TEMPORAL TRENDS IN BODY-BURDEN SUGGEST THAT DIOXIN EXPOSURES IN THE GENERAL POPULATION HAVE DECLINED SIGNIFICANTLY

Sean M. Hays[1] and Lesa L. Aylward[2]

Exponent, Inc. 4940 Pearl East Circle, Ste. 300 Boulder, CO 80301 shays@exponent.com [1]
BBL Sciences, Inc. 1943 Isaac Newton Sq. East., Ste. 24. Reston, VA 20190 lla@bbl-inc.com [2]

Introduction

Jackson and Michalek recently reported the mean serum lipid TCDD levels measured in 1987, 1992, and 1997 in 1419 U.S. Air Force Vietnam era veterans who were chosen to provide a comparison population for the Air Force (i.e., the "Ranch Hand" population of herbicide handlers).[1] The comparison population did not handle Agent Orange or other herbicides, and thus have exhibited serum TCDD levels similar to those measured in the general U.S. population (Patterson et al., 1990).[2] Jackson and Michalek reported a statistically significant decrease in mean serum lipid TCDD levels in the comparison population, from 4.5 parts per trillion (ppt) in serum lipid in 1987 to 2.0 ppt in 1997.[1] The 1997 mean levels (2.0 ppt) are similar to those currently measured in the general population in the U.S.[3] An even greater rate of decline has been reported by researchers in Europe.[4] Specifically, total TEQ levels in human blood have declined by more than 80% over the period of 1986 to 1996.

These measured decreases would seem to suggest that human exposure to TCDD and related compounds is declining significantly, particularly given the long half-life of elimination of TCDD in humans (approximately 7.5 years[5]) However, some researchers claim that the concentrations of PCDD/Fs in foods have not changed substantially over the last 10 years.[6] In order to more definitively assess the decline in TCDD dose associated with the measurements of Jackson and Michalek,[1] we simulated serum lipid TCDD level changes resulting from decreases in background intake of TCDD using standard kinetic assumptions. The results are evaluated with respect to current findings regarding environmental and dietary TCDD concentrations.

Methods and Materials

As reported in Jackson and Michalek, the serum sampling data were obtained from males with no known occupational exposures to TCDD.[1] Because the average age of the participants was 48 years, it is likely they were approaching steady state. The lipid-adjusted levels of 2,3,7,8-TCDD declined from 4.5 ppt in 1987 to 2.0 ppt in 1997. The difference in the mean levels measured in 1987 and 1997 was statistically significant at a confidence level of 0.001.. Assuming first-order kinetics with a 7.5-year half-life of elimination, body fat levels of approximately 25 percent, and a body weight of 70 kilograms, 1987 intake levels (absorbed dose) would have been approximately 0.25 pg/kg body weight per day. From this starting point, we simulated changes in serum lipid TCDD level resulting from changes in intake dose. We assumed a one-compartment model description for the intake and

elimination of TCDD. Microsoft Excel® (Microsoft Corporation) was used to perform the model simulations.

Results and Discussion

We found that steep decreases in TCDD intake are required to result in simulated serum lipid TCDD levels that match the measured serum data from Jackson and Michalek.[1] Figures 1A and 1B show that an assumption of either a simple linear decrease (Figure 1A) or an exponential decrease (Figure 1B) in dose rate predicts that TCDD intake levels must have decreased to essentially zero by 1992 to produce a corresponding serum lipid TCDD decrease from 4.5 to 2.0 ppt over the 10-year period.

Sources of variability or uncertainty in this analysis include inter-individual variations in half-life of elimination, changes in percent body fat in the study population, and the assumption that the serum lipid TCDD levels were at steady state in 1987. Estimates of the half-life of elimination for TCDD range from approximately 6 to 9 years.[5,7] A longer half-life than the one used in our analysis would result in estimates of even greater declines in intake needed to produce the observed changes in mean serum levels, while even a half-life as short as 6.0 years still requires orders-of-magnitude decreases in intake levels. The body mass index of the subjects reported on by Jackson and Michalek[1] changed only slightly over the 10-year period (27.9 and 28.2 in 1987 and 1997, respectively), so changes in this parameter are unlikely to have had a substantial effect on the observed serum lipid TCDD levels. We also examined the possibility that 1987 serum lipid TCDD levels had already decreased from earlier, higher levels. Although this assumption reduced the estimated 1987 dose rate, it did not change the conclusion that intake rates between 1987 and 1997 must have decreased dramatically. In short, it does not appear that different assumptions regarding half-life, body fat, or steady state would influence the outcome of our analysis.

