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Confirmation of and explanations for elevated blood lead and other disorders in children exposed to water disinfection and fluoridation chemicals

Myron J. Coplan [a,*], Steven C. Patch [b], Roger D. Masters [c], Marcia S. Bachman [a]

[a] Intellequity Technology Services Natick, Massachusetts, United States
[b] Environmental Quality Institute, University of North Carolina in Asheville, United States
[c] Dartmouth College Institute for Nuroscience and Society, United States

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Abstract

Silicofluorides (SiFs), fluosilicic acid (FSA) and sodium fluosilicate (NaFSA), are used to fluoridate over 90% of US fluoridated municipal water supplies. Living in communities with silicofluoride treated water (SiFW) is associated with two neurotoxic effects: (1) Prevalence of children with elevated blood lead (PbB > 10 μg/dL) is about double that in non-fluoridated communities (Risk Ratio 2, χ^2 $p < 0.01$). SiFW is associated with serious corrosion of lead-bearing brass plumbing, producing elevated water lead (PbW) at the faucet. New data refute the long-prevailing belief that PbW contributes little to children's blood lead (PbB), it is likely to contribute 50% or more. (2) SiFW has been shown to interfere with cholinergic function. Unlike the fully ionized state of fluoride (F-) in water treated with sodium fluoride (NaFW), the SiF anion, [SiF6]2- in SiFW releases F- in a complicated dissociation process. Small amounts of incompletely dissociated [SiF6]2- or low molecular weight (LMW) silicic acid (SA) oligomers may remain in SiFW. A German PhD study found that SiFW is a more powerful inhibitor of acetylcholinesterase (AChE) than NaFW. It is proposed here that SiFW induces protein mis-folding via a mechanism that would affect polypeptides in general, and explain dental fluorosis, a tooth enamel defect that is not merely ''cosmetic'' but a ''canary in the mine'' foretelling other adverse, albeit subtle, health and behavioral effects. Efforts to refute evidence of such effects are analyzed and rebutted. In 1999 and 2000, senior EPA personnel admitted they knew of no health effects studies of SiFs. In 2002 SiFs were nominated for NTP animal testing. In 2006 an NRC Fluoride Study Committee recommended such studies. It is not known at this writing whether any had begun.

Keywords: Elevated blood lead; Silicofluoride; Fluosilicate; Brass corrosion; Enzyme inhibition; Fluorosis

1. Introduction

Chronic ingestion of water bearing 1 ppm of fluoride ion (F^-) from NaF was thought harmless to humans when municipal water fluoridation began in 1945. NaFSA was substituted in 1947 and endorsed in 1950 by the US Public Health Service without prior animal testing because rats grew just as fast, their teeth got as much F^- as from NaF, and a community could save 4 cents per year per resident (McClure, 1950).

FSA (H_2SiF_6) and NaFSA, its sodium salt (Na_2SiF_6), share the $[SiF_6]^{2-}$ anion, a fluoride complex herein called ''silicofluoride'' (SiF) which dissociates in water, releasing F^-. The dissociation was predicted to be ''virtually complete'' at 1 ppm of F^- so that SiFW would be ''just like'' NaF treated water (NaFW). Today, 92% of US fluoridated drinking water is SiFW (CDC, 1993). Senior EPA personnel have found no evidence SiFW was ever tested for adverse health effects (Fox, 1999; Thurnau, 2000). In 2002, SiFs were ''nominated'' for animal tests (NTP, 2002) that had not begun as of July 2006.

The NRC report, ''Fluoride in Drinking Water...A Scientific Review of EPA's Standards'' (NRC, 2006) emphasizes the importance of such testing with questions about

* Corresponding author. Tel.: +1 508 653 6147; fax: +1 508 655 3677.
E-mail addresses: MYRONCOPLAN@aol.com (M.J. Coplan), patch@unca.edu (S.C. Patch), Roger.D.Masters@Dartmoth.edu (R.D. Masters), maribac@aol.com (M.S. Bachman).

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incompletely dissociated $[SiF_6]^{2-}$ end-products in human diets. It recommends study of SiFW of different hardness, mineral content, and silica native to the water, taking into account the reversible equilibrium aspects of $[SiF_6]^{2-}$ dissociation.

Neurotoxic and related effects associated with chronic ingestion of SiFW that have heretofore escaped attention are discussed here.

2. Effects associated with SiFW

2.1. Association of elevated PbB with SiFW

PbB data for 400,000 children (250,000 in Massachusetts, 150,000 in New York State, and 6,000 from NHANES III), consistently showed a statistically significant Risk Ratio around 2 for PbB > 10 μg/dL in SiFW communities compared with either non-fluoridated or NaFW communities. (Masters and Coplan, 1999; Masters et al., 2000) (see Tables 1–5 and Figs. 1 and 2). SiFW could increase PbB by (a) exacerbating plumbing corrosion, and/or (b) facilitating

Table 1
Community-Based PbB Parameters in 250,000 Massachusetts Children aged 0–5

WF status	Mean capillary PbB (μg/dL)	Prevalence PbB VB > 10 μg/dL (%)
Non-fluoridated	2.02	1.9
Sodium fluoride used	2.09	1.6
Sodium fluosilicate used	2.66	3.0
Fluosilicic acid used	2.78	2.9

Table 2
Comparison of matched Massachusetts communities

	30 non-fluoridated communities	30 SiF fluoridated communities
Total population	837,300	845,100
Pop children 0–5	57,031	56,446
Children tested (N)	37,310	39,256
VB PbB > 10 μg/dL (n)	283	762
Prevalence rate	283/37,130 = 0.76%	762/39,256 = 1.94%
Risk ratio	1.94/0.76 = 2.55	Chi sq $p < 0.001$

