WATER FLUORIDATION
RESOLUTION COMPENDIUM

Background
Fluoride

JUNE 17TH, 2015
PUBLIC UTILITIES COMMITTEE
CITY OF AUSTIN

RESOLUTION NO._____

WHEREAS, in the early 1970's, before any serious longitudinal study of the health effects of water fluoridation was conducted, voters of the City of Austin approved a referendum to fluoridate the municipal water supply; and,

WHEREAS, research from the 1940's through the 1960's argued that artificial water fluoridation resulted in acid-resistant teeth. But conflicting research, namely the 2006 National Research Council's review of 1,100 worldwide epidemiological and laboratory studies, found that to the contrary the current levels of fluoride added to the water results in the following "adverse health effects: moderate dental fluorosis, stage I skeletal fluorosis, decreased thyroid function, and detrimental effects on the brain."; and,

WHEREAS, a study of release by the Department of Environmental Science at Harvard School of Public Health in conjunction with China Medical University in 2011 urged the results not to be ignored while concluding that the study "supports the possibility of adverse effects of high fluoride exposure on children's neurodevelopment" and also that "children in high fluoride areas have significantly lower IQ scores than children in low fluoride areas."; and,

WHEREAS, in a letter written in 2006, scientists and other representatives of the United States' Environmental Protection Agency (EPA) pleaded with Congress, and the U.S. Public Health Service to immediately halt the artificial fluoridation of water, citing many studies, one of which from the Harvard School of Dental Medicine, found that "pre-adolescent boys who drink fluoridated water are at a seven-fold increased risk of osteosarcoma, an often fatal bone cancer."; and,

WHEREAS, while the benefits and risks of water fluoridation are now under contentious debate, infants, children, the elderly and other with compromised immune systems may be harmed by ingesting fluoride via drinking water; and,

WHEREAS, scientific studies are too copious to enumerate, but the results of many studies show negative effects including endocrine function, cognitive function, skeletal problems, dental fluorosis, and thyroid impairment; and,

WHEREAS, when hydrofluorosilicic acid is ingested the fluoride replaces calcium in the bones resulting in an increased susceptibility to certain bone cancers. Dartmouth scientist, Dr Roger Masters, and chemical engineer, Myron Coplan, published studies in 1999 and 2000 reporting that exposure to fluoridated water was associated with increased blood lead levels in children, and three other published studies in Neurotoxicology and National Institute of Environmental Health Science, 2006-2007, confirmed these findings; and,

WHEREAS, Center for Disease Control and Prevention (CDC) and National Center for Health Statistics (NCHS), determined in their study, Prevalence and Severity of Dental Fluorosis in the

United States, 1999–2004, that 40.7% of American teenagers have dental fluorosis. The prevalence of fluorosis increased 18.1% since 1987-1988 survey, and the prevalence of moderate and severe fluorosis increased from 1.3% to 3.6%; and,

WHEREAS, human breast milk naturally contains very low levels of fluoride (.004ppm) which is 175 times less than the levels in Austin's fluoridated drinking water (.7ppm). As a result, infants drinking reconstituted formula with fluoridated water are far exceeding the recommended dosage for themselves as well as for adults; and,

WHEREAS, hydrofluorosilicic acid is not a pharmaceutical-grade substance but rather a hazardous toxic waste product resulting from strip mining of phosphate for fertilizers and this waste product has strict guidelines for disposal; and,

WHEREAS, because topical fluoride is available through low cost toothpastes and supplements, stopping the practice of artificially fluoridating the Austin water supply does not deprive citizens of the benefits of fluoride; and,

WHEREAS, the current cost of opting-out of fluoride through avoidance measures such as purchasing reverse-osmosis and distillation equipment and unfluoridated bottled water far exceeds the expense of opting-in through topical use or supplementation. With high costs associated with treatment of dental fluorosis and other health care costs, low-income families are disproportionately burdened by the negative effects of water fluoridation; and,

WHEREAS, during initial fluoridation trials in the 1940's, it was believed that fluoride needed to be ingested, however since the 1980's, there is now a scientific consensus that the primary benefits of fluoride are topical. This new understanding undermines the premise of water fluoridation; and,

WHEREAS, because all Federal and State agencies and any company providing fluoride to municipalities for water fluoridation relinquish all legal responsibility to the purchasing municipality, the City of Austin is at risk if it is concluded that water fluoridation has specifically caused the ailments it is associated with; and,

WHEREAS, in recent decades the scientific research has convinced other developed nations that had previously fluoridated their water supply to cease the practice. Those countries include Finland, Sweden, Germany, Czechoslovakia, and Japan; and,

WHEREAS, it is unethical to force residents to consume any drug or nutrient especially when the condition is not deadly or contagious; **NOW, THEREFORE:**

BE IT RESOLVED BY THE CITY COUNCIL OF THE CITY OF AUSTIN:

That Resolution 720817-11 and Resolution 20111215-011 be repealed and rescinded and directs the the City Manager is directed to cease the addition of artificial fluoride, including hydrofluorosilicic acid, sodium fluoride, sodium fluorosilicate or any other methods of fluoridation, to the City of Austin's water supply by December 1, 2015.

NCHS Data Brief ■ No. 53 ■ November 2010

Prevalence and Severity of Dental Fluorosis in the United States, 1999–2004

Eugenio D. Beltrán-Aguilar, D.M.D., M.S., Dr.P.H.; Laurie Barker, M.S.P.H.; and Bruce A. Dye, D.D.S., M.P.H.

