VIETNAMESE DIOXIN BLOOD AND MILK LEVELS 1970-1999 AND IMPLICATIONS FOR FUTURE EPIDEMIOLOGY STUDIES

Arnold Schecter¹, Le Cao Dai², Lori Fischbach¹, and Olaf Päpke³

 ¹University of Texas-Houston School of Public Health, Satellite Program at University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, V8.112, Dallas, TX 75235, USA
² Vietnam Red Cross Agent Orange Fund, 82 Nguyen Du Street, Hanoi, Vietnam
³ERGO Forschungsgesellschaft mbH, Geierstrasse 1, 22305 Hamburg, Germany

Introduction

The largest known dioxin contamination is believed to have occurred in Vietnam between 1962 and 1971 from spraying of Agent Orange. Approximately 12,000,000 gallons of Agent Orange, half 2,4-D and half 2,4,5-T phenoxy herbicides, was sprayed heavily over discrete areas in the south of Vietnam for purposes of defoliation and crop destruction. Most, 85 %, was sprayed by fixed wing aircraft, with the remainder from back pack, helicopter or naval spraying. Several hundred pounds of 2,3,7,8-TCDD, the most toxic of the dioxins, contaminated the Agent Orange¹⁻

Dioxins are currently believed to lead to serious human health consequences including cancer mortality, ischemic cardiovascular disease mortality, immune system alteration, reproductive and developmental pathology, endocrine disruption in children and adults, nervous system damage, liver pathology, transient elevation of blood lipids, skin rashes, rarely including chloracne (rarely), and death⁴⁻⁶.

Vietnam provides a living laboratory for studying the health effects of dioxin contamination and of Agent Orange with its dioxin contaminant. We have previously documented marked elevation in dioxin levels from Agent Orange exposure in the breast milk of nursing Vietnamese mothers, in blood, and in fat tissue. Human milk collected in 1970 in two villages in the South that had been sprayed with Agent Orange had 2,3,7,8-TCDD levels as high as 1,850 ppt (lipid)⁷. Most Vietnamese, however, do not have elevated dioxin from Agent Orange.

We review our previous data after converting them to the new WHO dioxin toxic equivalency values and present new blood dioxin measurements from 1999 samples. We conclude that it is relatively easy to find large populations in Vietnam with elevated dioxin levels from Agent Orange (and sometimes from other sources), as well as a large population with low dioxin body burden, and that Vietnam offers a unique opportunity to learn about the consequences of dioxins in humans. Men, women and children have been exposed to dioxin for a number of decades in Vietnam and several generations can be studied.

Materials and Methods

Whole blood samples from Vietnam were collected in the early 1990s at nine sites in southern Vietnam, four sites in the central region, and two sites in Hanoi, in the North. Blood of 30 to 50 donors at each site was sometimes pooled⁷. During 1999, a single pooled sample from Ho Chi Minh City and eight individual samples from individuals thought by Vietnam Red Cross to have been exposed to Agent Orange were collected. All samples were collected in chemically

ORGANOHALOGEN COMPOUNDS 417 Vol. 44 (1999)

Epidemiology: Recent Results and Research Paths P415

cleaned glass jars, frozen at -20° C, and shipped to the dioxin laboratories. Analysis was performed using high resolution gas chromatography-mass spectrometry. The methods have been described previously and will not be repeated here⁸.

Results and Discussion

Results of dioxin analyses of pooled blood samples collected in Vietnam in 1991-92 are graphically presented in Figure 1, along with results of analyses of blood from the general population of the United States and Germany collected in 1996^{9,10}. Measured levels have been converted to dioxin toxic equivalents (TEQ) using the 1998 WHO toxic equivalency factors (TEFs)¹¹. These results have been reported previously using the older I-TEFs^{12,13}. Total TEQ for 3 regions of Vietnam, the United States, and Germany is presented using both sets of TEFs. Total TEQs using 1998 WHO TEFs are increased by 10-20% in comparison with the previous I-TEF results.

The increased mean level of 2,3,7,8-TCDD in pooled and individual samples of blood from Central and Southern Vietnam versus Northern Vietnam corresponds to the areas where Agent Orange was most heavily sprayed.

Epidemiologic studies have examined the association between dioxin exposure and the incidence of cancer, endometriosis, endocrine disorders, cognitive impairment, spontaneous abortion, congenital malformations, and immune deficiency in several populations, and have consistently reported a positive association between dioxin exposure and total cancer mortality, soft tissue sarcoma and non-Hodgkin's lymphoma³⁻⁶. However, only a few epidemiologic studies have examined the risk of health effects from dioxin exposure in exposed Vietnamese populations^{2, 14-16}. Inadequate individual measures of exposure and outcomes, and inadequate control of confounders can be noted in some of these studies. In one case-control study aimed at examining the association between Agent Orange exposure and the risk of gestational trophoblastic disease in Ho Chi Minh City, controls were matched to cases on residence, yet residence was also the method of measuring the exposure, thus diluting the estimated measure of effect¹⁴. Future high quality epidemiologic studies of individuals in Southern and Central Vietnam are needed to assess the long-term health effects of dioxin exposure, especially when the dioxin is a component of the phenoxy herbicide mixture found in Agent Orange. Due to the high cost of dioxin analyses and incomplete medical records in Vietnam, case control studies with appropriate control selection are the most feasible design to evaluate potential associations between elevated dioxin level and adverse health outcomes.