Table 3
Counties in NHANES III by fluoridation status

	County	State	Persons	Percent receiving fluoridated water
Low fluoride: counties: 8, total pop: 1.9 million, % on Fl: 4.0	Nassau	NY	1287348	0.0
	San Bernardino	CA	1418380	0.0
	San Diego	CA	2498016	0.1
	Fresno	CA	667490	0.4
	Ventura	CA	669016	3.9
	Bexar	TX	1185394	4.7
	Los Angeles	CA	8863164	4.8
	Orange	CA	2410556	9.9
Medium fluoride: counties: 8, total pop: 1.1 million, % on Fl: 51.6	Santa Clara	CA	1497577	11.6
	Palm Beach	FL	863518	16.8
	Westchester	NY	874866	27.3
	Maricopa	AZ	2122101	58.1
	Delaware	PA	547651	58.2
	Harris	TX	2818199	65.6
	Oakland	MI	1083592	68.6
	Middlesex	MA	1398468	77.1
High fluoride: counties: 19, total pop: 3 million, % on Fl: 97.2	King	WA	1507319	81.0
	El Paso	TX	591610	81.1
	Tarrant	TX	1170103	86.4
	Hamilton	OH	866228	88.0
	Dade	FL	1937094	96.3
	Cook	IL	5105067	98.5
	Dallas	TX	1852810	99.0
	Kings	NY	2300664	100.0
	New York	NY	1487536	100.0
	Philadelphia	PA	1585577	100.0
	Queens	NY	1951598	100.0
	Duval	FL	672971	100.0
	Wayne	MI	2111687	100.0
	Cuyahoga	OH	1412140	100.0
	Providence	RI	596270	100.0
	Alameda	CA	1279182	100.0
	Allegheny	PA	1336449	100.0
	Erie	NY	968532	100.0
	St. Louis	MO	993529	100.0

Table 4
NHANES III study participants by race and silicofluoride exposure ages 3–17 with PbB test and poverty/income information

	Number	Black-Non-Hisp	White Non-Hisp	Mexican-American
Total	6645	2375	1876	2394
Probability of SiF Exposure				
95%	1361	754	320	287
50/50	544	164	183	197
5%	1085	137	111	837
Unknown	3655	1320	1262	1037

Table 5
NYS Study ORs as Function of Criterion for Elevated PbB

Criterion (μg/dL)	Exposed to SiF		Not exposed to SiF		OR
	N	Prev %	*N*	Prev%	
5	4991	57.5	3,710	38.8	2.1
10	1786	20.6	673	7.0	3.4
15	857	9.9	262	2.7	3.9
20	458	5.2	137	1.4	3.8

lead transport across the gut/blood membrane, whatever the lead source might be.

2.2. Elevated PbW effect on PbB

EPA and CDC have estimated that 14–20% of PbB for all ages is due to PbW (EPA, 1993). This estimate is too low for children, considering reduced exposure to other lead sources and new data on PbW due to brass plumbing corrosion. Besides, children ingest more water per pound of body weight than adults, and absorb a higher fraction of any lead in that water (Houk et al., 1989; CDC, 2004). Newborns are the most seriously affected (White, 2004).

A fetus will get lead from placental blood due to PbW in a mother's current diet or released from her bones absorbed many years earlier (Gomaa et al., 2002). The worst and most likely irreversible lead damage is done to a fetus in the first trimester (Hu et al., 2006).

A breast-fed infant may ingest lead in its mother's milk; a formula-fed infant's diet may include tap-water lead, and any child may ingest PbW in home- or commercially-prepared foods. PbW contributes at least half of an infant's PbB (Houk et al., 1989; Skipton and Hay, 2006). PbW should be considered as important as lead paint and low calcium intake (Goyer, 1996) as a factor in PbB, particularly for Blacks (Enattah et al., 2002).

2.3. Plumbing corrosion and PbW

Plumbing corrosion has been studied under many conditions other than fluoridation (EPA, 1993; Lyttle and Schock, 1996). Recent high PbW episodes prompted a University of North Carolina Environmental Quality Institute (EQI) study which found high PbW from brass corrosion by water treated with fluoridating agents combined with chlorine or chloramine disinfecting agents (Maas et al.,in press). (See companion article in this issue and Table 6 here). This comports with field experience of high PbW in Washington DC (Edwards, 2004) and Boston (Estes-Smargiassi, 2005) pointing to brass corrosion as the problem. The effect of chloramine alone on lead corrosion has been explored (Switzer et al., 2006) as well as the effect of chloramine combined with fluoridating agents on blood lead (Miranda et al., 2007).

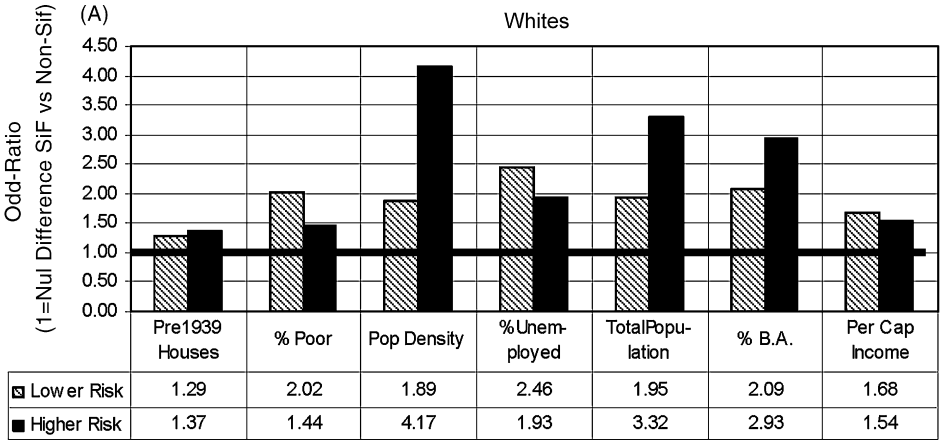
CDC's Fluoridation Manual says SiFs may enhance plumbing corrosion but can be mitigated by the simple pH control used for chlorine or alum (Reeves, 1994). However, this doesn't account for pH effects of SiF dissociation. The same error was made in ''proving'' SiFW and NaFW are identical (Jackson et al.,2004). Neutralizing the initial two protons released from H_2SiF_6 still leaves 4 more to neutralize when the 6 F^- ions are released by dissociation of $[SiF_6]^{2-}$.