Key findings

Data from the National Health and Nutrition Examination Survey, 1999–2004 and the 1986–1987 National Survey of Oral Health in U.S. School Children

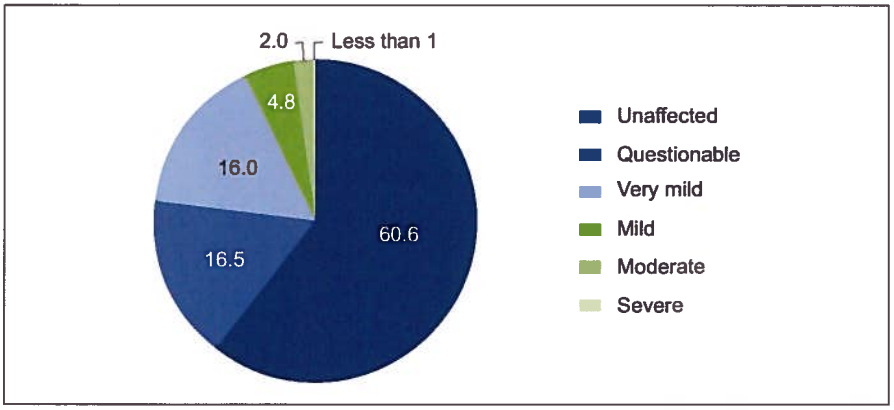
- Less than one-quarter of persons aged 6–49 in the United States had some form of dental fluorosis.
- The prevalence of dental fluorosis was higher in adolescents than in adults and highest among those aged 12–15.
- Adolescents aged 12–15 in 1999–2004 had a higher prevalence of dental fluorosis than adolescents aged 12–15 in 1986–1987.

Dental fluorosis refers to changes in the appearance of tooth enamel that are caused by long-term ingestion of fluoride during the time teeth are forming (1). Studies conducted in the 1930s showed that the severity of tooth decay was lower and dental fluorosis was higher in areas with more fluoride in the drinking water (2). In response to these findings, community water fluoridation programs were developed to add fluoride to drinking water to reach an optimal level for preventing tooth decay, while limiting the chance of developing dental fluorosis (3). By the 1980s, studies in selected U.S. communities reported an increase in dental fluorosis (4,5), paralleling the expansion of water fluoridation and the increased availability of other sources of ingested fluoride, such as fluoride toothpaste (if swallowed) and fluoride supplements (6). This report describes the prevalence of dental fluorosis in the United States and changes in the prevalence and severity of dental fluorosis among adolescents between 1986–1987 and 1999–2004.

Keywords: children • dental public health • National Health and Nutrition Examination Survey • National Survey of Oral Health in U.S. School Children

Less than one-quarter of persons aged 6–49 had dental fluorosis.

Figure 1. Percent distribution of dental fluorosis among persons aged 6–49: United States, 1999–2004



NOTES: Dental fluorosis is defined as having very mild, mild, moderate, or severe forms and is based on Dean's Fluorosis Index. Percentages do not sum to 100 due to rounding.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2004.

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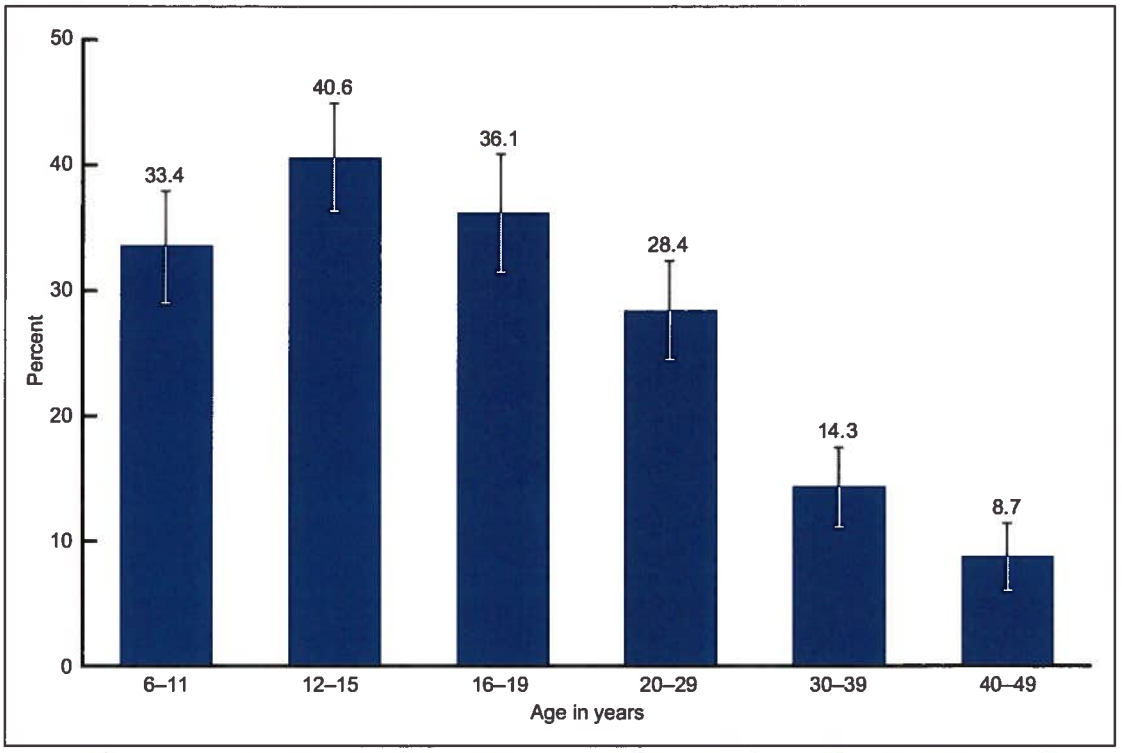
Among persons aged 6–49, 16.0% had very mild fluorosis, 4.8% had mild fluorosis, 2.0% had moderate fluorosis, and less than 1% had severe fluorosis (Figure 1).

For the remaining three-quarters of persons in this age group, 60.6% were unaffected by dental fluorosis and 16.5% were classified as having questionable dental fluorosis.

Prevalence of dental fluorosis was higher among younger persons and ranged from 41% among adolescents aged 12–15 to 9% among adults aged 40–49.

