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Agent Orange/Dioxin and Causation of Human Disease  
Spina Bifida and Birth Defects

There are people that for selfish reasons are shocked by the decision of the Department of Veterans Affairs to award service connected disability compensation to the children of Vietnam Veterans whom suffer spina bifida. The children are the offspring of American soldiers whom were exposed to Agent Orange/Dioxin during the Vietnam War. The scientific evidence shows that there is a strong connection between exposure in the parent to phenoxy herbicides, dioxins, difurans, PCBs, and birth defects including spina bifida in their offspring.

Public Law 96-151 enacted in 1979 mandated the Veterans Administration to do a worldwide literature review and scientific analysis on Agent Orange/Dioxin and other phenoxy herbicides. Volume III of this analysis was done by Clement and Associates and published in 1983 by the Veterans Administration. I will quote page 185-186 in the chapter on TERATOGENICITY AND REPRODUCTIVE TOXICITY, animal studies, summary and conclusions:

"The results for TCDD in particular and to a lesser extent for 2,4,5-T and 2,4-D in a number of non human species are cumulatively so compelling that it is difficult to believe that humans might not be susceptible to the reproductive effects of these compounds."

The little human reproductive studies in 1983 were essentially negative; however, Clement and Associates suggested that larger epidemiological studies might prove conclusive evidence of a positive association.

The studies on Vietnam Veterans, which have been done by the U.S. Government, have been small and therefore, the results have to be interpreted with caution. If a birth defect study of a large population of Vietnam Veterans were done, the results would be more significant. The U.S. Government has been able to utilize this flaw as a criticism when significant results have been achieved.

~~if we examine~~

The Ranch Hand Reproductive Outcome studies ~~showed~~ e. In the Ranch Hand Study released February 24, 1984 there was a statistically significant increase in all birth defects in Ranch Hand offspring. The one released on December 17, 1984 showed even higher elevated risks of birth defects. It is probably this reason that made the National Academy of Sciences attach the significance it did to these reports. BECAUSE a larger study would very likely achieved shocking results and this would be particularly true for spina bifida. The

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Ranch Hand birth defect study published in 1995 did not show a clear pattern of spina bifida in excess but indeed there was an excess. This study was of high quality and the National Academy of Sciences recognized this fact. Once again, if the numbers of participants ~~were~~ <sup>had</sup> been larger, the results would have been more definitive.

~~It~~ <sup>hit me</sup> ~~illustrates~~ <sup>Some in</sup> the point about exposure in a large group of Vietnam Veterans. The U.S. Government ~~has~~ <sup>have</sup> argued that the only veterans that had any significant exposure to Agent Orange/Dioxin were the sprayers. It is precisely this hypothesis that is incorrect. We know now that there was significant exposure to Agent Orange/Dioxin by Vietnam Veterans who ~~were~~ were not sprayers. Military records show that some 300 gallons were sprayed into the water supply at the massive base in Long Binh in 1969. If an independent study were done on Vietnam Veterans and birth defects utilizing an exposure index that was practical, there would be a statistically significant higher rate of birth defects including spina bifida in the more likely exposed. The only problem being that <sup>??</sup> the Long Binh report shows, ~~it~~ <sup>it</sup> would be hard to rule out any in-country Vietnam Veteran from high exposure. If, however, Vietnam Veterans were compared to other veterans of the same era utilizing a practical index of exposure, the results might very well be startling. <sup>their children's</sup>

The 1988 Centers for Disease Control study may be an example of the utility of exposure indexes. The estimated risk for fathering babies with spina bifida was higher for Vietnam Veterans with a higher opportunity for exposure to Agent Orange/Dioxin. Interestingly, other birth defects showed the same relationship, such as cleft palate.

Lets now look at a recent study which did utilize a large population in relation to exposure to amongst other chemicals - phenoxy herbicides. These phenoxy herbicides had to have some amount of dioxin contamination but keep in mind that phenoxy herbicides are hormone disruptors in themselves.

The newest study on chemicals and birth defects is titled "Pesticide Applicators, Biocides, and Birth Defects in Rural Minnesota". It is published in the April, 1996 edition of "Environmental Health Perspectives", page 394-399. The hypothesis that related to this study was that there might be a high rate ~~x~~ of birth defects in the offspring of pesticide applicators. The Environmental Protection Agency in conjunction with the University of Minnesota studied 4935 births to 3472 pesticide applicators. "The birth defect rate for all birth anomalies was significantly increased in children born to private appliers." The conclusion of the study was that "the pattern of excess frequency of birth anomalies by

pesticide use, season, and alteration of sex ratio suggests exposure-related effects in appliers and the general population of the crop growing region of western Minnesota". This finding itself is significant but there are even more significant findings. I will quote three paragraphs here to ~~elicit~~ <sup>highlight</sup> the significance of Agent Orange/Dioxin type chemicals. The first quote is taken from page 397 and it states the following"

"The data show that in regions where chlorophenoxy herbicides and/or fungicides are frequently used, infants conceived in spring show a significant increase in birth defects compared to infants conceived in other seasons."