CDC also recommends a 60 second flush of water that has been stagnant a few hours (CDC, 2003). This is now considered insufficient in many common situations (eg schools and multi-story apartment buildings). In the wake of Washington DC's water lead debacle of 2001–2004, CDC also dismissed as ''much ado about nothing'' public concern about high PbB from ingesting PbW as high as 300 ppb (Renner, 2006). EPA's Lead/Copper Rule sets 15 ppb as a limit on PbW and specifies 60 second flushing of water stagnated for several hours (EPA,

Table 6
Maas 2007 Water Lead Data Illustrating Enhanced Brass Corrosion By Combinations of Water Fluoridation and Disinfection Agents

Agent[a] Combinations	Water Lead (ppb) Found after overnight dwell[b] during 6 weeks of flow-through exposure			
	Mean lead ppb for		Spike increment due to	
	All 18 samples	Last 6 samples	ppb	Added F agent
(a) CA + FSA	60	39	300	
(b) CA, extra NH_3 + FSA	61	98	150	b/c 2.1, 2.8, 3.0
(c) CA, extra NH_3	29	35	50	
(d) CA, extra NH_3 + NaF	36	51	100	d/c 1.2, 1.5, 2.0
(e) Cl_2 + FSA	202	45	1000	e/g 1.8, 0.5 5.3
(f) Cl_2 + NaF	151	107	210	f/g 1.3 1.2 1.1
(g) Cl_2 alone	115	88	190	

[a] Agents added as 2 ppm: CA: chloramine; Cl_2: chlorine; FSA: fluosilicic acid; NH_3: ammonia in solution; NaF: sodium fluoride in solution; pH held at 7.2–7.5.
[b] Three samples taken per week for six weeks.



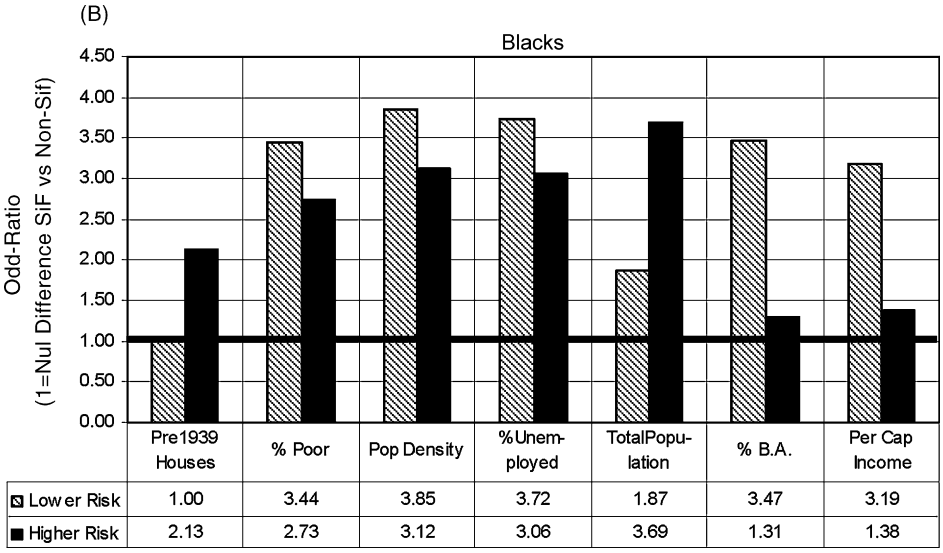


Fig. 1. Odds Ratios for VB > 10 μg/dL Comparing Children in 105 New York State Communities (pop. 15,000–75,000) With and Without SiF Treated Water Controlling for 7 Risk Factors for High Blood Lead.

2002; EPA, 2005). This might suffice for a ground floor faucet but not for upper floors of ''triple-deckers'' or apartment buildings (EPA, 1993). Several minutes may still be inadequate for some conditions. High PbW would explain association of elevated PbB with population density due to multi-story buildings. Similar considerations would apply to school PbW (Arizona, 2004; EPA, 2005; Karr et al.,2004).

Table 7
Average daily fluoride metabolism experience of young male rats (derived by MJ Coplan from Kick et al Data Cited by McClure)

	Fluoride Source		Na_2SiF_6/NaF
	Na_2SiF_6 (mgm)	NaF (mgm)	Ratio
Average Daily:			
(a) Fluoride ''Dosage''	4.00	3.91	1.02
(b) Fluoride Absorbed (c + f)	2.60	1.75	1.49
(c) Total Fluoride Retained	1.22	1.27	0.96
(d) Total Fluoride Excreted	2.78	2.64	1.05
(e) Fluoride Excreted in Feces	1.40	2.16	0.63
(f) Fluoride Excreted in Urine	1.38	0.48	2.67