Adolescents aged 12–15 had the highest prevalence of dental fluorosis (40.6%) (Figure 2). The prevalence is lower among older age groups. The lowest prevalence was among those aged 40–49 (8.7%). The prevalence of dental fluorosis among children aged 6–11 (33.4%) was lower than the prevalence among those aged 12–15 (40.6%).

Figure 2. Prevalence of dental fluorosis among persons aged 6–49, by age group: United States, 1999–2004



NOTES: Dental fluorosis is defined as having very mild, mild, moderate, or severe forms and is based on Dean's Fluorosis Index. Error bars represent 95% confidence intervals.

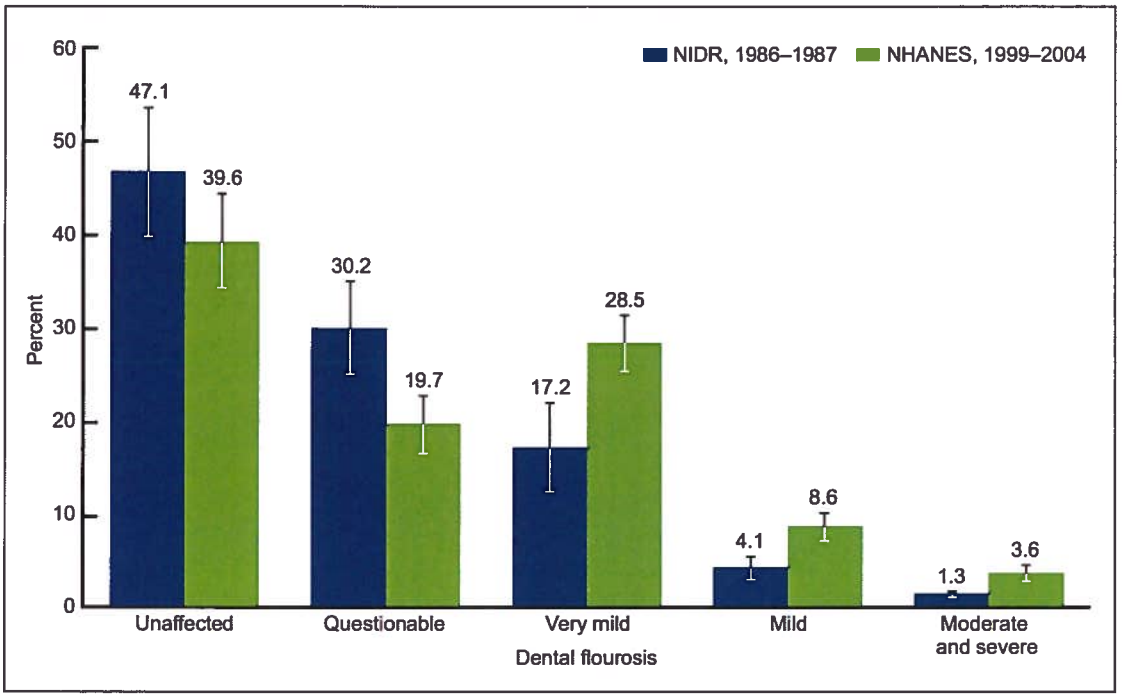
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2004.

Children aged 12–15 in 1999–2004 had higher prevalence of dental fluorosis compared with the same aged children in 1986–1987.

In 1986–1987, 22.6% of adolescents aged 12–15 had dental fluorosis, whereas in 1999–2004, 40.7% of adolescents aged 12–15 had dental fluorosis (Figure 3). The estimates for severe alone were statistically unreliable.

The prevalence of very mild fluorosis increased from 17.2% to 28.5% and mild fluorosis increased from 4.1% to 8.6%. The prevalence of moderate and severe fluorosis increased from 1.3% to 3.6%.

Figure 3. Change in dental fluorosis prevalence among children aged 12–15 participating in two national surveys: United States, 1986–1987 and 1999–2004



NOTES: Dental fluorosis is defined as having very mild, mild, moderate, or severe forms and is based on Dean's Fluorosis Index. Percentages do not sum to 100 due to rounding. Error bars represent 95% confidence intervals.

SOURCES: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2004 and National Institute of Dental Research, National Survey of Oral Health in U.S. School Children, 1986–1987.

Summary

Twenty-three percent of persons aged 6–49 had dental fluorosis in 1999–2004. Approximately 2% had moderate dental fluorosis and less than 1% had severe dental fluorosis. Dental fluorosis was most prevalent among children aged 12–15, and less prevalent among older age groups. The prevalence of dental fluorosis among children aged 6–11 was lower than the prevalence among adolescents aged 12–15. This may be explained by an incomplete set of permanent teeth among children aged 6–11; some posterior permanent teeth, including premolars and second molars, erupt between ages 10 and 12.

The levels of very mild, mild, and moderate or severe dental fluorosis were higher among adolescents aged 12–15 in 1999–2004 than in 1986–1987.

In the analyses of changes in prevalence between both national surveys, moderate and severe dental fluorosis were aggregated into one category because all estimates of severe fluorosis were statistically unreliable after stratification (standard error of the percentage was greater than 30% the value of the percentage).

Definitions

Dental fluorosis: Defined as a change in the mineralization of the dental hard tissues (enamel, dentin, and cementum) caused by long-term ingestion (eating and drinking) of fluoride during the period of tooth development prior to eruption into the mouth (first 8 years of life for most permanent teeth excluding third molars). Once the tooth erupts, dental fluorosis refers to a range of visually detectable changes in enamel. Changes range from barely visible lacy white markings in milder cases to converged opaque areas and pitting of the teeth in severe forms. After eruption the pitted areas can become stained yellow to dark brown.

