Testing and Risk Assessment of Chemicals that Impact Highly Adaptive Biological Systems: The Case of Endocrine Systems.

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Animals have evolved a variety of mechanisms for responding to toxic chemicals of both natural and anthropogenic origin. Well-known examples include activation of cellular repair pathways and induction of metabolizing enzymes. From a governmental regulatory perspective, these and other adaptive responses may complicate efforts to establish acceptable levels of chemical exposure. To illustrate this point, we consider endocrine systems as potential targets for chemical effects. Although limited, existing data suggest that these systems possess a robust capacity to adapt to and potentially recover from chemically-induced insults. Using the hypothalamo-pituitary-thyroid (HPT), gonad (HPG), and adrenal (HPA) axes as case examples, we highlight structural attributes of these systems that provide for this capability. In doing so, a distinction is made between endocrine systems of adult animals and those of developing organisms. Emerging data suggest that disturbance of these systems during early development may lead to epigenetic programming, resulting in differences in phenotypic expression later in life. Risk assessments of chemicals that impact highly regulated systems must consider the dynamics of these systems in relation to complex environmental exposures. A largely unanswered question is whether “successful” adaptation exerts a fitness cost on individual animals with adverse consequences for populations. Mechanistically-based mathematical models of endocrine systems may provide a means for better understanding adaptation and recovery in species that exhibit different life history strategies. With appropriate modification, bioassays developed in support of U.S. EPA’s endocrine disruptor screening program could be used to assess the potential for adaptation and recovery and inform the development of mechanistically-based models. This abstract does not necessarily reflect U.S. EPA policy.