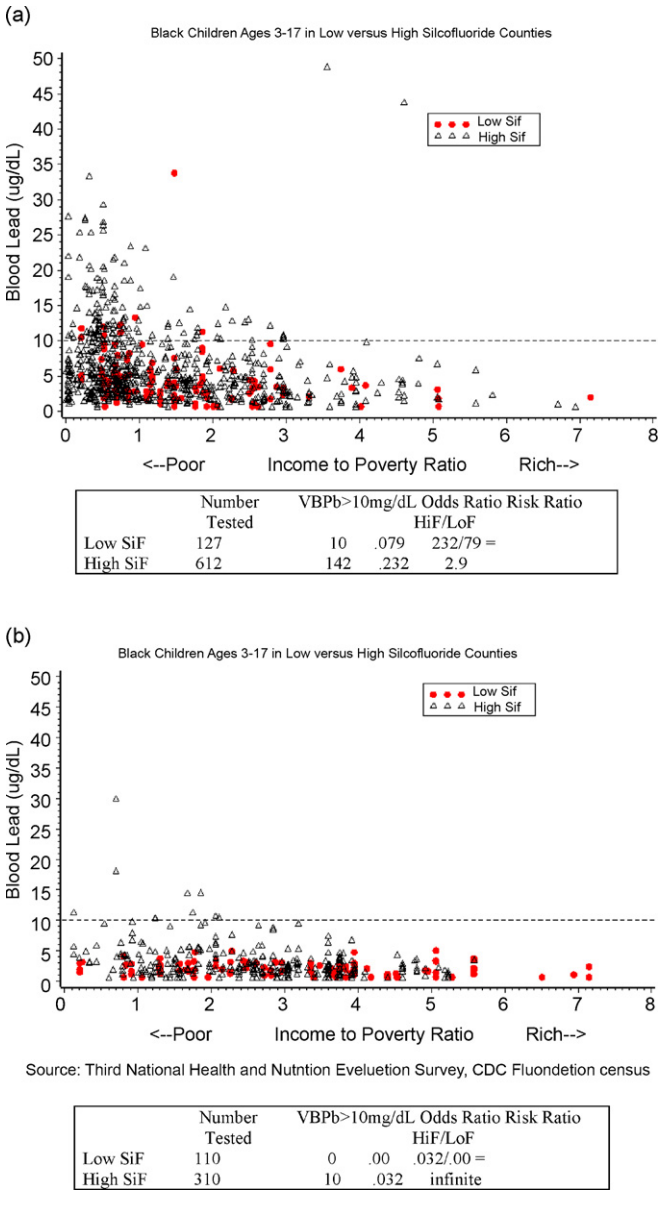
2.4. Metabolism of ingested fluoride

The 1950 US PHS endorsement of NaFSA noted that more F^- from SiFW was eliminated in urine of young male rats than from NaFW (Kick et al., 1935) (Table 7). A related metabolic effect was observed when urine of boys and men was collected (separately) in two communities from the start of fluoridation, one using NaF the other SiF. Urine F^- level was tracked until equilibrium with ingested F^- was reached. This occurred later for boys than men with no time difference for men exposed to NaF or SiF. However, a longer time to reach equilibrium was required for boys drinking SiFW compared with those drinking NaFW (Zipkin et al., 1956).

Kick et al., 1935; Zipkin et al., 1956 results imply that soft tissue of young male mammals suffer more exposure to F^- from SiFW than NaFW. This is consistent with reversible equilibrium chemistry since the fluoride-bearing dissociation species in SiFW should undergo re-association at stomach pH around 2, regenerating membrane-permeable fluorinated silicic acid (SA) derivatives that would not be produced from NaFW.

Table 8
Degree of complex dissociation at physiological conditions, pH 7.4, $T = 37\ ^{\circ}C$

Complex used	Concentration $[10^{-4}M]$ pH 7.4; $T = 37\ ^{\circ}C$	Level of hydrolysis at saturation	Number of F ions separated per complex
$MgSiF_6$	5.7	0.593	4
$MgSiF_6$	1.01	0.622	4
$MgSiF_6$	0.232	0.625	4
$MgSiF_6$	0.116	0.630	4
K_2GeF_6	1.82	0.83	5
K_2SnF_6	1.42	1.00	6
Na_3AlF_6	1.76	0.659	4
KPF_6	1.67	0.0209	0
KBF_4	2.34	0.068	0



	Number Tested	VBPb>10mg/dL	Odds Ratio HiF/LoF	Risk Ratio HiF/LoF
Low SiF	127	10	.079	232/79 =
High SiF	612	142	.232	2.9

	Number Tested	VBPb>10mg/dL	Odds Ratio HiF/LoF	Risk Ratio HiF/LoF
Low SiF	110	0	.00	.032/.00 =
High SiF	310	10	.032	infinite

Fig. 2. (a) Blood Lead Versus Poverty to Income Ratio of NHANESIII Children. Black Children Ages 3–17 in Low versus High Silicofluoride Counties. (b) Blood Lead Versus Poverty to Income Ratio of NHANESIII Children. White Children Ages 3–17 in Low versus High SilioDfluoride Counties.

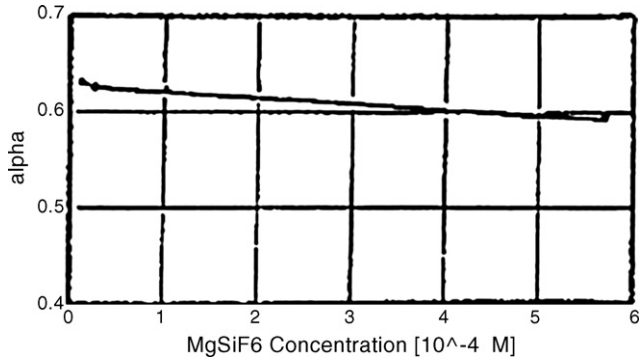


Fig. 3. Level of Hydrolysis of SiF_6^{2-} as a Function of Concentration (Westendorf Figure 17).

Kick's rat fluoride metabolism data were recently disputed (Whitford and Johnson, 2003, see also MCG Anon). Female rats were fed NaFW or SiFW for 4 months before their urine was tested. No difference was found for fluoride intake, excretion, and retention. However, Whitford's rat urine was collected from adult females and Kick's from juvenile males. Whitford himself had shown that children metabolize fluoride differently than adults (Whitford, 1999). It is also known that girls' boney tissue matures earlier than boys' (Gajewska et al., 2005).

Both acute short-term high level F^- and chronic low level F^- exposures impair calcium-dependent processes, including those associated with neural as well as kidney functions (Borke and Whitford, 1999). This is consistent with the damage found in squirrel monkeys exposed to SiFW at 1–5 ppm F^- for