Dean's Fluorosis Index: Developed in the 1930s by H.T. Dean to assess the prevalence and severity of dental fluorosis in various communities in the United States (2). Major criteria for each category are listed below:

- *Unaffected*: The enamel is translucent. The surface of the tooth is smooth, glossy, and usually has a pale creamy white color.
- *Questionable*: The enamel shows slight changes ranging from a few white flecks to occasional white spots. This classification is utilized in those instances in which a definitive determination of the mildest form of fluorosis is not warranted and a classification of unaffected is not justified.
- *Very mild*: Small opaque paper-white areas are scattered over the tooth surface, but do not involve as much as 25% of the surface.
- *Mild*: White opaque areas on the surface are more extensive, but do not involve as much as 50% of the surface.
- *Moderate*: White opaque areas affect more than 50% of the enamel surface.
- *Severe*: All enamel surfaces are affected. The major aspect of this classification is the presence of discrete or confluent pitting.

Prevalence of dental fluorosis: Defined as the proportion of the population with very mild or higher levels of dental fluorosis, by convention established by H.T. Dean (2). The questionable category is excluded.

Data source and methods

Data from the National Health and Nutrition Examination Survey (NHANES) were used for most of these analyses. NHANES is a cross-sectional survey designed to monitor the health and nutritional status of the civilian noninstitutionalized U.S. population. The oral health exam was conducted in mobile examination centers by trained dentists. In 1999, NHANES became a continuous survey with each year of data collection based on a representative sample covering all ages. The NHANES sample is selected through a complex, multistage design that includes selection of primary sampling units (PSUs) (counties or county equivalents), household segments within the PSUs, and finally, sample persons from selected households. The sample design includes oversampling in order to obtain reliable estimates of health and nutritional measures for population subgroups. In 1999–2004, oversampling included non-Hispanic black and Mexican-American persons as well as adolescents. Additional information on NHANES can be located at http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm.

Data from the 1986–1987 National Survey of Oral Health in U.S. School Children were also used, which was conducted by the National Institute of Dental Research (NIDR, currently the National Institute of Dental and Craniofacial Research). The oral health exam was conducted using portable dental equipment on the school premises by trained dentists. The 1986–1987 NIDR sample was selected through a multistage design that included selection of school districts, schools, and classrooms. Because the 1986–1987 NIDR survey was school-based, children not attending school were not part of the sampling frame. Additional information for the 1986–1987 NIDR survey is available in the public-use data file documentation and survey methodology report (7).

Both surveys included intraoral assessment of all permanent teeth conducted by trained and standardized dental examiners who used the Dean's Fluorosis Index (2). Accordingly, each tooth was assigned one of six diagnostic codes: unaffected, questionable, very mild, mild, moderate, and severe. Examiners in both surveys reached acceptable levels of interexaminer reliability against a standard examiner (8–10). Data from the 1986–1987 NIDR survey represent the first national data on dental fluorosis, while data from the 1999–2004 NHANES represent the most recent national data. The age group 12–15 was used to compare changes between surveys because, on average, all permanent teeth are fully erupted at that age.

Publicly available datasets from both surveys were used to calculate a person-based score for dental fluorosis following Dean's criteria, that is, using the score corresponding to the two most affected teeth. For example, in order to have a category of "moderate" fluorosis, the person should have at least two permanent teeth with the score of moderate. For analyses using age, data from the 1999–2004 NHANES were grouped into six age groups (6–11, 12–15, 16–19, 20–29, 30–39, and 40–49) and comparisons to the 1986–1987 NIDR survey used data from respondents aged 12–15.

Population estimates and standard errors were calculated in SAS-callable SUDAAN software (release 9.0; Research Triangle Institute, Research Triangle Park, N.C.). Sample weights provided by the National Center for Health Statistics and NIDR to account for differing probabilities of selection, nonresponse, and noncoverage, were used for analysis. The standard errors of the percentages were estimated using Taylor Series Linearization to take into account the complex sampling design. Graphs include 95% confidence intervals.

About the authors

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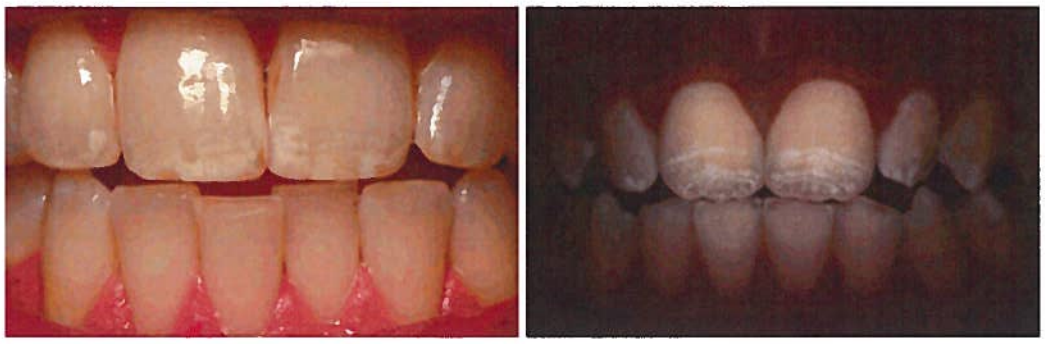
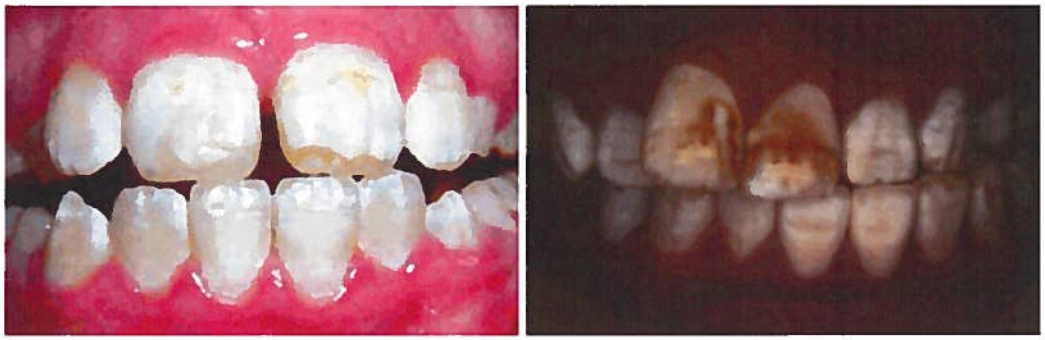
DENTAL FLUOROSIS

