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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 (Na_2SiF_6) or fluosilicic acid (H_2SiF_6) — 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

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independent relationships for blood lead levels and "median per capita income, percentage of housing built before 1950, percentage of the population who were Black, percentage of children screened, and a 'poverty index'." (Sargent *et al.*, 1995). Although not found in that study, other researchers have also found higher blood lead levels among Hispanics (Snyder *et al.*, 1995).

Recently, we carried out a further analysis of the Massachusetts blood lead data used by Sargent *et al. (op cit)*. We found that there was a statistically significant ($p = 0.001$ or better) correlation between community use of SiFs as reported by the CDC's fluoridation census (CDC, 1992) and a higher level of children's blood lead parameters, controlling for community factors commonly associated with blood lead, such as rates of housing built before 1950 and exposure to water containing over 15ppb first draw lead (Masters and Coplan, 1999a). Moreover, as predicted by our model (Masters and Coplan, 1999b), there were statistically significant interactions between these risk-factors and SiF usage as predictors of higher blood lead.

A second study has recently been completed, based on the Third National Health and Nutrition Evaluation Survey (NHANES III). Blood lead data for over 4,000 children living in 35 counties with a population over 500,000 was compared with county fluoridation status using the CDC's 1992 Fluoridation Census. The percent of each county population receiving silicofluoride treated water was calculated and each county was assigned to one of three groups. The "high" group comprised counties in which a total of 92% of the population received SiF-treated water. The "low" group comprised a population only 6% of which received SiF-treated water. A relatively small group of counties with "intermediate" exposure comprised a population with about a 50% chance of receiving SiF-treated water. Controlling at the individual level for covariates usually associated with lead uptake, elevated blood lead was statistically significant, again with $p = 0.001$ or better, with High/Low risk ratios in the range of 1.5 to 2.0 depending on age and race (Masters, Coplan and Hone, 1999 and in preparation).

The new analysis reported here is completely consistent with these earlier analyses of data from Massachusetts and NHANES III. Using New York State Health Department individual blood lead data for children 0-6, collected mostly between 1994 and 1998 by the Bureau of Children's Health[7], a multivariate study was done on data for over 151,225 children living in New York communities between 15,000 and 75,000 in population, of which 28 use SiF and 77 do not (one community using mixed chemicals had to be dropped from the analysis). We find that SiF is consistently associated with increased risk of having VBL>10mg/dL for virtually any race/age group, controlling for most factors commonly associated with increased blood lead.

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 race and age 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 10μg/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 15μg/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 10μg/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 10μg/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>10mg/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

Number of communities	28 (SiF)	77 (Non-F)
Mean community sample size	310 (SiF)	124 (Non-F)
Total number tested	8,685 (SiF)	9,556 (Non-F)

A. Prevalence and Odds Ratios by VBL Interval

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

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)

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

to 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: Odds Ratios of VBL>10µg/dL Comparing Children in 105 NY Communities (pop. 15,000-75,000) With and Without SiF Treated Water, Controlling for 7 Risk Factors for High Blood Lead

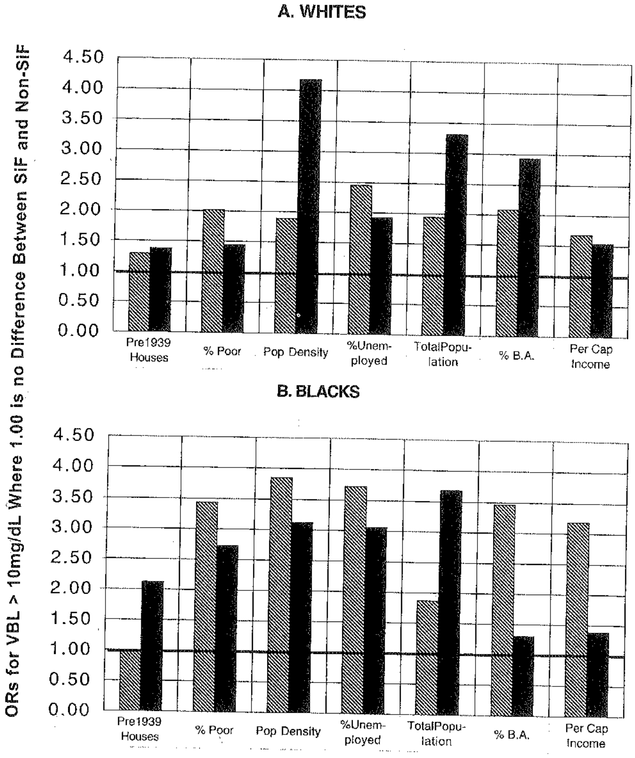


FIG. 1. Age adjusted logistic regression analysis of Odds Ratios for VBL > 10µg/dL in children 0-6 (Whites n = 72,542; Blacks, n = 18241) living in communities using and not using SiFs, ranked above and below the median for seven risk factors listed in Table 2. Light bars represent ORs for below the 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).

