Association of Silicofluoride Treated Water with Elevated Blood Lead

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Abstract: Previous epidemiological studies have associated silicofluoride-treated community water with enhanced child blood lead parameters. Chronic, low-level dosage of silicofluoride (SiF) has never been adequately tested for health effects in humans. We report here on a statistical study of 151,225 venous blood lead (VBL) tests taken from children ages 0-6 inclusive, living in 105 communities of populations from 15,000 to 75,000. The tests are part of a sample collected by the New York State Department of Children's Health, mostly from 1994-1998. Community fluoridation status was determined from the CDC 1992 Fluoridation Census. Covariates were assigned to each community using the 1990 U.S. Census. Blood lead measures were divided into groups based on race and age. Logistic regressions were carried out for each race/age group, as well as above and below the median of 7 covariates to test the relationship between known risk factors for lead uptake, exposure to SiF-treated water, and VBL >10µg/dl. RESULTS: For every age/race group, there was a consistently significant association of SiF treated community water and elevated blood lead. Logistic regressions above and below the median value of seven covariates show an effect of silicofluoride on blood lead independent of those covariates. The highest likelihood of children having VBL>10µg/dl occurs when they are both exposed to SiF treated water and likely to be subject to another risk factor known to be associated with high blood lead (e.g., old housing). Results are consistent with prior analyses of surveys of children's blood lead in Massachusetts and NHANES III. These data contradict the null hypothesis that there is no difference between the toxic effects of SiF and sodium fluoride, pointing to the need for chemical studies and comprehensive animal testing of water treated with commercial grade silicofluorides. © 2000 Intox Press, Inc.

Key Words: Lead Neurotoxicity, Silicofluorides, Water Fluoridation, Venous Blood Tests, Public Health

INTRODUCTION

Over 91% of US fluoridated water is treated with either sodium silicofluoride (Na2SiF6) or fluosilicic acid (H2SiF6) — henceforth, the silicofluorides or SiFs. Less than 10% is treated with simple sodium fluoride (NaF). Whereas NaF was the model compound used in the 1940s for demonstrating safety and efficacy, and has been submitted to exhaustive animal testing for decades (e.g., McClure, 1962; Largent, 1961; Dunipace et al., 1995, 1996, 1998a, 1998b; Jackson et al., 1997), the same cannot be said of the SiFs. The Assistant Administrator of the EPA recently acknowledged (Fox, 1999) that his agency knew of no study of human health effects of chronic low-level exposure to either of the SiFs. Here we report data suggesting that SiF may enhance the uptake of lead from other environmental sources.

As is well known, many environmental and behavioral risk factors have previously been associated with increased lead levels among children. Among these are age, race, sex, income (or poverty), size of community (esp. between urban areas of greater and less than 1 million as well as between urban, suburban, and rural communities), location of community (including presence of soils with high lead levels), age of housing (presence of lead paint), lead in excess of 15 ppb in public water supplies, individual calcium or iron deficiency, maternal smoking, parental education and alcohol consumption (e.g., Needleman, 1992; Hense et al., 1992; Cezard et al., 1992; Weitzman et al., 1993). Using community rates, a recent study of over 238,000 Massachusetts children found...
METHODS

Over 1.2 million blood lead tests were collected by the State of New York, mostly between the years 1994 and 1998. We analyzed records in all communities between 15,000 and 75,000 in population (as determined using the 1990 US Census) which had at least 100 blood lead tests (five had fewer than 100 tests). Selecting communities in this size range avoided the complication of non-comparable large cities (such as New York City) and controlled for the effects of large population size as well as the environmental conditions in inner cities. For each community, we determined whether it uses SiF using the CDC 1992 Fluoridation Census. Olean, New York — the sole community using sodium fluoride — and towns using multiple chemicals were dropped from the multivariate comparisons, which focus on the contrast between non-fluoridated communities and those using one of the silicofluorides (fluosilicic acid or sodium silicofluoride) at 1.0 ppm. Levels of other factors associated with increased blood lead, such as age of housing and % aged 0-5 who are poor were determined from the 1990 U.S. Census. We are thus able to control at the individual level for factors such as race, age, community size and SiF exposure, but only indirectly for such factors as age of housing and poverty.