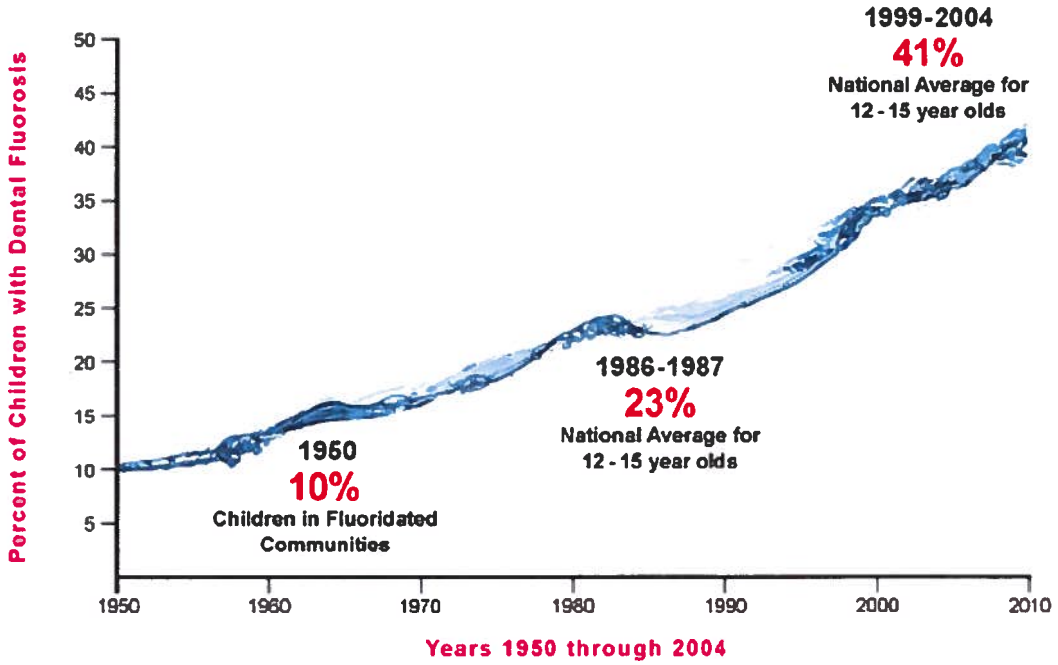


"Very Mild" "Mild"



"Moderate" "Severe"

Dental Fluorosis Rates in the United States: 1950 through 2004



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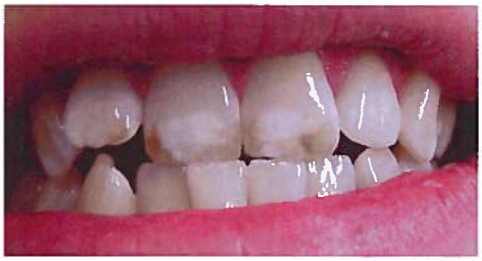
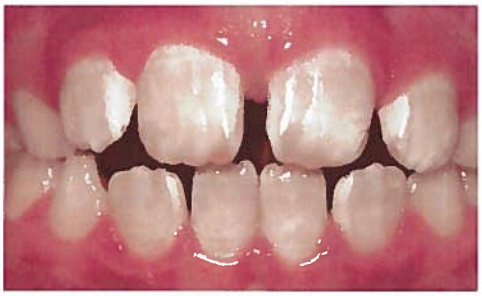
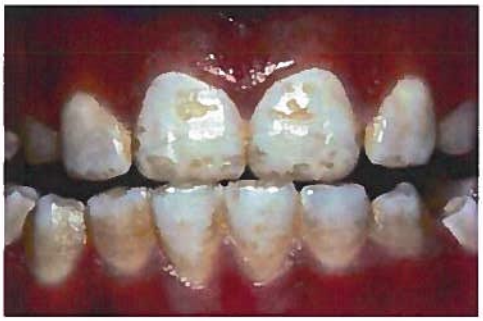
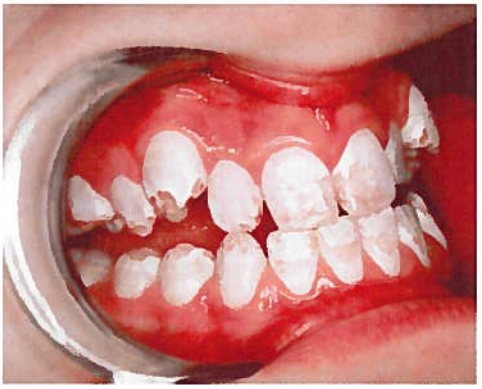
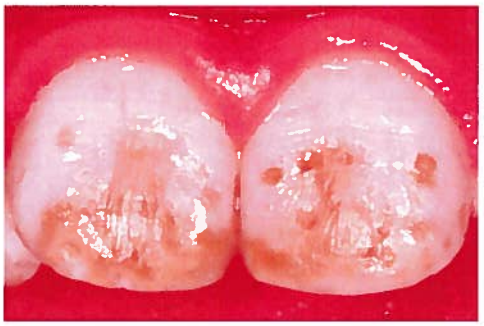
DENTAL FLUOROSIS