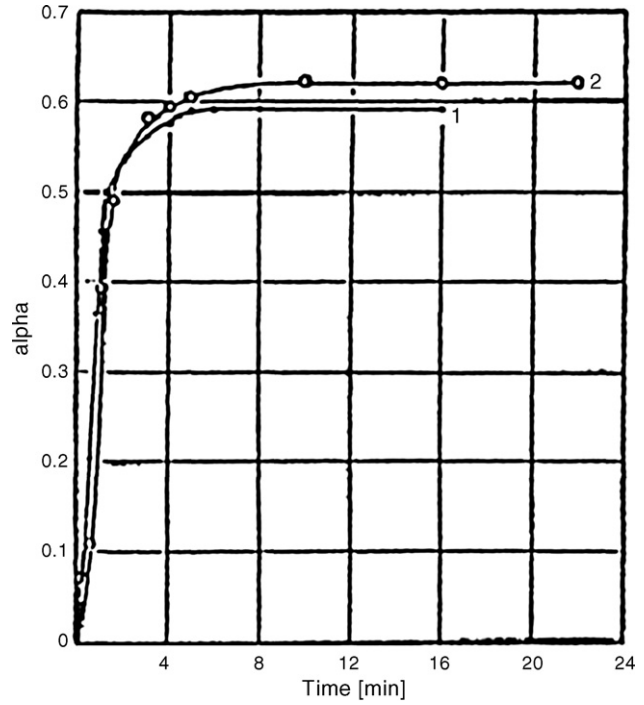


Fig. 4. Dependence of the Level of Hydrolysis of SiF_6^{2-} on Time. (Westendorf Figure 16). (1) 6.45 ppm of F^- (5.7×10^{-4} M of $MgSiF_6$). (2) 1.14 ppm of F^- (1.01×10^{-4} M of $MgSiF_6$). Hydrolysis is initially rapid; no more change occurred after 15 minutes.

18 months (Manocha et al., 1975). Early development of rat kidney is very sensitive to toxic insult (Alexander et al., 1997) with hypertension later in life a probable outcome of damage inflicted *in utero* (Alexander, 2006). The same F^- levels impairing rat kidney phospholipid cell membranes is associated with dental fluorosis (Guan et al., 2000). Similar damage to cell membranes results from prolonged low level exposure to reactive oxygen species produced by internal radiation, according to the ''Petkau Effect'' (Graueb, 1994).

2.5. Caries/Fluorosis/PbW/SiFW linkage

Contrary to common belief, fluorotic enamel *per se* does not prevent caries (Wondwossen et al., 2004). NRC, 2006 identifies fluorosis damage to tooth enamel as a cause of caries in about 10% of children living today where water F^- exceeds 3 ppm. Twenty years ago, the National Institute for Dental Research warned that fluorosis from natural F^- over 2 ppm could lead to caries (Heifetz et al., 1988). The CDC recently recommended that even very low levels of fluoride in infant formula should be avoided (CDC, 2006). Caries has also been associated with elevated PbB (Moss et al., 1999) and in newborn mice with lead in the dam's diet (Watson et al., 1997).

Before water fluoridation began (1945), 10–12% of children drinking 1 ppm F^- in natural fluoridated water exhibited dental fluorosis, mostly mild (Dean, 1938). In 1993, half the children in some fluoridated areas had fluorosis, 14% moderate-to-severe and some severe (NRC, 1993). Fluoridation advocates claim fluorosis is only ''cosmetic'' but NRC, 2006 says severe fluorosis is a ''toxic effect that is consistent with prevailing risk assessment definitions of adverse health effects'' and drinking water is a major fluoride source.

Dental fluorosis is believed due to inhibition of the enzyme that removes amelogenin after enamel formation in nascent tooth buds (Den Besten, 1986, 1999). Severe fluorosis was reported in India where naturally occurring fluoridated water had ''silicon'' in it (Anasuya et al.,1996). The silicon couldn't have been metallic or in sand, it had to come from natural SiFW (Ockerse, 1946; Sahlbom and Hinrichsen, 1906). Thus, chronic ingestion of SiFW is a major factor in the linkage of dental fluorosis with fluoridated water.

3. SiFW delivers more than fluoride

3.1. Incomplete dissociation of SiF in SiFW (Westendorf, 1975, 1974a,b)

Fluorides in general inhibit enzyme function. Voluntary and involuntary muscle action is stimulated by acetylcholine (ACh) which is cleaved by the enzyme acetylcholinesterase (AChE) to end the stimulation. Without that, muscle excitation would persist as spasm with potentially lethal effect, as caused by a nerve gas. ACh modulated by AChE also induces saliva flow. Intense salivation is a symptom of fluoride poisoning; less severe fluoride exposure should increase flow of fluoride bearing saliva. With caries prevention in mind, a German PhD study compared inhibition of AChE by NaFW and SiFW (Westendorf, 1975).

Inhibition was measured in cells or as purified products in 37 °C solutions buffered at pH 7.4 or 8.6, to which NaFW and SiFW were added at stoichiometric concentrations as low as 1 ppm F^-. HF from the F^- in NaFW caused ''competitive'' inhibition; (*ie* it blocked enzyme active sites). SiFW inhibition was more complicated. As measured by ion selective electrode *without* adding ''TISAB'' (see part B, below), only 2/3rds of the F^- bound in $[SiF_6]^{2-}$ was detected. The balance was present either in partially dissociated $[SiF_6]^{2-}$ such as $[SiF_2(OH)_4]^{2-}$ or in some fluorinated SA species (See Table 8 and Figs. 3 and 4).

Whichever one it was, it caused ''non-competitive'' inhibition by distorting enzyme shape making active sites inaccessible. Hence, for the same total fluoride in the system, SiFW competitive plus non-competitive AChE inhibition was more powerful than that by NaFW. Westendorf also studied butyrylcholinesterase (BuChE) and got the same result. Unlike AChE, the role of BuChE is not well-defined, but it is important as a scavenger of blood-borne toxins and back-up for AChE in some situations (Cokugras, 2003).

The mechanism for ''non-competitive'' enzyme inhibition by incomplete SiF dissociation products has broader implications than interference with normal AChE cholinergic activity. SA binds with a wide array of amides (Clark et al., 1957; Coradin and Livage, 2001; Coradin et al., 2005). Evidence of this is that LMW SA oligomers ''denature'' proteins (Iler, 1979).