Acknowledgments

This work was partially funded by a number of sources, which are gratefully acknowledged. They include the CS Fund, the Christopher Reynolds Foundation, the Samuel Rubin Foundation, and the Kunstadter Family Foundation. We also thank the Vietnam Red Cross and the Ministry of Science, Technology and the Environment (M.O.S.T.E.) for assistance during the 1999 work in Vietnam.

References

1. Westing, A.H. Herbicides in War: The Long-term Ecological and Human Consequences, London: Taylor & Francis, 1984.

ORGANOHALOGEN COMPOUNDS 418 Vol. 44 (1999)

Epidemiology: Recent Results and Research Paths P415

- 2. Harada M, Sakai T, Hattori R, et al. *Herbicides in War: The long-term effect on man and nature.* 2nd International Symposium, Hanoi, pp.167-9, 1993.
- 3. Institute of Medicine. Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides. *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam*, National Academy Press (1994).
- 4. Schecter AJ. Dioxins and Health, Plenum Press, New York (1994).
- Institute of Medicine. Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides. *Veterans and Agent Orange: Update 1996*, National Academy Press (1996).
- World Health Organization International Agency for Research on Cancer, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 69 Polychlorinated dibenzo-paradioxins and polychlorinated dibenzofurans, 1997.
- Schecter A, Dai LC, Thuy LTB, Quynh HT, Minh DQ, Cau HD, Phiet PH, Phuong TN, Constable JD, Baughman R, Päpke O, Ryan JJ, Fürst P, and Räisänen S. Agent Orange and the Vietnamese: The persistence of elevated dioxin levels in human tissues. *Am. J. Public Health* 85:516-22, 1995.
- 8. Päpke O, Ball M, Lis ZA, and Scheunert K. PCDD/PCDF in whole blood samples of unexposed persons, **1989**, *Chemosphere* 19:941-8.
- 9. Päpke O. PCDD/PCDF: Human background data for Germany, a 10-year experience. *Environ Health Perspect* 106 (Suppl 2): 723-31,1998.
- Schecter A and O Päpke. Dioxins, dibenzofurans and coplanar PCBs in blood of persons residing near a PCB manufacturing facility in the United States. *Organohalogen Compounds* 38:175-178, 1998.
- Van den Berg M, Birnbaum L, Bosveld ATC, Brunström B, et al. Toxic equivalency factors (TEFs) for PCBs, PCDDs, PCDFs for humans and wildlife. *Environ Health Perspect* 106:775-92, 1998.
- 12. North Atlantic Treaty Organization, Committee on the Challenges of Modern Society., International Toxicity Equivalency Factor (I-TEF) Method of Risk Assessment for Complex Mixtures of Dioxins and Related Compounds, Pilot study on international information exchange on dioxins and related compounds Report No. 176, 1988, 1-26.
- North Atlantic Treaty Organization, Committee on the Challenges of Modern Society. Scientific Basis for the Development of the International Toxicity Equivalency Factor (I-TEF) Method of Risk Assessment for Complex Mixtures of Dioxins and Related Compounds, Pilot study on international information exchange on dioxins and related compounds, Report No. 178, 1988, 1-56.
- 14. Ha MC, Cordier S, Bard D, et al. Agent Orange and the risk of gestational trophoblastic disease in Vietnam, *Arch Environ Health* 51(5):368-74, 1996 Sep-Oct.
- Nguyen TNP, Tran TT, Pham KP. An estimate of reproductive abnormalities in women inhabiting herbicide sprayed and non-herbicide sprayed areas in the south of Vietnam, 1952-1981. *Chemosphere* 18(1-6):843-6, 1989.
- Tanh V, Chi HTK, Thai PN. Cohort study on reproductive anomalies in two villages in Song be province, Vietnam. *Herbicides in War: The long-term effect on man and nature*. 2nd International Symposium, pp.184-9, 1993.

ORGANOHALOGEN COMPOUNDS 419 Vol. 44 (1999)

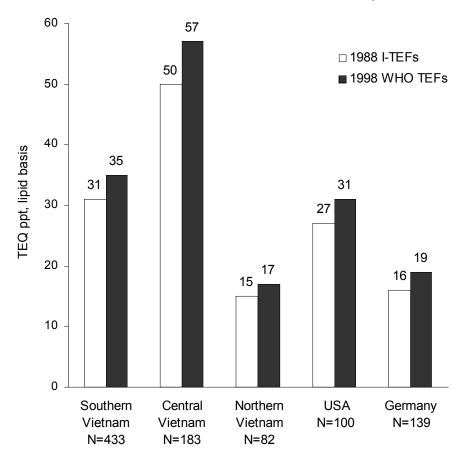


Figure 1. Blood TEQ for dioxins and dibenzofurans in three regions of Vietnam, 1991-92, and in the USA and Germany, 1996

Totals calculated with 1988 I-TEFs 12,13 and with WHO 1998 TEFs 11 pg/g (ppt) lipid basis non-detects=1/2 limit of detection

ORGANOHALOGEN COMPOUNDS Vol. 44 (1999) 420