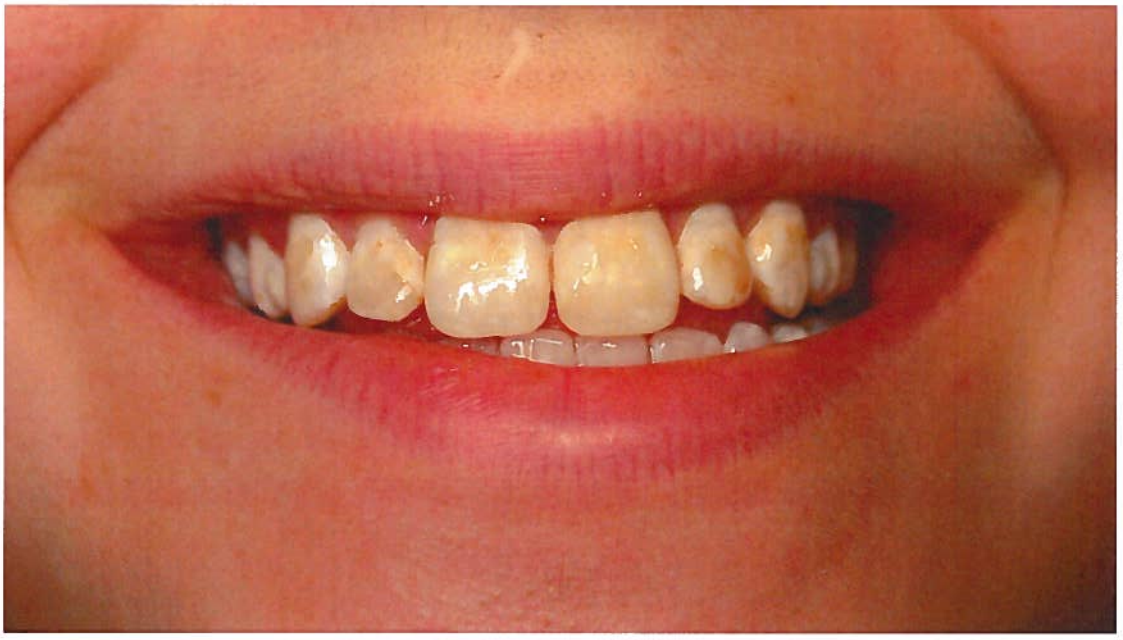












Review

Developmental Fluoride Neurotoxicity: A Systematic Review and Meta-Analysis

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Background: Although fluoride may cause neurotoxicity in animal models and acute fluoride poisoning causes neurotoxicity in adults, very little is known of its effects on children's neurodevelopment.

Objective: We performed a systematic review and meta-analysis of published studies to investigate the effects of increased fluoride exposure and delayed neurobehavioral development.

Methods: We searched the MEDLINE, EMBASE, Water Resources Abstracts, and TOXNET databases through 2011 for eligible studies. We also searched the China National Knowledge Infrastructure (CNKI) database, because many studies on fluoride neurotoxicity have been published in Chinese journals only. In total, we identified 27 eligible epidemiological studies with high and reference exposures, end points of IQ scores, or related cognitive function measures with means and variances for the two exposure groups. Using random-effects models, we estimated the standardized mean difference between exposed and reference groups across all studies. We conducted sensitivity analyses restricted to studies using the same outcome assessment and having drinking-water fluoride as the only exposure. We performed the Cochran test for heterogeneity between studies, Begg's funnel plot, and Egger test to assess publication bias, and conducted meta-regressions to explore sources of variation in mean differences among the studies.

Results: The standardized weighted mean difference in IQ score between exposed and reference populations was −0.45 (95% confidence interval: −0.56, −0.35) using a random-effects model. Thus, children in high-fluoride areas had significantly lower IQ scores than those who lived in low-fluoride areas. Subgroup and sensitivity analyses also indicated inverse associations, although the substantial heterogeneity did not appear to decrease.

Conclusions: The results support the possibility of an adverse effect of high fluoride exposure on children's neurodevelopment. Future research should include detailed individual-level information on prenatal exposure, neurobehavioral performance, and covariates for adjustment.

Key words: fluoride, intelligence, neurotoxicity. *Environ Health Perspect* 120:1362–1368 (2012). http://dx.doi.org/10.1289/ehp.1104912 [Online 20 July 2012]

A recent report from the National Research Council (NRC 2006) concluded that adverse effects of high fluoride concentrations in drinking water may be of concern and that additional research is warranted. Fluoride may cause neurotoxicity in laboratory animals, including effects on learning and memory (Chioca et al. 2008; Mullenix et al. 1995). A recent experimental study where the rat hippocampal neurons were incubated with various concentrations (20 mg/L, 40 mg/L, and 80 mg/L) of sodium fluoride *in vitro* showed that fluoride neurotoxicity may target hippocampal neurons (Zhang M et al. 2008). Although acute fluoride poisoning may be neurotoxic to adults, most of the epidemiological information available on associations with children's neurodevelopment is from China, where fluoride generally occurs in drinking water as a natural contaminant, and the concentration depends on local geological conditions. In many rural communities in China, populations with high exposure to fluoride in local drinking-water sources may reside in close proximity to populations without high exposure (NRC 2006).

Opportunities for epidemiological studies depend on the existence of comparable population groups exposed to different levels of fluoride from drinking water. Such circumstances are difficult to find in many industrialized countries, because fluoride concentrations in community water are usually no higher than 1 mg/L, even when fluoride is added to water supplies as a public health measure to reduce tooth decay. Multiple epidemiological studies of developmental fluoride neurotoxicity were conducted in China because of the high fluoride concentrations that are substantially above 1 mg/L in well water in many rural communities, although microbiologically safe water has been accessible to many rural households as a result of the recent 5-year plan (2001–2005) by the Chinese government. It is projected that all rural residents will have access to safe public drinking water by 2020 (World Bank 2006). However, results of the published studies have not been widely disseminated. Four studies published in English (Li XS et al. 1995; Lu et al. 2000; Xiang et al. 2003; Zhao et al. 1996) were cited in a recent report from the NRC (2006), whereas the World Health Organization (2002) has considered only two (Li XS et al. 1995; Zhao et al. 1996) in its most recent monograph on fluoride.

