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Review

Why endocrine disrupting chemicals (EDCs) challenge traditional risk assessment and how to respond

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HIGHLIGHTS

- Endocrine disrupting chemicals (EDCs) considered in relation to traditional risk assessment.
- Many characteristics pronounced in EDCs challenge traditional risk assessment.
- Human health can be best protected with a future risk framework tailored to EDCs.
- For now EDC risk may be transparently assessed with available tools and methods.

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ABSTRACT

Endocrine disrupting compounds (EDCs) are a diverse group of "chemicals of emerging concern" which have attracted much interest from the research community since the 1990s. Today there is still no definitive risk assessment tool for EDCs. While some decision making organizations have attempted to design methodology guidelines to evaluate the potential risk from this broadly defined group of constituents, risk assessors still face many uncertainties and unknowns. Until a risk assessment paradigm is designed specifically for EDCs and is vetted by the field, traditional risk assessment tools may be used with caution to evaluate EDCs. In doing so, each issue of contention should be addressed with transparency in order to leverage available information and technology without sacrificing integrity or accuracy. The challenges that EDCs pose to traditional risk assessment are described in this article to assist in this process.

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1. Introduction

More than at any other time risk assessment is at a crossroads—one path leads to retaining the status quo the other to a challenging but less certain future.

Let's hope we have the wisdom to choose correctly. [56].

"Chemicals of emerging concern" have attracted much attention in the last half decade [1–8]. One group among them, endocrine disrupting chemicals (EDCs)—also known as endocrine disrupting compounds, endocrine disruptor contaminants, hormonally active agents, and endocrine active substances—make headlines regularly [9–12]. Broadly speaking, EDCs are substances that influence processes associated with the endocrine system and alter its functioning [13,14]. The endocrine system is responsible for the release of hormones, chemicals which help control and connect the systems of the body, and thus plays a major role in the health of humans and wildlife [15]. EDCs interfere with steroids such as estrogen, anti-androgen and androgen, as well as other hormone action [14].

As the endocrine system is tightly regulated during certain life stages, small changes in hormonal conditions, even for a brief time, can have acute and enduring impacts on exposed populations [16]. According to the World Health Organization (WHO) and the Organisation for Economic Co-Operation and Development (OECD), changes to natural hormonal functions (i.e., synthesis, secretion, transport, binding, action, elimination) [16] can cause adverse health effects in an intact organism, or its progeny or (sub) populations, consequent to changes in endocrine function [17,18]. Though the term EDC is often thought of as referring only to synthetic chemicals, natural agents can also be endocrine-active [19]. EDCs can be grouped in many ways, by structure or function (see Appendix B for examples of EDC categories). For example, estrogenic EDCs produced naturally by plants are called phytoestrogens (e.g., isoflavones), and synthetically are called xenoestrogens (e.g., phthalates) [20,21]. A large portion of identified EDCs are xenoestrogens [22], although their precise number in the ecosystem is unknown [23].

The term "endocrine disruptor" came into use in 1991 after a working session on chemically-induced alternations in sexual development as part of the Wingspread Conference [24]. This was the first time a group of researchers reached a public consensus that endocrine disrupting chemicals in the environment were disturbing reproductive health [25,26]. Five years later, a book called "Our Stolen Future" [27] brought attention to the widespread ecological and human health consequences of EDCs. These events sparked a wave of research, and brought to light the high potential for risk to human health posed by EDC exposure [28,29]. Still, progress in developing the method for systematic assessment of associated risks from these chemicals has been only modest [30] relative to methods for quantifying other types of health threats such as carcinogens [31,32] and natural hazards [33,34].

It is proposed here that risk assessment (RA) of EDCs should be undertaken promptly by leveraging available methods and analytical tools, but should be done with caution and should be accompanied by appropriate risk communication. This will help keep provisional results from being misconstrued as definitive risk values, and resulting in unwise decisions and unsafe situation. Subsequently, comprehensive guidelines should be developed specifically for EDC risk assessment in which the unique characteristics of this chemical group are addressed. Table 1 lists some of these challenges which make conventional risk assessment complicated or ill-suited for application to EDC human health risk.

There are also some challenges to exposure assessment and RA that, while not unique to EDCs, are prominent in this chemical group and worth noting. These are discussed in Appendix A:

- EDCs have been transported all over the globe and are ubiquitous in the environment,
- Effective exposure to EDCs is complex to calculate,
- Limitations in epidemiological and toxicological study limit reliable data for RA, and