On page 398 the following is stated:

"In the production of <sup>which was one of the investigations in Agent Orange</sup> spring wheat, about 90% of the acreage is treated with herbicide. In 1991 more than 70% of the treated acreage was treated with chlorophenoxy herbicides (2,4-D and or MCPA) accounting for approximately 90% of state use. Approximately 6% of the wheat crop was treated with fungicides".

On page 398 is the following quote:

"With regard to fertility, a recent clinical epidemiologic study of 2,4-D reports that the herbicide may be spermatotoxic in appliers. Along these same lines, preliminary data gathered by our laboratory (unpublished) in regard to birth rate indicate that in the 1990 census year, the frequency of births among appliers (ages 15-44) in the five counties with the highest 2,4-D herbicide/fungicide use was approximately half that of the general population (males ages 15-44) living in the same five county area ( $p < 0.001$ )."

I would like to point out that "specific birth defect categories circulatory/respiratory, urogenital, and musculoskeletal/integumental showed significant increases". These categories would include spina bifida.

~~I think at this time it would be a practical idea to suggest that~~ There are a number of plausible biological mechanisms by which Agent Orange/Dioxin chemicals could be <sup>be</sup> cause birth defects from parents who were exposed to these chemicals. This ~~is~~ <sup>is</sup> very significant ~~in~~ <sup>in</sup> ~~an~~ <sup>an</sup> ~~analysis~~ <sup>analysis</sup> paternally mediated birth defects.

The Minnesota study indicated that 2,4-D could be spermatotoxic to appliers. This is one way that paternally mediated birth defects could take place in males exposed to Agent Orange/Dioxin type chemicals.

Another possible mechanism by which Agent Orange/Dioxin

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could cause paternally mediated birth defects is by direct transmission of dioxin from the male to the egg of the female. Dr. Arnold Schecter of the State University of New York at Binghamton studied the semen analysis of Michigan Vietnam Veterans. Dr. Schecter found dioxin in a pooled sample of seminal fluid from these veterans. It is very likely that the dioxin in the seminal fluid would reach the egg of a female.

~~I suppose that one could~~ <sup>Some</sup> argue that dioxin at the part per trillion level would not be toxic to a developing fetus. However, Dr. Peterson at the University of Wisconsin found that dioxin at the low part per trillion level could cause damage to the developing fetus in animals.

A book recently published <sup>er</sup> titled "Our Stolen Future" documents the field of emerging scientific research on how dioxin type chemicals disrupt "delicate human systems". On page 112 the author Theo Colburn documents the potency of dioxin. I quote the following in relation to dioxin in pregnant rats:

"As they had expected, the dioxin did damage to the male reproductive system if the pups were exposed during a critical period in their prenatal development. What surprised the scientists was how little dioxin it took to do the damage. They hadn't given a large dose or repeated doses, but they saw long-term effects on male pups when the mother rats had ingested only one dose of an astonishingly tiny amount of dioxin at a critical moment. It had taken just a single hit".

"The lowest doses given to the mother rats had been very near to the levels of dioxin and related compounds reported in people in industrialized countries such as the United States, Japan, and those in Europe".

One last note; A study of immense magnitude has just been released. It is titled "Reproductive Effects of Paternal Exposure to Chlorophenolate Wood Preservatives in the Sawmill Industry". It is published in the Scandanavian Journal of Work, Environment and Health, Vol. 22, page 267-273, 1996. I will quote directly from this study.

The abstract states the following:

"The offspring of male sawmill workers were at increased risk for developing anomalies of the eye, particularly congenital cataracts; elevated risks for developing anencephaly or spina bifida and congenital anomalies of genital organs were shown according to specific windows of exposure".

On page 272 the following is stated:

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"The maximal index of exposure to chlorophenols during the preconception period was positively related to the prevalence of anencephaly or spina bifida in the exposed father's progeny".

This study shows exactly what I ~~said~~ <sup>suggested earlier in this document that</sup> a large study on dioxin type chemicals would show. This study was done to determine "whether paternal exposure to DIOXIN-contaminated chlorophenols is associated with an increased risk of congenital anomalies or other adverse reproductive outcomes in offspring". This study has the numbers which were 19675 births between 1952 and 1988 in a cohort of 9512 fathers. The results are statistically significant. This study also documents the plausible mechanisms of toxicity for paternally mediated birth defects. Precision of exposure was "enhanced by restricting the exposure variable to relevant time windows or critical periods related to time of conception or birth".

~~This is the extent of my small analysis but I think the evidence will show that the National Academy of Sciences made the right decision. However, I believe with the Minnesota study and Sawmill study there is sufficient evidence of an association between Agent Orange/Dioxin and spina bifida. Also, we should be looking at other birth defects.~~ <sup>for a com</sup> <sup>Institute of Medicine</sup>

George Claxton



to move the next finding from 10M to move spinal bifida to 2nd top category of "Sufficient Evidence of an ASSOCIATION" ~~and that~~