is a leading principle in some environmental law, such as in Germany [37] and in much of Europe [38], where it is sometimes explicitly referred to. It is embodied in some U.S. legislation (e.g., Toxic Substances Control Act), but not by name. In the United States, it does not offer legal standing [38]. It was adopted by the countries in the charter of the European Union (EU Treaty, 1993 [29]). They wish to use the precautionary principle to reduce the use of toxic chemicals by developing safe industrial technologies and invoking criminal sanctions for suppression and manipulation of information about chemicals and their effects [39]. The precautionary principle only recently has entered environmental policy debates in the United States [29]. Applegate [29] argued that while U.S. law contains some elements of the precautionary principle, precaution is usually balanced against cost.

There are four main elements to the precautionary principle: (1) trigger for regulatory action, (2) timing of the regulatory action, (3) nature of the regulatory response, and (4) a regulatory strategy [29]. While Applegate and others have focused on the regulatory nature of the precautionary principle, others have focused more on environmental management. Recently, Kriebel et al. [40] suggested a different set of guidelines suggested by the precautionary principle: (1) taking preventive action in the face of uncertainly, (2) shifting the burden of proof to those who want to do an action or use a chemical, (3) exploring a range of alternatives, and (4) increasing public participation in decisions and management. In other words, the principle suggests that regulators, policy-makers, and law-makers should err on the side of caution.

The precautionary principle has been invoked in such diverse areas as conservation [41], salmon farming and other fisheries [42,43], marine ecosystems [44], occupational medicine standards [45], and breast cancer reduction [46]. In the latter case, Davis et al. [46] suggested that prudent precautionary principles suggest that reducing exposure to avoidable risk factors should receive high priority. To some extent, it is this aspect that has been applied to the issue of endocrine active substances. The precautionary principle can provide guidance for regulatory initiatives to reduce the risks caused by chemicals [47], particularly to children [48].

Remarkably, in the refereed literature the precautionary principle has not been linked with endocrine active substances. For example, a search of papers on MedLine for the last five years yielded 252 papers on the precautionary principle, but none linked either weight of evidence or precautionary principle with the term. Both terms, however, have been used extensively, although mention of the precautionary principle began only in the mid-1980s (Fig. 1, MedLine). An environmental science and pollution search indicated only four papers linking endocrine disruption with the precautionary principle, and seven linking endocrine disruption with weight of evidence. The two terms have been used extensively mainly over the last ten years in other contexts (Table 1). Similarly, weight of evidence has been mentioned less over the last five years, compared to the precautionary principle (Fig. 2, Cambridge Scienctific Abstracts, environmental science and pollution search).

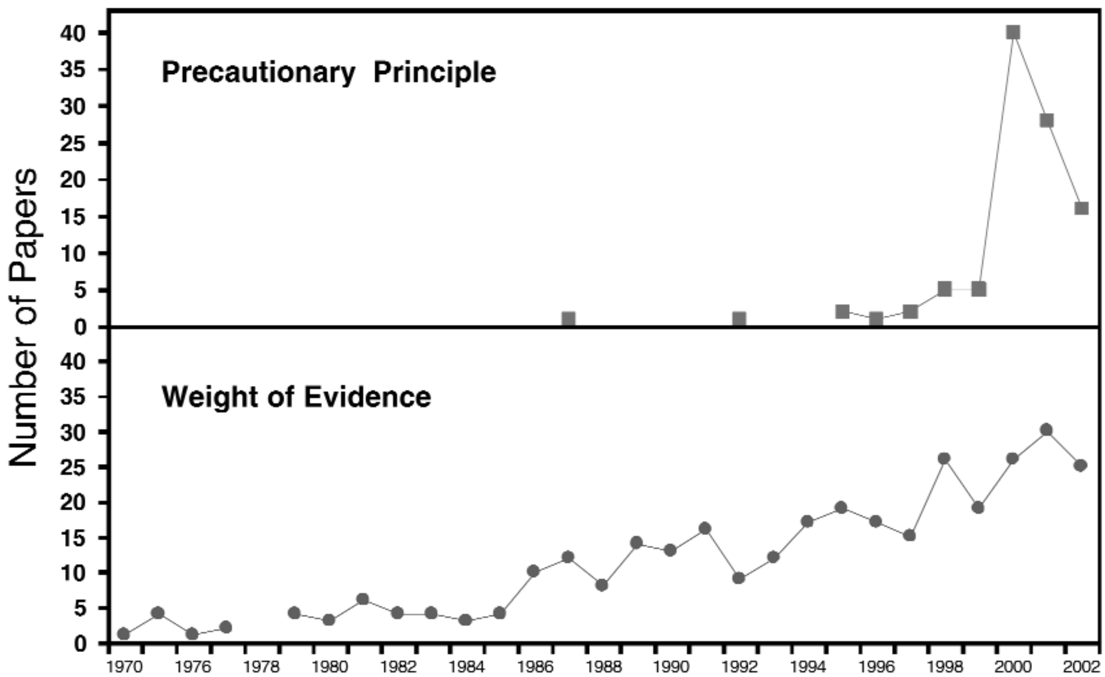

Fig. 1 Number of papers mentioning the precautionary principle and weight-of-evidence approaches, from a MedLine search.

