ARE DIOXIN BODY BURDENS SURROGATES FOR OTHER RISK FACTORS IN ASSOCIATIONS BETWEEN DIOXIN AND DIABETES?

Haws LC[1], Scott PK[2], Unice KM[2], Gough M[3]; Harris MA[4]; Staskal DS[1], Paustenbach DJ[5], and Pavuk M[6]

[1]ChemRisk, Austin, TX, USA; [2]ChemRisk, Pittsburgh, PA, USA; [3]Consultant, Bethesda, MD, USA; [4]ChemRisk, Houston, TX, USA; [5]ChemRisk, San Francisco, CA, USA; [6]SpecPro Inc., San Antonio, TX, USA.

Introduction

In 1999, the National Academy of Science's Institute of Medicine (IOM) established a committee to examine the evidence regarding an association between Type II diabetes and exposure to dioxin and other chemicals in herbicides used in Vietnam. As a result of their review, the IOM committee concluded that there was "limited/suggestive evidence of an association between exposure to the herbicides used in Vietnam or the contaminant dioxin and Type II diabetes"[1]. In reaching this conclusion, the IOM committee stated, "No one paper or study was determinative in reaching this decision. Instead, the committee found that the information accumulated over years of research now meets the definition established for limited/suggestive evidence-that is, *evidence is suggestive of an association between herbicides and the outcome, but limited because chance, bias, and confounding could not be ruled out with confidence*" (emphasis in original)[1]. Examples of limitations cited by the IOM committee include the apparent lack of a dose-response in studies relating dioxin and diabetes, the inability to rule out potential confounders, and conflicting findings (e.g., negative [inverse] trend between diabetes mortality and cumulative TCDD exposure reported by Steenland and coworkers[2]).

The IOM Committee relied heavily upon data from the Air Force Health Study (AFHS), an ongoing prospective epidemiological study that compares the health of veterans of Operation Ranch Hand, the Air Force unit responsible for spraying millions of gallons of Agent Orange during the Vietnam War, with a Comparison population of Air Force veterans who served in Southeast Asia during the same time period (1962-1971) but were not involved in any spraying activities (hereafter referred to as "Comparisons")[3]. Comparisons were individually matched to Ranch Hands based on age, race, and military occupation. Physical examinations and interviews were conducted in 1982, 1985, 1987, 1992, 1997, and 2002.

In this paper, we describe our analyses of the relationships between known risk factors for diabetes, as well as between dioxin and diabetes. Henriksen and coworkers first reported an association between increasing blood lipid TCDD and diabetes prevalence in the Ranch Hands[4]. However, as the IOM noted, this apparent relationship "is difficult to understand, however, given that the diabetes rates in the comparison subjects were as high as in Ranch Hand Veterans despite the much lower dioxin levels in the comparison group"[1]. Longnecker and Michalek reported that diabetes increased with increasing dioxin serum levels in the Comparisons as well[5]. In a subsequent analysis, Michalek and Ketchum divided both populations into quintiles based on dioxin serum levels[6]. They found dose responses in both populations, but at different dioxin serum levels. Diabetes prevalence was 26% in the fifth (i.e., highest-exposed) quintile of Comparisons and 25% in the fifth quintile of Ranch Hands. However, the serum levels of dioxin differed significantly: the fifth quintile of Comparisons ranged from 6 to 55 ppt dioxin, whereas the fifth quintile of Ranch Hands from 36 to 618 ppt dioxin. We believe that these findings warrant further investigation of the association between Type II diabetes and dioxin.

Materials and Methods

Air Force researchers overseeing the AFHS provided us with study data regarding age, race, length of tour of duty, start and end dates for tour of duty, family history of diabetes, serum dioxin levels, changes in body weight, body mass index, percent body fat, severity of diabetes, and fasting glucose and insulin measurements in Comparisons