In summary, it would appear that substantial and rapid decreases in background TCDD intake (i.e., orders-of-magnitude decreases between 1987 and 1997) are the most plausible explanation for the observed serum TCDD decrease from 4.5 to 2.0 ppt. Because similar decreases (50 to 70 percent) in background total serum lipid toxic equivalency (TEQ) of all dioxins and furans have been observed over this same time period,[4] it is likely that similarly dramatic decreases in intake have occurred for other dioxin-like congeners. This suggests that we need to re-examine our current general population dioxin intake level estimates and the underlying data, recognizing that current levels of background exposure may be dramatically different from those of only a few years ago.

Given that TCDD and related congeners can still be found in foods, this finding draws into question the hypothesis that diet has been the primary source of exposures to dioxin. Another possible source of significant exposure to TCDD in the past is emissions from combustion of leaded gasoline.[8] As leaded gasoline use has been phased out, exposures to dioxins and furans from this source have decreased as well, and if these emissions were a significant source of dioxin and furan exposure, relative to diet, the decrease in such emissions may have had a significant impact on background body burdens.

Jackson and Michalek conclude that their results are "consistent with the hypothesis that efforts to reduce emissions from industry are having beneficial effects."[1] Our analysis indicates that the effects of these reductions on general population exposure (and any associated reductions in potential health risks) may be far greater than has been generally recognized to date.

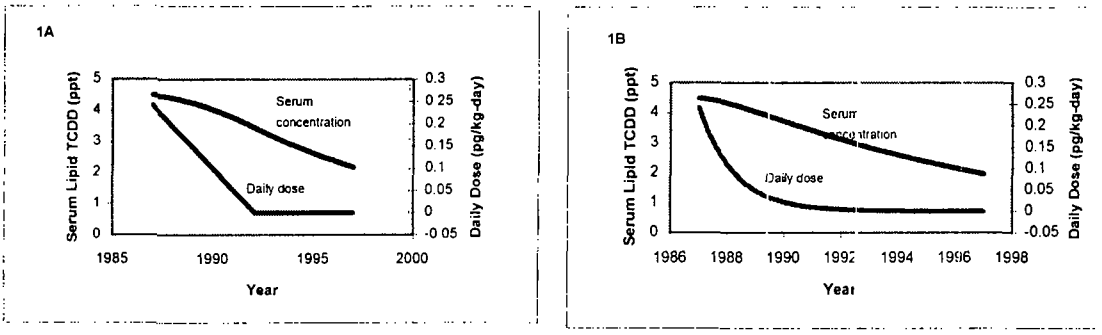

Figure 1: Simulated serum lipid TCDD concentration and required dose changes assuming first-order kinetics and assumptions specified in the text, assuming A) a linear decline in dose from estimated 1987 levels, or B) an exponential decline in dose from estimated 1987 levels.

References

1. Jackson Jr. W.G. and Michalek J.E. (2001) J Exposure Anal Environ Epidemiol. 11, 50-55.
2. Patterson D.G., Needham L.L., and Andrews J.S. (1990) In: Clinical Management of Poisoning and Drug Overdose (L.M. Haddad and J.F. Winchester, Eds.), W.B. Saunders Co., Philadelphia, pp. 528-537.
3. U.S. Environmental Protection Agency (EPA) (2000) Exposure and human health reassessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. Appendix to Part 1: Estimating exposure to dioxin-like compounds. May Draft Final.
4. Papke O. (1998) Environ Health Perspect. 106(Suppl. 2), 723-731.
5. Michalek J.E. and Tripathi R.C. (1999) J Toxicol Environ Health Part A. 57, 369-378.
6. Schecter, A., Cramer, P., Boggess, K., Stanley, J., Papke, O., Olson, J., Silver, A. and Schmitz, M. (2001) J Toxicol. Environ. Health. 63(1), 1-18.
7. Flesch-Janys D., Becher H., Gurn P., Jung D., Konietzko J., Manz A., Papke O. (1996) J Toxicol Environ Health. 47(4), 363-78.
8. Marklund, S., Rappe, C., Tysklind, M., and Egeback, K.E. (1987) Chemosphere. 16(1), 29-36.