Of over 256,000 children tested, data for 151,225 were from venous blood tests, whereas the remaining 105,148 only had data from capillary blood. Because some researchers suggest greater reliability for the former (Sargent, Dalton and Klein, 1999; Morris et al., 1999), we limit this paper to VBL (cf. Schlenker et al., 1993; Hernandez-Avila et al., 1998). In the future, it may be possible to study both methods. To minimize effects within the range of resampling error (Morris et al., 1999; Sargent and Dalton, 1996), we focus on the percent of children whose venous blood lead was in excess of 10μg/dL.

Researchers have differed widely on the threshold level of blood lead level representing danger to humans: although the conventional level for identifying threats to health and behavior has been 10μg/dL, both higher and lower levels have been proposed. Some (e.g., Sargent, Dalton and Klein, 1999) claim it is not necessary to report levels below 15μg/dL, others (e.g., Lanphear, 1999) suggest that any detectable lead in blood indicates unacceptable risks to development, health, and cognition. For evidence that this choice does not bias our findings, see Results below.

In a study such as this, it is also of utmost importance to test for covariance in order to avoid spurious correlation. We were able to control for age and race at the individual level by analyzing each age/race group separately. For other possible correlates of elevated VBL, we were only able to control at the community level.
We chose seven variables from the U.S. census which tend to predict elevated VBL as likely covariates of elevated blood lead. Because children in communities with high levels of one or more of these variables are more likely to have high blood lead levels, our analysis computes a separate logistic regression for each race above and below the median of each covariate. By doing this one can determine whether there is an effect of SiFs independent of these covariates and, indeed, that was found to be the case.

RESULTS

As a measure of the likelihood of dangerous lead levels in children, we have selected the conventional cutting point of 10 µg/dL in venous blood lead (VBL). To confirm that this choice would not bias our results, however, we first considered blood lead levels at increments of 5 µg/dL to assess effects of silicofluoride among Blacks in our sample. The data show that, for lead levels above 5 µg/dL, as the measured range increases from between 10 and 15 µg/dL to over 20 µg/dL, there are progressively higher odds ratios attributable to SiF (Table 1). These findings indicate that, for a dichotomous measure, the traditional cutting point (10 µg/dL) does not bias our findings and the choice of another measurement would not change the results in a material way. Indeed, using a higher cut-off point such as 15 µg/dL (as proposed by Sargent, Dalton, and Klein, 1999) might be viewed as biased in favor of our hypothesis because odds ratios among Blacks are so much higher for lead levels of 15 to 20 µg/dL (3.5) or over 20 µg/dL (3.8) than for lead levels between 10 and 15 µg/dL (2.7) or between 5 and 10 µg/dL (1.3). Moreover, by focusing on the percent of children whose venous blood lead was in excess of 10 µg/dL, we should minimize effects within the range of resampling error (Morris et al., 1999; Sargent and Dalton, 1996).

Multivariate statistical analysis was performed for those variables which were known individually (age, race, exposure to SiF). Logistic regression was used to compare percentages of children with blood lead exceeding 10 µg/dL in communities using SiF versus communities not using these chemicals. Because the odds ratios are consistently significant, for this sample as for others studied, the association between exposure to SiF and VBL >10 mg/dL does not seem to be an artifact and deserves further study as a potentially serious issue of public health.

For each of the 105 communities, values for 7 risk factors were assigned based on the seven covariates listed in Table 2. To assess the overall vulnerability of those in high risk environments (cf. Binns et al., 1999), we assigned

| TABLE 1. Prevalence And OR of Elevated VBL for Black Children 0-6 in NY Communities of 15,000-75,000, Using And Not Using SiF to Treat The Municipal Water Supply |
|-----------------|-----------------|-----------------|
| Interval        | Using SiF        | Not Using SiF   | Odds Ratio |
| µg/dL           | n               | Prev %          | n               | Prev %          | SIF/Non-F |
| 0-5             | 3,694           | 42.5            | 5,846           | 61.2            | 0.5     |
| 5-10            | 3,205           | 36.9            | 3,037           | 31.8            | 1.3     |
| 10-15           | 929             | 10.7            | 411             | 4.3             | 2.7     |
| 15-20           | 402             | 4.6             | 125             | 1.3             | 3.5     |
| 20+             | 455             | 5.2             | 137             | 1.4             | 3.8     |
| B. Prevalence and Odds Ratios by VBL Threshold Level |
| Threshold       | Using SiF        | Not Using SiF   | Odds Ratio |
| µg/dL           | n               | Prev %          | n               | Prev %          | SIF/Non-F |
| < 5             | 3,694           | 42.5            | 5,846           | 61.2            | 0.5     |
| > 5             | 4,991           | 57.5            | 3,710           | 38.8            | 2.1     |
| > 10            | 1,786           | 20.6            | 673             | 7.0             | 3.4     |
| > 15            | 857             | 9.9             | 262             | 2.7             | 3.9     |
| > 20            | 455             | 5.2             | 137             | 1.4             | 3.8     |

