Noncancer Health Effects and Exposure to 2,3,7,8-TCDD

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Exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) among humans has been associated with adverse health effects in a number of organ systems. Conditions such as chloracne, elevated liver enzymes, nervous system disorders, porphyria cutanea tarda, lipid, endocrine and immunologic changes and reproductive effects have been reported in a number of exposed populations. The majority of effects have been reported among occupationally exposed groups, including chemical production workers, pesticide users, and individuals handling materials treated with 2,3,7,8-TCDD-contaminated pesticides, and among residents of communities contaminated with tainted waste oil (Missouri, USA) and industrial effluent (Seveso, Italy). The purpose of this paper is to highlight the salient results of the studies which evaluated the association between exposure to 2,3,7,8-TCDD and noncancer health effects.

The information describing human health effects attributed to exposure to 2,3,7,8-TCDD-contaminated materials is derived from a wide variety of sources including clinical assessments (case reports) of exposed individuals and analytic epidemiologic studies using case-control, cross-sectional, and cohort mortality designs. The case reports describe the acute outcomes of exposure to 2,3,7,8-TCDD and provide the basis for hypothesis generation for controlled epidemiologic studies; however, they are not suitable for testing causal relationships between exposure and related health effects.[1,2,3]

Cohort mortality and case-control studies have been used to investigate hypothesized increases in malignancies among the various 2,3,7,8-TCDD exposed populations.[4,5,6,7] Cross-sectional studies have been conducted to evaluate the prevalence or extent of disease in living 2,3,7,8-TCDD exposed

groups.[8,9,10,11,12,13,14,15] Many of the earliest studies were unable to define exposure-outcome relationships due to a variety of shortcomings in the studies, including small sample size, poor participation, short latency periods, selection of inappropriate controls, and the inability to quantify exposure to 2,3,7,8-TCDD or to identify confounding exposures. In more recent cross-sectional studies of US chemical workers,[13] US Air Force Ranch Hand personnel,[12] and Missouri residents,[15] serum or adipose tissue levels of 2,3,7,8-TCDD were measured to evaluate 2,3,7,8-TCDD-associated noncancer effects in exposed populations. The ability to measure tissue or serum levels of 2,3,7,8-TCDD for all or a large sample of the subjects confirmed exposure to 2,3,7,8-TCDD and permitted the investigators to test hypothesized dose-response relationships.

Based on the results of two or more studies, recent evidence suggests that chloracne,[6,8,9,16,17,18,19] elevated GGT levels,[9,12,16,20,21,22,23] an increased risk of diabetes,[12,24] and altered male reproductive hormone levels (luteinizing hormone, follicle stimulating hormone and testosterone)[12,25] appear to be long-term consequences of exposure to 2,3,7,8-TCDD. In contrast, studies show possible acute effects but few chronic exposure-related effects for dermatologic endpoints other than chloracne, such as eye lid cyst, hypertrichosis, hyperpigmentation, actinic keratosis and Peyronie's disease.[8] Possible acute but few chronic effects were also observed for liver diseases such as cirrhosis, liver enlargement and hepatic enzyme levels (LDH, AST, ALT and D-glucaric acid) other than GGT, and for porphyrias,[12,16,26] renal, neurologic[8,27] and pulmonary disorders.[12,28] Certain outcomes require further study before their respective relationships to 2,3,7,8-TCDD can be more definitively assessed. These include circulatory and heart diseases,[12] reproductive outcomes[29,30,31,32,33,34] immunologic disorders,[12,35] lipid levels,[8,12,22] and thyroid function.[12,36]

The body of research to date suggests that human exposure to 2,3,7,8-TCDD does produce a variety of metabolic or health effects, some which are short-term, and others which are chronic. The health effects have generally been observed in highly exposed populations.

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