When a stream of concentrated FSA or NaFSA enters water, $[SiF_6]^{2-}$ dissociates, releasing SA and F^- in close proximity and F^- catalyzes SA ''oligomerization'' (Rabinovich and Wood, 1986). Hydrogen bonding sites of linear SA oligomer molecules are spaced apart the same distance as polypeptide backbone repeat units. Properly juxtaposed, they are likely to zip together (Clark and Holt, 1957), creating the ''mis-folded proteins'' described by Ellis (2002) and Temussi et al. (2003). Protein mis-folding would explain SiFW non-competitive enzyme inhibition as well as other health problems associated with blood-borne polypeptides (Kayed et al.,2004).

3.2. SiF dissociation complexity; analysis for total fluoride

SiF dissociation has been studied for a century (e.g. Hudleston and Bassett, 1921) with little agreement other than that it involves a series of reversible equilibrium steps influenced by temperature and pH. Total fluoride in NaFSA (AWWA, 1994a) and FSA (AWWA, 1994b) is quantitatively assayed at pH 9 at the boil. The $[SiF_6]^{2-}$ anion is sufficiently stable at pH 7 to permit standard base titration of the ordinary hydronium ion acidity of FSA without producing SiF dissociation *per se* (Colton, 1958).

$$2OH^- + H_2SiF_6 \xrightarrow{pH\,7} [SiF_6]^{2-} + H_2O$$

The Ion Selective Electrode (ISE) method to measure ionic F^- in the water plant involves sample dilution with an equal volume of Total Ionic Strength Adjustment Buffer (TISAB).

The 2:1 dilution *per se* causes some dissociation but TISAB also carries a chelating agent to break up fluoride complexes. Other agents control pH at 5.5 (EPA, 1996). None of this is replicated in water plant treatments and certainly not in the digestive tract. Thus, it is unlikely the free F^- ion levels read on an ISE meter faithfully reflect SiF dissociation status in water leaving the plant, at the faucet, or in the digestive tract.

4. EPA's refutation of SiF adverse health effects

4.1. Urbansky and Schock

Without studying data or statistical methodology of the findings summarized in II A, EPA chemists produced an EPA ''Work Product'' detailing why SiFs are ''almost completely'' dissociated at 1 ppm $F^-$and can't influence PbB (Urbansky and Schock, 2000). The issue was framed as a question of residual concentration of the fluosilicate ion $[SiF_6]^{2-}$ after hydrolysis which should be predictable from reversible equilibrium thermodynamics and reaction kinetics theory. If theory applied, no $[SiF_6]^{2-}$ would remain in drinking water at equilibrium with 1 ppm of F^-.

However, residual $[SiF_6]^{2-}$, as such, is not the issue. Its total absence does not obviate survival of some fluorine-bearing SiF derivatives. Moreover, ''at equilibrium'' implies an end state that cannot be predicted without precise knowledge of SiF's *ab initio* status. As much as 30 ppm of silica may already be in raw water (ASTM, 1994) and silicates are sometimes used in the water plant for flocculation. Both of these conditions would influence dissociation end results. This is further confounded by what a phosphate fertilizer expert told an international technical conference of peers (Smith, 1999):

''The chemical formula of fluosilicic acid [FSA] is H_2SiF_6. However, things are not as simple as that due to the fact that rarely is fluosilicic acid present as pure H_2SiF_6. . .there are well reported references to the existence of H_2SiF_6 •SiF_4. . . Hereon in this presentation, FSA means a mixture of HF, H_2SiF_6 and H_2SiF_6 •SiF_4''.

In 2001, EPA research managers concluded it was necessary to clarify SiF dissociation. In 2002, EPA issued a ''Request for Assistance'' (RFA) inviting research proposals on methods to detect and measure SiF dissociation products. For the benefit of prospective bidders, Urbansky wrote an extensive review of SiF dissociation studies (Urbansky, 2002), in which he concluded that hydroxo-fluoro SiF derivatives could survive in drinking water and opined:

> ''. . . it is probably best to stop using qualified expressions such as 'virtually complete' or 'essentially complete' in favor of more rigorous and quantitative descriptions [of SiF dissociation] even if that hinders communication with the lay public.''

In connection with a response to questions raised by a Congressional committee (Fox, 1999), an EPA Information Sheet (Donohue, 1999) defined ''virtually complete'' dissociation of $[SiF_6]^{2-}$ as 99%. This was based on a study that reported 99% dissociation at 1 ppm but it also reported only 95% dissociation at 2 ppm (Crosby, 1969).

At 99% dissociation, six of the 600 fluorine atom originally bound in 100 $[SiF_6]^{2-}$ anions remain bound to silicon in some species. If these fluorines are distributed randomly over 100 silicons, 6% of the 100 pre-dissociation $[SiF_6]^{2-}$ anions remain as some fluorine-bearing species. Without stipulating any particular one, it is reasonable to assume that if that species mobilizes a lead atom it does so1 to1. The atomic weight of lead being about ten times that of fluorine, for each ppm of silicon-bound fluorine, 10 ppm of lead would be mobilized.

With 1 ppm of free F^- and 1% of initial bound F^- remaining bound, 10 ppb (ie 0.01 ppm) of F^- would be in the lead mobilizing species, so 100 ppb of lead would be mobilized. For reasons discussed in Maas et al., in press, many water systems deliver water with 1.5–2 ppm of F^- which should magnify the 100 ppb several-fold. PbW at 100 ppb has been estimated to increase an infant's PbB by 15 μg/dL (White, 2004) and school age children's by 2.5 μg/dL (Karr et al.,2004). A recent mega-study (Lanphear et al., 2005) reports that PbB at 2.5 μg/dL reduces a child's IQ measurably.

4.2. Morris/Finney

NRC, 2006 mentions ''Morris 2004,'' work funded pursuant to the EPA, 2002 RFA cited above, to be conducted in the laboratory of a Raman spectroscopy expert. The mission was to find better ways to quantify SiF dissociation end-products; results are reported in Finney et al., 2006. Although the EPA RFA did not ask for assistance in epidemiology or enzyme inhibition, the introduction of Finney et al., 2006 suggests another agenda, namely to prove that SiFW does not pose a public health danger.