Fluoride readily crosses the placenta (Agency for Toxic Substances and Disease Registry 2003). Fluoride exposure to the developing brain, which is much more susceptible to injury caused by toxicants than is the mature brain, may possibly lead to permanent damage (Grandjean and Landrigan 2006). In response to the recommendation of the NRC (2006), the U.S. Department of Health and Human Services (DHHS) and the U.S. EPA recently announced that DHHS is proposing to change the recommended level of fluoride in drinking water to 0.7 mg/L from the currently recommended range of 0.7–1.2 mg/L, and the U.S. EPA is reviewing the maximum amount of fluoride allowed in drinking water, which currently is set at 4.0 mg/L (U.S. EPA 2011).

To summarize the available literature, we performed a systematic review and meta-analysis of published studies on increased fluoride exposure in drinking water associated with neurodevelopmental delays. We specifically targeted studies carried out in rural China that have not been widely disseminated, thus complementing the studies that have been included in previous reviews and risk assessment reports.

Methods

Search strategy. We searched MEDLINE (National Library of Medicine, Bethesda, MD, USA; http://www.ncbi.nlm.nih.gov/pubmed), Embase (Elsevier B.V., Amsterdam, the Netherlands; http://www.embase.com), Water Resources Abstracts (Proquest, Ann Arbor, MI, USA; http://www.csa.com/factsheets/water-resources-set-c.php), and TOXNET (Toxicology Data Network; National Library of Medicine, Bethesda, MD, USA; http://toxnet.nlm.nih.gov) databases to identify studies of drinking-water fluoride and neurodevelopmental outcomes in children. In addition, we searched the China National Knowledge Infrastructure (CNKI; Beijing, China; http://www.cnki.net) database to identify studies published in Chinese journals only. Key

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Supplemental Material is available online (http://dx.doi.org/10.1289/ehp.1104912).

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The authors declare they have no actual or potential competing financial interests.

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words included combinations of "fluoride" or "drinking water fluoride," "children," "neurodevelopment" or "neurologic" or "intelligence" or "IQ." We also used references cited in the articles identified. We searched records for 1980–2011. Our literature search identified 39 studies, among which 36 (92.3%) were studies with high and reference exposure groups, and 3 (7.7%) studies were based on individual-level measure of exposures. The latter showed that dose-related deficits were found, but the studies were excluded because our meta-analysis focused on studies with the high- and low-exposure groups only. In addition, two studies were published twice, and the duplicates were excluded.

Inclusion criteria and data extraction. The criteria for inclusion of studies included studies with high and reference fluoride exposures, end points of IQ scores or other related cognitive function measures, presentation of a mean outcome measure, and associated measure of variance [95% confidence intervals (CIs) or SEs and numbers of participants]. Interpretations of statistical significance are based on an alpha level of 0.05. Information included for each study also included the first author, location of the study, year of publication, and numbers of participants in high-fluoride and low-fluoride areas. We noted and recorded the information on age and sex of children, and parental education and income if available.

Statistical analysis. We used STATA (version 11.0; StataCorp, College Station, TX, USA) and available commands (Stern 2009) for the meta-analyses. A standardized weighted mean difference (SMD) was computed using both fixed-effects and random-effects models. The fixed-effects model uses the Mantel–Haenszel method assuming homogeneity among the studies, whereas the random-effects model uses the DerSimonian and Laird method, incorporating both a within-study and an additive between-studies component of variance when there is between-study heterogeneity (Egger et al. 2001). The estimate of the between-study variation is incorporated into both the SE of the estimate of the common effect and the weight of individual studies, which was calculated as the inverse sum of the within and between study variance. We evaluated heterogeneity among studies using the I^2 statistic, which represents the percentage of total variation across all studies due to between-study heterogeneity (Higgins and Thompson 2002). We evaluated the potential for publication bias using Begg and Egger tests and visual inspection of a Begg funnel plot (Begg and Mazumdar 1994; Egger et al. 1997). We also conducted independent meta-regressions to estimate the contribution of study characteristics (mean age in years from the age range and year of publication in each study) to heterogeneity among the studies. The scoring standard for the Combined Raven's Test–The Rural edition in China (CRT-RC) test classifies scores of ≤ 69 and 70–79 as low and marginal intelligence, respectively (Wang D et al. 1989). We also used the random-effects models to estimate risk ratios for the association between fluoride exposure and a low/marginal versus normal Raven's test score among children in studies that used the CRT-RC test (Wang D et al. 1989). Scores indicating low and marginal intelligence (≤ 69 and 70–79, respectively) were combined as a single outcome due to small numbers of children in each outcome subgroup.

