Health Effects of Dioxin

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Notes:


Dr. Schettler notes that this summary is not exhaustive.

The health effects of dioxin have been extensively studied in animals and to a lesser extent, in humans. Binding of a dioxin molecule to a cellular receptor seems to be necessary for expression of biochemical and toxic effects, though some investigators question whether this is how dioxin interferes with the immune system. The dioxin-receptor combination is further processed and transported to the nucleus of a cell where it binds to DNA, interfering with the normal expression of genes. Observed effects include stimulation of enzyme production and alteration of production and metabolism of various hormones, growth factors, and other naturally-occurring chemicals.

Dioxin causes cancer in laboratory animals, and several studies of humans show an increased incidence of various forms of cancer. It is also toxic to the immune system and interferes with normal reproduction and development. Primate studies show an association between dioxin exposure and endometriosis. Dioxin interferes with thyroid hormone levels in infants. These effects may occur at extremely low exposure levels. Large accidental or occupational exposures cause a skin rash (chloracne), weight loss, fatigue, decreased libido, altered glucose metabolism, and neurological damage. In animals studies, susceptibility to the various forms of toxicity varies considerably among species. Species variability is less marked, however, among fetuses and infants, with some health effects detectable after extremely low


Kang HK, Weatherbee L, Breslin PP, exposures even in species whose adults are relatively resistant. There is also evidence of considerable variability of susceptibility among individuals.

Cancer

Dioxin repeatedly causes cancer in virtually all studies in experimental animals at doses well below those which are otherwise toxic. Carcinogenesis is a multi-stage process. Though dioxin does not appear to initiate the events leading to cancer, it behaves as a potent cancer promoter - i.e., once the initial events have occurred, dioxin triggers others necessary for a malignant tumor to appear. It modifies hormones involved in cell growth and differentiation. This undoubtedly explains how dioxin exposure causes an increased incidence of many different types of tumors. Experimental animals exposed to very low doses of dioxin under varying circumstances may develop cancers of different organs, including the liver, adrenal gland, thyroid , skin, lung, nose, and palate.

Studies of cancer in humans exposed to dioxin have produced mixed results. Some show increased incidence of soft-tissue sarcoma, non-Hodgkin's lymphoma, and nasal cancer. A particularly comprehensive study of workers from 12 different industrial facilities showed increased mortality from soft-tissue sarcomas and all cancers among those exposed to dioxin. Others have not found similar increases. Dioxin is classified as a known human carcinogen by the International Agency for Research on Cancer (IARC), and probable human carcinogen by the Environmental Protection Agency (EPA).

Immune system toxicity

Effects on antibody response and other forms of immune-system expression have been extensively studied and documented. Effects on the immune system of the developing organism appear to be among the most sensitive endpoints studied. Extraordinarily low single doses in


17 Luster MI, Boorman GA, Dean JH. Examination of bone marrow, immunologic parameters, and host susceptibility following pre- and postnatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). n J Immunopharmacol 2:301-310, 1980.


Prenatal exposure to dioxin at low levels causes increased growth of transplanted tumor cells in offspring. This may well represent immune-system toxicity since the immune system plays an important role in cancer surveillance and suppression.

A number of studies in humans exposed to dioxin have shown effects on various measurements of the immune system in blood tests. The importance of these changes is not clear. More research is needed to determine if these changes are correlated with increased susceptibility to infection or more severe disease.

Reproductive and developmental toxicity

Animal studies show that dioxin exposure is associated with decreased fertility and litter size and inability to carry pregnancies to term. Offspring have lowered testosterone levels, decreased sperm counts, birth defects, and learning disabilities. Many of these effects are seen at very low exposure levels, demonstrating the exquisite sensitivity of the developing fetus to dioxin. In one rat study, a single low maternal dose of dioxin (0.16 micrograms/kg) on day 15 of pregnancy reduced male testosterone levels, delayed descent of the testicles, made the genital area more female-like, and reduced sperm production and prostate weight in male offspring. It also demasculinized their behavior in months that follow. These results have been replicated in many different laboratories.

Human studies have shown lowered testosterone levels in exposed workers and birth defects in offspring of Vietnam veterans exposed to Agent Orange, an herbicide containing dioxin.

In the U.S., a breast-feeding infant is exposed to...


approximately 50-60 picogram dioxin (TEQ)/kg/day, a level considerably higher than average adult exposure levels of approximately 3 picograms/kg/day. Nursing infant exposures are at levels which cause abnormalities in animal studies. All studies of dioxin toxicity indicate that early development is the lifestage of greatest sensitivity to many of its health effects. However, since many of the adverse effects of fetal or infant dioxin exposure may be apparent only much later in life, human epidemiological studies of the results of those exposures have yet to be conducted since early exposures are impossible to estimate with accuracy.