The EPA contracted for work to be performed in the laboratory of an expert in Raman spectroscopy, but the published report does not mention the use of Raman spectroscopy. Instead, ^{19}F NMR spectroscopy was employed but it could not detect SiF hydrolysis intermediates because SA oligomers formed and interfered. Another approach was tried, FSA was added incrementally to buffered solutions and pH change, if any, measured.

Based on these data, Finney/Morris challenge Westendorf's enzyme inhibition results, claiming that added FSA lowered pH enough at 1 ppm F^- to explain the AChE inhibition he attributed to SiF derivatives. The problem is that, while their graph shows a line plotted from theory predicting pH shifts, the actual data points show no effect on pH from adding SiF at 1–5 ppm F^- and only a fraction of 0.1 pH unit at 50 ppm.

Finney/Morris had an easier way to refute Westendorf. They could have tried his way of measuring F^- released by $[SiF_6]^{2-}$ without the use of TISAB to see whether 67% dissociation was correct or not. They didn't, but in the course of their NMR experiments, they had inadvertently confirmed the formation of SA oligomers during $[SiF_6]^{2-}$ disociation.

Finney et al., 2006Finney, 2006 says Westendorf studied ''effects of fluoride and hydrofluoric acid on AChE inhibition''. Hydrofluoric acid is hydrogen fluoride dissolved in water, the

inhibitor derived from NaF. Unless the word ''fluoride'' was meant to denote $[SiF_6]^{2-}$, the phrase quoted above is equivalent to saying Westendorf studied ''effects of hydrogen fluoride and hydrogen fluoride on AChE inhibition''.

To summarize: Morris and Finney (a) misinterpreted Westendorf's experimental results; (b) didn't try to measure free F^- by ISE without TISAB to break up fluoride complexes, as Westendorf did; (c) didn't measure SiF derivatives by Raman spectroscopy; (d) tried NMR spectroscopy without success; and (e) measured pH as a secondary attribute of SiF dissociation, producing data that do not support their claims about AChE inhibition.

5. CDC's dismissal of an SiF/PbB linkage

CDC funded a former employee to either verify or refute Section 2.1 findings. Results first appeared as an abstract (Macek et al., 2003), the full report is published in Environmental Health Perspectives (Macek et al., 2006). NHANES III provided children's PbB data and the CDC Fluoridation Census (CDC, 1993) provided residence community fluoridation status (WFS). PbB data were grouped by WFS and housing age in four categories (See Appendix, Macek Table A.1). Other variables were similar to those underlying Section 2.1 analyses which Macek rejects on three counts:

(1) Macek says Section 2.1 analyses lacked data on covariates at the individual level. However, for the 150,000 NY State children (see Fig. 1A and B) Masters et al., 2000 says:

> ''Controlling at the individual level for covariates usually associated with lead uptake, elevated blood lead was statistically significant with $p < 0.001$ and Hi/Low risk ratios in the range of 1.5–2.0 depending on age and race''.

(2) Macek says Section 2.1 analyses used unclear sampling methods. However, the data for Massachusetts children were collected under State regulations by qualified agencies. Overall ascertainment rate was over 60% with 80% in most large communities (Masters and Coplan, 1999). The data were considered satisfactory by State health authorities for other epidemiologic analyses by Dartmouth-Hitchcock Hospital staff with partial CDC funding (Bailey et al., 1994; Sargent et al., 1995). Data for New York State children provided by the State Health Department for individuals included race, age, and poverty status. SiF exposure was determined from CDC information about community fluoridation status. The study was as close to case/control as possible (Masters et al., 2000). Moreover, the NHANES III data for the Section 2.1 analyses were collected the same way Macek's NHANES III data were collected.

(3) Macek objects to Section 2.1 analyses using skewed untransformed data to compare community mean PbB values. However, using log transformed, less skewed data to find a central tendency does injustice to worst case children. Suppressing the statistical effect of their high outlier PbB values makes it seem that the risk of elevated PbB where these children reside is closer to the norm for other communities. The CDC recently pledged ''intensified efforts to target areas at highest risk, evaluate preventive measures, and improve the quality of surveillance data'' (CDC Sept 12, 2003). Making comparisons based on geometric mean data does not foster that objective.

While Macek et al., 2006 claims its results are based on a superior analytic approach, it could not refute or confirm the results summarized in II A. The probable reason for this ambiguous outcome can be explained as follows:

(a) Macek used 5 μg/dL rather than 10 μg/dL as the criterion for elevated PbB. This downshifted OR values comparing the same two populations (Table 9). An OR based on 10 μg/dL can be 50% greater than if 5 μg/dL is used. Fig. 2a and b demonstrate how skewed untransformed PbB data can be used more effectively than GM values to reveal PbB problem populations. This isn't meant to suggest that PbB 5 μg/dL is acceptable for individuals. Rather, it means that using 5 μg/dL as an action trigger for alleviating community elevated PbB makes it easier to ignore the effect of PbW.

(b) While referring to the lead leaching capacity of ''silicofluoride compounds'' as a single class, Macek treated FSA and NaFSA as different SiF classes for statistical analysis. There was no reason to analyze PbB data for children drinking FSA treated water separately from those drinking NaFSA treated water. This produced two smaller groups of children exposed to SiFW. The OR confidence intervals in these smaller groups had to have broader band-widths with lower bounds near 1.0, based solely on an arbitrary statistical artifact.

Table 9
Blood lead data used by Macek et al., 2006 re-analyzed, confirming an association of silicofluoride with elevated blood lead for children aged 1–16 in NHANES III database

WF status	Number sampled	Number with[a] PbB > 5 μg/dL	Percentage with PbB > 5 μg/dL (%)
SiF treated[b]	3170	524	16.5
All other[c] known	4004	568	14.2

Odds Ratio: 1.20, Wald Chi-Square p-value: 0.006. Wald 95% Confidence Interval: (1.05, 1.36).

[a] The standard criterion for elevated blood lead is >10 μg/dL; an OR of 1.2 found using >5 μg/dL predicts an OR greater then 1.2 using >10 μg/dL as the criterion.

[b] Fluosilicic acid and sodium silicofluoride combined.

[c] Natural, NaF treated, and non-fluoridated combined.