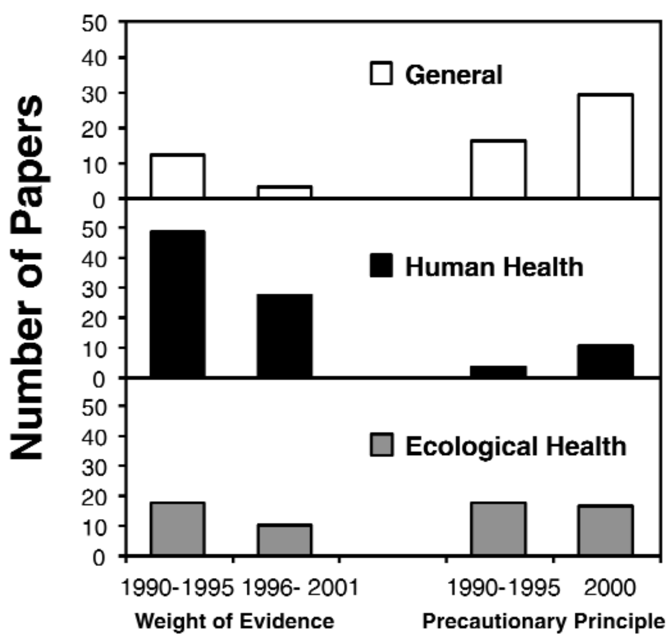

Fig. 2 Number of papers mentioning the precautionary principle and weight-of-evidence approaches, from a Cambridge Scientific Abstracts search.

Table 1 References to weight of evidence and precautionary principle in the CSA–Environmental Science and Pollution database.

	Weight of evidence		Precautionary principle	
Number of papers	1990–1995	1996–2001	1990–1995	1996–2001
General				
Laws, regulations, and guidelines	2	1	3	6
Risk assessment	5	1	3	8
General theory	2	1	6	13
Global warming	3		4	2
Total	12	3	16	29
Human health				
Endocrine disruptors	3	4		2
Chemicals	28	18	2	5
Physical agents	2			
Carcinogenicity	5	1	1	3
Neurotoxicity	3			
Occupational health	1			
Social (seat belts, EMF)	2	1		
Epidemiology	3	2		
Surgery/medicine	3			
Toxicity testing	1	1		
Total	48	27	3	10
Ecological health				
Endocrine disruptors				2
Marine ecosystems and pollution	2	3	7	7
Marine ecosystem function	1	2	2	1
Freshwater and pollution	4	4	1	3
Freshwater and chemicals/pollutants	2		1	
Invertebrates	3			1
Fish	3			1
Other vertebrates	1		1	
Sustainability/biodiversity	1	1	5	1
Total	17	10	17	16

CONCLUSIONS

Recently, Goldstein [49] argued that the precautionary principle is really the modern formulation of the Hippocratic principle that says "above all do no harm". Since human health is tied to global health, there are, he argues, reasons to act cautiously. Yet, the imprecise definition of the principle restricts its usefulness as a goal. Further, he argues persuasively that the use of this principle should not preclude further scientific inquiry to further our knowledge of the initial problem, and to ascertain whether our precautionary actions were warranted [49]. The "principle" and scientific research are not antithetical [50], as Holm and Harris [51] have lamented. This seems to be an important aspect to bear in mind, particularly for endocrine active substances where the scientific evidence is often contradictory.

Goldstein's [49] arguments, and those of others, suggest that while the precautionary principle may be useful in formulating our current public policy decisions regarding endocrine active substances, caution would also argue that we continue to conduct research to determine cause-and-effect and mechanisms [52]. While European and American environmental agencies are acting on the precautionary principle with respect to possible endocrine disruption [19], it is clear that on-going research on endocrine disruption is critical to our future actions. Uncertainties in themselves should not stifle future research, but instead should inform and stimulate research.

There are some criticisms of the precautionary principle, including that current regulations are already precautionary, it is not scientifically sound because it advocates making decisions without scientific justification, and it might stifle new technologies [40]. While these are not unfounded, there are situations where it might be difficult to obtain sufficient scientific justification until it is too late to prevent disaster, particularly in the case of ecological receptors (such as endangered species). The precautionary principle is useful in public policy when the failure to act may cause potentially serious of irreversible threats to health or the environment [35].

In summary, there is a continuum of three approaches that are used for regulation: traditional scientific data leading to regulation, weight of evidence, and the precautionary principle. I would argue that all three approaches are useful in the realm of management, regulation, and policy-making (Fig. 3). The problem is determining when to use each of the approaches. Clearly, scientific certainty and the degree of consequences influence when each is used.

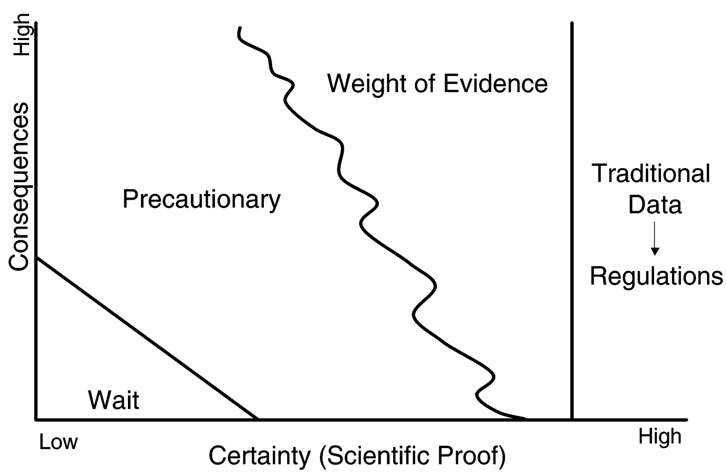

Fig. 3 Schematic of the relationship between differing approaches to risk management based on traditional scientific data, weight of evidence, and precautionary principle as a function of certainty and consequences.

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