Figure 2: Percent Tested with Venous Blood Lead>10µg/dLin New York State

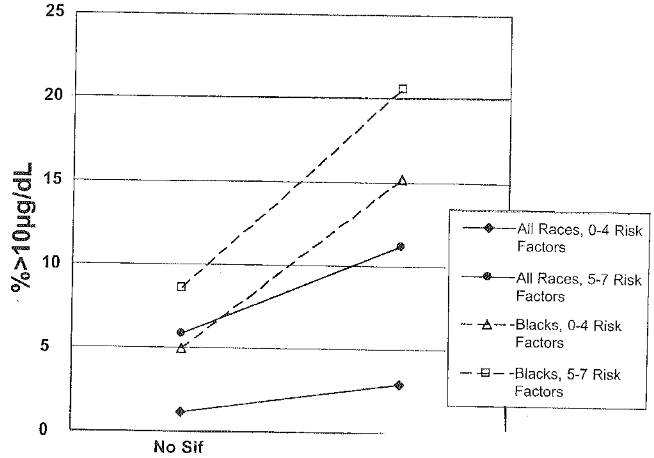
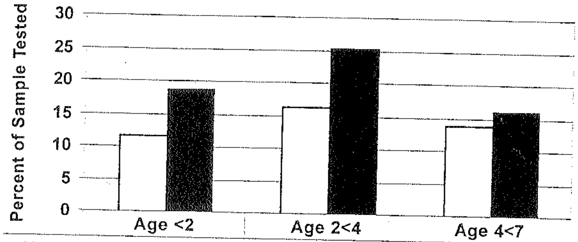


FIG. 2. Each of the [illegible] factors from those listed in Table 2. [illegible] communities with five or more and those with 4 or fewer risk factors and further grouped by use or non-use of SiF. Broken lines indicate the prevalence of VBL >10µg/dL among Black children and the solid lines the prevalence of VBL >10µg/dL for all races

Figure 3: Percent Black Children Tested With >10µg/dL by Silicofluoride Use in NYState Communities Pop 15,000-75,000 with high % Old Housing and Childrens Poverty



	Age <2	Age 2<4	Age 4<7
□ No SiF	11.8	16.4	13.8
■ SiF	18.8	25.4	16

FIG. 3.

	n	Odds Ratio	CI	p <
All Ages	10,481	1.626	1.412, 1.873	0.0001
Age <2	4,076	1.729	1.354, 2.208	0.0001
Age 2<4	3,900	1.736	1.396, 2.150	0.0001
Age 4<7	2,505	1.277	0.959, 1.700	0.0949

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.

FIGURE 4: ORs for VBL>10μg/dL in Massachusetts SiF vs Non-SiF Communities Controlling For 4 Risk Factors

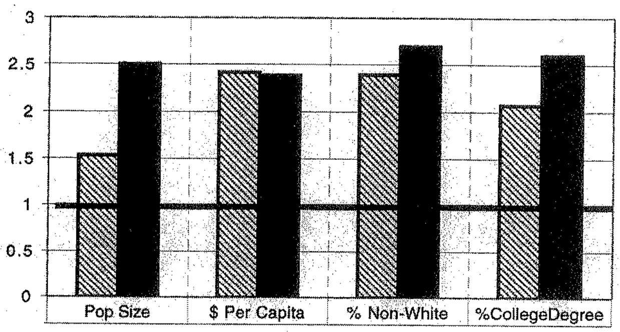


FIG. 4 ORs for VBL >10μg/dL in 30 SiF and 30 non-SiF Massachusetts comparable mid-size communities were determined for above and below median values of 4 risk factors: population size, per capita income, % non-white, and community average parent education level. ORs for VBL >10μg/dL in the communities with below median values for the referenced risk factor are represented by the gray bars; above the median, by the black bars. All ORs are close to 2.5 except for communities with below-median populations, where there is still a 50% greater chance of finding children with VBL > 10μg/dL if SiFs are used to treat the municipal water supply.

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 re-analyzed 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 H_2SiF_6 and Na_2SiF_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 factors. Complex models of multivariate analysis are thus probably necessary. For example, when the presence or absence of SiF water treatment is considered along with other risk factors for lead uptake dichotomized at sample median, the analyses of variance (ANOVA) often show a significant interaction term ($p < .05$). Moreover, sometimes these interaction effects are different for children of different races. Whereas many studies of environmental toxins assume that variables of concern are causally independent, more attention thus needs to be devoted to multifactorial, interactive models of neurotoxicity (Masters and Coplan, 1999b). Recent research on the inhibitory effects of multiple sulfhydryl-reactive metals on the "adaptive and protective response to toxic metal exposure" by glutathione and metallothioneins (Quigg, 1998) confirms the importance of extending research to more complex mixtures and relationships than have typically been considered by either scholars or regulatory agencies (e.g., Calderon, 2000).

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 (Emsley *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 biomechanisms 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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