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TABLE 2. Community Demographics and Risk Factors (Distribution of 1990 U.S. Census Variables in 105 NY State Communities of population 15,000-75,000, by SIF Status)

<table>
<thead>
<tr>
<th></th>
<th>SIF</th>
<th>Non-SIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUMBER OF COMMUNITIES</td>
<td>28</td>
<td>77</td>
</tr>
<tr>
<td>DEMOGRAPHICS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean community population</td>
<td>34,778</td>
<td>25,627</td>
</tr>
<tr>
<td>Children 0-5 as % of population</td>
<td>8.5%</td>
<td>8.0%</td>
</tr>
<tr>
<td>No. of children 0-5 per community</td>
<td>2,960</td>
<td>2,046</td>
</tr>
<tr>
<td>TOTAL NUMBER OF CHILDREN TESTED 1994-1998</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of VBL tests</td>
<td>58,934</td>
<td>94,291</td>
</tr>
<tr>
<td>Total number of capillary tests</td>
<td>36,791</td>
<td>68,357</td>
</tr>
<tr>
<td>Total of all blood lead tests</td>
<td>95,725</td>
<td>162,648</td>
</tr>
<tr>
<td>VBL Tests as % of total</td>
<td>61%</td>
<td>58%</td>
</tr>
<tr>
<td>RISK FACTORS ASSOCIATED WITH HIGH BLOOD LEAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housing built before 1939</td>
<td>49.4%</td>
<td>23.3%</td>
</tr>
<tr>
<td>Children 0-5 in poverty</td>
<td>22.3%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Community unemployment rate</td>
<td>3.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Parents with Bachelor Degree</td>
<td>7.4%</td>
<td>9.3%</td>
</tr>
<tr>
<td>Population density (persons per sq. km.)</td>
<td>155</td>
<td>143</td>
</tr>
<tr>
<td>Total population of group</td>
<td>973,785</td>
<td>1,973,336</td>
</tr>
<tr>
<td>Per capita income</td>
<td>$14,698</td>
<td>$19,415</td>
</tr>
</tbody>
</table>

For each individual a value indicating whether his/her community was above or below the sample median for each covariate risk factor. We then used these as covariates in our analysis, dividing the sample of individuals into those who live in communities above and below the median of each covariate. Age-adjusted logistic regressions above and below the community median for each of the seven covariates (Figs 1a and 1b, and Appendix) showed, in most cases, a significant relationship between SIF use and elevated blood lead. An Odds Ratio (OR) of 1.0 (bold line in Figures 1a-1b) reflects an equal probability of elevated VBL for children living in communities with or without SIF treated water. In no case is an OR significantly lower than 1.0 where SIFs are in use. In contrast, for 49 of 56 regressions, the ORs are significantly over 1.0 for children exposed to SIF, with 35 over 2.0 (all significant), of which 23 are over 3.0. Moreover, ORs are significant in all 28 regressions for children in communities above the mean of a known risk-factor for lead uptake. Four of these ORs—all for Whites—are under 2.0 (range 1.4 - 1.9).

For Blacks and Hispanics exposed to both some other known risk-factor and SIF treated water, ORs range from 2.1 to 6.4 and are always significant. (See Appendix). ORs are significant 10 of 14 times for SIF use without any other risk factor. More striking, ORs are often doubled and sometimes quadrupled where Black and Hispanic children are exposed to both a risk factor such as old housing and SIF treated water.