(c) Macek used three dwelling age categories when two would have sufficed. A cut-off of 1940 or 1950 could have determined ''older housing'' as a risk of elevated PbB due to lead plumbing or lead paint. Data for pre-1946 housing were actually available and could have been used to compare with the others, rather than ''1974-present''.
(d) Macek required 90% of a county be fluoridated with a single agent (or none) for a child living there to be assigned any fluoridation status. Many children could arbitrarily remain unassigned in a county less than 90% fluoridated by either FSA or NaFSA alone when combined they could comprise 90% or more getting SiFW.

These flaws notwithstanding, Macek's raw data (see Appendix A) can be properly analyzed, using NHANES III weighting, to show that SiFW is associated with higher PbB levels than where other WFS prevails. For each housing age, the percent of children with PbB $>$ 5 ug/dL multiplied by the number of children tested from any category gives the likely number of children with elevated PbB in a random sampling of that category. Since ''Unknown/mixed'' fluoridation category provides no data on SiF effects, it should be excluded.

PbB data for children in communities delivering NaFSA and FSA treated water combined as one SiF group and summed across all housing ages should be compared with PbB data for all other children, also summed across housing ages. The comparison in Table 9 shows that children getting SiFW had statistically significant higher PbB than all others combined.

The OR of 1.2 might seem inconsequential but it is based on 5 μg/dL, not the usual 10 μg/dL criterion. Since raising the cut-off of a continuous variable also raises an observed OR, if 1.2 is valid for 5 μg/dL the OR for 10 μg/dL would be meaningfully higher, possibly 2 or greater.

While Macek data analysis could neither confirm nor refute a PbB effect of SiF treated water, the same data does confirm that association when properly analyzed. On that count alone, under the Precautionary Principle, the two CDC policy positions embodied in the following quote are questionable, but Maas et al., in press also provides compelling evidence of the linkage between SiFW and PbB ''demonstrated by additional research''. Macek's policy position is not supported by the facts.

> ''Efforts to decrease exposure to lead among children by targeting prevention efforts at high-risk communities and/or populations as well as efforts to prevent dental caries via the use of fluoridated drinking water should continue unless a causal impact of certain fluoridation methods on PbB concentration is demonstrated by additional research.'' (Macek et al., 2006).

6. Conclusions

The effect of PbW on elevated PbB in children has been underestimated on several counts: (a) a fetus *in utero* is exposed to lead in the mother's blood released from her bones and/or ingested with her food and drink; (b) a newborn ingests more water per pound of body weight than an adult; (c) all children absorb more of the lead they ingest than adults; (d) their developmental state renders them more susceptible to neurotoxic damage; (e) lead in drinking water extracted from brass plumbing fixtures by combinations of disinfection and fluoridation chemicals is more important than previously thought and has not had the attention it deserves.

The role of silicofluorides with significant capacity for enzyme inhibition and other bio-activity adverse to neural health, among other problems, has not been properly explored. On the other hand, several studies designed to rebut this conclusion not only fail to do so, they provide evidence of its validity.

It is proposed here that geometric mean values for community based blood lead levels obscure real problem populations by suppressing high side ''outlier'' cases that would otherwise be evident in simple scatter diagrams of non-transformed data for individuals.

Finally, an NRC Committee appointed in 2003 to review MCLG for fluoride (a) noted the widespread use of

Table A.1
Prevalence and adjusted odds of an elevated PbB concentration at the 5-μg/dL cut-off for U.S. children 1–16 years of age, by water fluoridaticn method and year in which dwelling was built, 1988–1934 (n = 9,477)[a]

Water fluoridation method[b]	Before 1946			1946–1973			1974-Present			Unknown		
	No.	Percent[c]	OR (95% CI)[d]	No.	Percent	OR (95% CI)	No	Percent	OR (95% CD	No.	Percent	OR (95%CI)
Unknown/mixed status	473	24.7	0.9 (0.4–1.9)	837	11.4	1.1(0.4–2.7)	674	8.3	1.2 (0.5–3.2)	319	21.9	3.8 (2.0–7.0)
Sodium silicofluoride	141	20.7[e]	0.9 (0.3–2.8)	420	16.8	0.8 (0.3–2.5)	289	6.5[e]	1.0 (0.4–2.5)	71	30.1	2.8 (0.8–9.8)
Hydrofluosilicic acid	448	30.1	1.2 (0.6–2.5)	839	14.7	1.4 (0.7–2.9)	605	5.4	1.7 (0.6–4.3)	257	24.7	5.3 (2.7–10.5)
Sodium fluoride	78	20.9	0.8 (0.3–1.7)	127	7.6[e]	1.5 (0.4–5.3)	81	6.0[e]	0.6 (0.1–4.6)	60	6.6[e]	1.0 (0.3–3.6)
Natural fluoride	113	19.4	0.3 (0.1–01.6)	419	17.3	1.5 (0.7–3.2)	413	7.3[e]	1.1 (0.3–3.8)	182	16.6	1.0 (0.4–2.2)
No fluoride	307	26.4	Reference	1176	16.0	Reference	707	6.4	Reference	341	18.4	Reference
Adjusted Wald-F p-value			<0.01			0.76			0.76			<0.01

[a] From the Third National Health and Nutrition Examination Survey (1988–1994) and 1932 Fluoridation Census.
[b] Weighted to reflect the civilian noninstitutionalized population of the United States; persons with unknown blood lead levels were excluded from analysis.
[c] Percentage of the population with an elevated blood lead concentration (≥5 μg/dL).
[d] Adjusted OR of an elevated blood lead concentration at the 5-μg/dL cut-off, controlling for age, sex, race/ethnicity, poverty status, urbanicity, and duration of residence.
[e] Does not meet the standard for statistical reliability.

silicofluorides in its March 22, 2006 report; (b) warned that a 4 ppm F^- MCLG was not protective of human health as regards dental and skeletal fluorosis; (c) included neurotoxic and behavioral issues in its studies; and (d) reinforced the need for the NTP to do animal tests of SiFs that have been on its ''nomination'' agenda since 2002.

Appendix A

Table A.1.

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