Determination of the Potential Toxicity of Contaminants in the Water Requires Improving the Understanding of Low-Concentration Effects

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The identification of contaminants, often at very low concentrations, in ground, surface, and drinking water raises concern. Toxicology studies and risk assessment on water contaminants are done at unusually high levels of exposures. Usually, rodent studies use a maximum level of tolerated exposure with several lower concentrations at one-half to one-fourth of the maximum concentration. The results must then be extrapolated from the toxic levels tested to the potential health effects of environmental concentrations. The linear extrapolation used to extrapolate from high to low concentrations has some serious defects. First, it assumes the mechanism of toxicity at high concentrations is similar to the mechanisms of toxicity at lower concentrations. However, for several chemicals, including chloroform, this is simply not the case. The carcinogenicity found at high concentrations is a reflection of repeated cellular toxicity. Second, linear extrapolation assumes that the response to toxicants at low-dose concentrations is similar to the response to high concentrations where adverse health effects are known. Linear extrapolations ignore the fact that cells can repair damage and can respond to minimally toxic exposures. These repair and response systems are necessary because normal cellular processes create endogenous toxicants such as free radicals. Thus, the body has evolved many ways in which to protect itself from many otherwise potent toxicants. These low-dose protection systems potentially provide for a threshold below which exposure has little consequence and above which there could be health problems. It is only when an exposure level is high enough to overwhelm the body's innate protection system that adverse health effects occur.

The National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) are investigating the molecular pathways of toxicant action and the mechanisms by which the body repairs damage from toxicants. Such knowledge is crucial to the interpretation of the rodent studies at high concentrations. This new research opportunity stems from the dramatic increase in our understanding of biological mechanisms at the cellular and molecular levels and the corresponding increase in our capabilities in the area of analytical chemistry. For example, it is possible to measure DNA damage by quantification of adducts with great precision examining the response to chemicals at low concentrations. Further, quantification of various cellular DNA repair systems has now become standard. Incorporation of relevant mechanistic research from all exposures into the risk-assessment enterprise will reduce uncertainties and produce more accurate and realistic estimates of human risk. While toxicologists are more comfortable working at toxic levels, a paradigm shift will be required to focus on the lower more relevant concentrations. The NIEHS/NTP currently is working on a targeted low-dose/threshold research initiative because the state of the science now allows for such an undertaking. The ultimate goal is to ensure that exposure standards truly protect the health of the public and are based on sound science.

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