The magnitude of some ORs might have been affected by sampling bias if conscious efforts were made to select children from high risk households in the SIF communities. We have, however, no information about such sampling procedures and sample size is robust (see Table 2). More important, because our statistical analysis considers risk-factors one at a time in accordance with standard multivariate methods, there is no reason to doubt the trend of ORs even should their magnitude sometimes be over-stated due to biased sampling.

To explore the relationship between SIF and combinations of the seven known risk factors ORs were computed by dividing the sample into those living in communities with four or fewer risk factors and those in communities with five or more risk factors. Exposure to five or more risk factors in combination always increases the risk of elevated blood lead. Where SIF is used to treat community water, exposure to this number of risks is associated with doubled values of OR (Figure 2). Although robust for all children tested (solid lines), the effect is substantially worse for Blacks (dashed lines).

Finally, it is commonly assumed that those at highest risk for high blood lead are poor Black children in old housing. For three age groups, logistic regressions indicated that if their community provided SIF-treated water, children in this group were at higher risk of elevated blood lead. Except for the age-group 4 to 6, which had the smallest sample, the effect was highly significant (Figure 3).
Figure 1: Age adjusted logistic regression analysis of Odds Ratios for VBL > 10µg/dL in children 0-6 (Whites n = 72,542; Blacks, n = 18241) living in communities using and not using SIFs, ranked above and below the median for seven risk factors listed in Table 2. Light bars represent ORs for below the median of each identified risk factor and dark bars the ORs for above the median. An OR of 1.0 would mean that there is the same chance of VBL > 10µg/dL with and without SIF exposure; it does not mean low VBL.

UNRESOLVED ISSUES AND DISCUSSION

We are aware that statistical association should not be confused with causation. Moreover, since privacy limits have made it impossible to ascertain each individual's exposure to such risk factors as living in a house built before 1939, the assignment of community level covariates might artificially inflate significance levels (increasing the risk of Type I error). Though it is theoretically possible that there could be no effect, this conclusion seems unlikely when evidence from the present study is combined with congruent data from other studies. Prudence dictates, moreover, that a chemical delivered by government policy to 140 million people should have been tested and shown to be reasonably safe. As the Rio Declaration puts it in formulating the "precautionary principle," lack of "full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation" (Foster et al., 2000).

Our analysis does not concern sodium fluoride, which is not used in a sufficient number of communities in this NY sample. Combined with our previous studies of data for children's blood lead in Massachusetts (Masters and Coplan, 1999a) and in the NHANES III sample (Masters, Coplan and Hone, in preparation) these findings point to a statistically significant risk of elevated blood lead associated with chronic ingestion of water treated with SIFs. In our experience, the data for NY State children reported here are not exceptions.
In Massachusetts we found risk ratios around 2.5 for elevated lead levels in venous and capillary blood tests by two independent methods. One compared the prevalence of VBL >10μg/dL among 37,000 children in 30 communities that use SiF with the prevalence of VBL >10μg/dL in 39,000 children living in 30 comparable communities that do not fluoridate. The other method compared mean capillary blood lead values of large populations of children in SiF and Non-F communities. To compare these results with the NY data, we reanalyzed our Massachusetts risk ratio data as OR values along the same lines as those reported here and depicted in Figure 1.

The Massachusetts OR results are summarized in Figure 4. Considering that similar ORs have now been found for two separate large populations from data collected and analyzed by entirely different agencies, it is unlikely that the results reported here are artifacts of sampling. Moreover, in a sample of over 30,000 criminals in 129 cities studied by the National Institute of Justice, behaviors associated with enhanced lead uptake vary in a manner consistent with the apparent effect of SiF (Masters and Coplan, 1999b).

Admittedly, in the absence of new chemical testing using contemporary methods of neurotoxicology, it is impossible to do more than hypothesize about the precise mechanisms that could account for these results. Nevertheless, these findings are extremely important for several reasons:

First, as noted above, it is not widely recognized that over 91% of fluoridated water has been treated with sodium silicofluoride or fluosilicic acid. Because less than 10% of the populace living in fluoridated communities receives water treated with sodium fluoride (NaF), the familiarity and widespread use of fluoridated toothpaste is not evidence of SiF safety. Despite MSDS data, (e.g., LCI, 1997) water plant managers and health agency personnel have little understanding of the toxic properties and behavior of the SiFs.

