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Veterans *and Agent Orange*

Update 2008

Committee to Review the Health Effects in
Vietnam Veterans of Exposure to Herbicides
(Seventh Biennial Update)

Board on Population Health and Public Health Practice

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the metabolism of estrogen, and this leads to a decrease in the amount of estrogen available for binding and activating the estrogen receptor. The ultimate effect of TCDD is an interference with all the bodily functions that are regulated by estrogens. Similarly, the actions of TCDD on the adrenal steroids can adversely affect their ability to regulate glucose tolerance, insulin sensitivity, lipid metabolism, obesity, vascular function, and cardiac remodeling. In addition to changing the amount of hormone present, TCDD has been found to interfere with the ability of receptors to fulfill their role in transmitting hormone signals. Animal models have shown that exposure to TCDD can increase the amounts of enzymes in the body and interfere with the ability of hormones to activate their specific hormone receptors. Those actions of TCDD on enzymes and hormone receptors are thought to underlie, in part, observed developmental and reproductive effects and cancers that are hormone-responsive.

TCDD alters the paths of cellular differentiation. Research performed primarily in cultured cells has shown that TCDD can affect the ability of cells to undergo such processes as proliferation, differentiation, and apoptosis. During the proliferative process, cells grow and divide. When cells are differentiating, they are undergoing a change from less specialized to more specialized. Cellular differentiation is essential for an organism to mature from a fetal to an adult state. In the adult, proper differentiation is required for normal functions of the body, for example, in maintaining a normally responsive immune system. Processes of controlled cell death, such as apoptosis, are similarly important during development of the fetus and are necessary for normal physiologic functions in the adult. Apoptosis is a way for the body to eliminate damaged or unnecessary cells. The ability of a cell to undergo proliferation, differentiation, and apoptosis is tightly controlled by an intricate network of signaling molecules that allows the body to maintain the appropriate size and number of all the specialized cells that form the fabric of complex tissues and organs. Disruption of that network that alters the delicate balance of cell fate can have severe consequences, including impairment of the function of the organ because of the absence of specialized cells. Alternatively, the presence of an excess of some kinds of cells can result in the formation and development of tumors. Thus, the ability of TCDD to disrupt the normal course of a specific cell to proliferate, differentiate, or undergo apoptosis is thought to underlie (at least in part) its adverse effects on the immune system and the developing fetus and its ability to promote the formation of certain cancers.

Definition of Dioxin-like Compounds and TEF and TEQ Terminology

Many compounds have dioxin-like properties: they have similar chemical structure, have similar physiochemical properties, and cause a common battery of toxic responses. Because of their hydrophobic nature and resistance to me-

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