Second, it also true but not widely realized, that extensive tests on animals exposed to sodium fluoride in their diets have never been replicated by exposure to commercial grades of sodium fluosilicate or fluosilicic acid. Both federal health agencies and academic researchers customarily employ simple sodium fluoride in animal studies and extrapolate the results to humans ingesting silicofluoride treated water (Bucher et al., 1997; Collins et al., 1995; Dunipace et al., 1998a; Dunipace et al., 1998b; Dunipace et al., 1995; Dunipace et al., 1996; Jackson et al., 1997; McClure, 1962; Sprando et al., 1995; Sprando et al., 1997; Sprando et al., 1998). Moreover, this practice is reinforced by the habit of discussing “fluoridation” without any reference to the chemicals used (e.g., Newbrun and Horowitz, 1999). A detailed search of the literature which was relied upon for judging health safety of the SiFs for mass-fluoridation has produced only three comparative studies of the effects of sodium silicofluoride vs. sodium fluoride. One showed that rats and other animals process SiF differently from NaF (Kick et al., 1935). Another showed that young children absorb fluoride from sodium silicofluoride over a substantially longer time than adults (Zipkin et al., 1956). A third simply confirmed previous work of Zipkin, which had shown equivalent uptake of ingested fluoride by teeth and bones (Zipkin and McClure, 1951).

Third, officials at all levels responsible for water fluoridation often appear to lack an understanding of fundamental chemical principles relating to the use of silicofluorides. The silicofluoride anion that $\text{H}_2\text{SiF}_6$ and Na$_2$SiF$_6$ have in common must dissociate to release fluoride ion. This process is both complex and reversible, differing distinctly in many ways from release of fluoride from NaF by simple solution/ionization. Fluoridating water with either silicofluoride can thus create problems which are not experienced when adding NaF for that purpose (Reeves, 1994). The only extensive examination of the actual biochemical effects of SiF that we have encountered is a German study (Westendorf, 1975) — to our knowledge never cited before in the debates surrounding water fluoridation in the U.S. This research, which shows substantial changes in membrane permeability and enzymatic changes capable of substantially modifying neuronal excitability, suggests plausible chemical mechanisms that would be consistent with our empirical findings.

Finally, our findings (especially Figure 3) indicate that SiF treated water probably exacerbates the risks of absorbing lead from other known environmental risk
CONCLUSIONS

In the light of the foregoing discussion, the extent of subtle health effects associated with long term exposure to SiF is thus still unknown. Apart from the possibility of direct toxicity, freshly released monomeric silicic acid as well as fluoride ion bind calcium. If diets are low in milk products and other sources of calcium, the products of silicofluoride dissociation can exacerbate the competition between calcium and lead for bone and soft tissue sites. In addition, F has a high affinity for proteins (Emseley et al., 1981) and is known to modify enzyme action (Westendorf, 1975; Padmanabhan and Shelanski, 1998) with potential for disrupting a wide range of endocrine, immune and neural processes. It has also been implicated in disturbing the functionality of calcium, both directly (ATSDR, 1993) and indirectly in interaction with vitamin D (Bayley et al., 1990).

Studies of the long-term effects of exposure to fluorides in general and silicofluorides in particular must therefore take into account the strong possibility of multiple pathways and diverse mechanisms for intoxication. Even more important, recent biochemical findings link lead uptake in the brain to the replacement of zinc by lead in synaptotagmen, thereby changing its folding and greatly reducing its functional effectiveness (Godwin, 2000). Such new research apparently provides a precise neurochemical explanation for the well-known link between lead and lower cognitive ability (Needleman, 1992) and illustrates radically new methods to analyze lead neurotoxicity.

In the light of these facts and hypotheses, the congruent statistical findings from three populations totaling almost 400,000 children (over 238,000 in Massachusetts, over 150,000 in New York and over 4,000 in the NHANES III sample) indicate an urgent need for further study of the possible links between exposure to SiF and increased lead uptake as well as the behavioral dysfunctions associated with lead neurotoxicity. Given the paucity of direct knowledge about bio-mechanisms depending on exposure to commercial silicofluorides, and the magnitude of the potential risks—especially to poor and minority children—large-scale epidemiological studies, chemical analyses, and animal experimentation on silicofluorides and their effects deserve the highest priority.

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