Results

Six of the 34 studies identified were excluded because of missing information on the number of subjects or the mean and variance of the outcome [see Figure 1 for a study selection flow chart and Supplemental Material, Table S1 (http://dx.doi.org/10.1289/ehp.1104912) for additional information on studies that were excluded from the analysis]. Another study (Trivedi et al. 2007) was excluded because SDs reported for the outcome parameter were questionably small (1.13 for the high-fluoride group, and 1.23 for the low-fluoride group) and the SMD (–10.8; 95% CI: –11.9, –9.6) was > 10 times lower than the second smallest SMD (–0.95; 95% CI: –1.16, –0.75) and 150 times lower than the largest SMD (0.07; 95% CI: –0.083, 0.22) reported for the other studies, which had relatively consistent SMD estimates. Inclusion of this study in the meta-analysis resulted with a much smaller pooled random-effects SMD estimate and a much larger I^2 (–0.63; 95% CI: –0.83, –0.44, I^2 94.1%) compared with the estimates that excluded this study (–0.45; 95% CI: –0.56, –0.34, I^2 80%) (see Supplemental Material, Figure S1). Characteristics of the 27 studies included are shown in Table 1 (An et al. 1992; Chen et al. 1991; Fan et al. 2007; Guo et al. 1991; Hong et al. 2001; Li FH et al. 2009; Li XH et al. 2010; Li XS 1995; Li Y et al. 1994; Li Y et al. 2003; Lin et al. 1991; Lu et al. 2000; Poureslami et al. 2011; Ren et al. 1989; Seraj et al. 2006; Sun et al. 1991; Wang G et al. 1996; Wang SH et al. 2001; Wang SX et al. 2007; Wang ZH et al. 2006; Xiang et al. 2003; Xu et al. 1994; Yang et al. 1994; Yao et al. 1996, 1997; Zhang JW et al. 1998; Zhao et al. 1996). Two of the studies included in the analysis were conducted in Iran (Poureslami et al. 2011; Seraj et al. 2006); the other study cohorts were populations from China. Two cohorts were exposed to fluoride from coal burning (Guo et al. 1991; Li XH et al. 2010); otherwise populations were exposed to fluoride through drinking water. The CRT-RC was used to measure the children's intelligence in 16 studies. Other intelligence measures included the Wechsler Intelligence tests (3 studies; An et al. 1992; Ren et al. 1989; Wang ZH et al. 1996), Binet IQ test (2 studies; Guo et al. 1991; Xu et al. 1994), Raven's test (2 studies; Poureslami et al. 2011; Seraj et al. 2006), Japan IQ test (2 studies; Sun et al. 1991; Zhang JW et al. 1998), Chinese comparative intelligence test (1 study; Yang et al. 1994), and the mental work capacity index (1 study; Li Y et al. 1994). Because each of the intelligence tests used is designed to measure general intelligence, we used data from all eligible studies to estimate the possible effects of fluoride exposure on general intelligence.

In addition, we conducted a sensitivity analysis restricted to studies that used similar tests to measure the outcome (specifically, the CRT-RC, Wechsler Intelligence test, Binet IQ test, or Raven's test), and an analysis restricted to studies that used the CRT-RC. We also performed an analysis that excluded studies with co-exposures including iodine and arsenic, or with non-drinking-water fluoride exposure from coal burning.

Pooled SMD estimates. Among the 27 studies, all but one study showed random-effect SMD estimates that indicated an inverse association, ranging from –0.95 (95% CI: –1.16, –0.75) to –0.10 (95% CI:

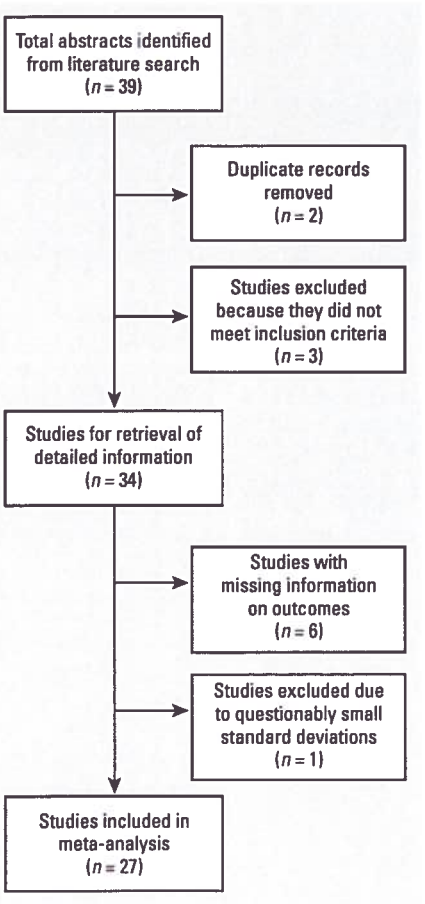

Figure 1. Flow diagram of the meta-analysis.

–0.25, 0.04) (Figure 2). The study with a positive association reported an SMD estimate of 0.07 (95% CI: –0.8, 0.22). Similar results were found with the fixed-effects SMD estimates. The fixed-effects pooled SMD estimate was –0.40 (95% CI: –0.44, –0.35), with a p-value < 0.001 for the test for homogeneity. The random-effects SMD estimate was –0.45 (95% CI: –0.56, –0.34) with an I^2 of 80% and homogeneity test p-value < 0.001 (Figure 2). Because of heterogeneity (excess variability) between study results, we used primarily the random-effects model for subsequent sensitivity analyses, which is generally considered to be the more conservative method (Egger et al. 2001). Among the restricted sets of intelligence tests, the SMD for the model with only CRT-RC tests and drinking-water exposure (and to a lesser extent the model with only CRT-RC tests) was lower than that for all studies combined, although the difference did not appear to be significant. Heterogeneity, however, remained at a similar magnitude when the analyses were restricted (Table 2).

Sources of heterogeneity. We performed meta-regression models to assess study characteristics as potential predictors of effect. Information on the child's sex and parental education were not reported in > 80% of the studies, and only 7% of the studies reported household income. These variables were therefore not included in the models. Among the two covariates, year of publication (0.02; 95% CI: 0.006, 0.03), but not mean age of the study children (–0.02; 95% CI: –0.094, 0.04), was a significant predictor in the model with all 27 studies included. I^2 residual 68.7% represented the proportion of residual between-study variation due to heterogeneity. From the adjusted R^2, 39.8% of between-study variance was explained by the two covariates. The overall test of the covariates was significant (p = 0.004).

When the model was restricted to the 16 studies that used the CRT-RC, the child's age (but not year of publication) was a significant predictor of the SMD. The R^2 of 65.6% of between-study variance was explained by the two covariates, and only 47.3% of the residual variation was attributable to heterogeneity. The overall test of both covariates in the model remained significant (p = 0.0053). On further restriction of the model to exclude the 7 studies with arsenic and iodine as coexposures and fluoride originating from coal burning (thus including only the 9 with fluoride exposure from drinking water), neither age nor year of publication was a significant predictor, and the overall test of covariates was less important (p = 0.062), in accordance with the similarity of intelligence test outcomes and the source of exposure in the studies included.

Table 1. Characteristics of epidemiological studies of fluoride exposure and children's cognitive outcomes.

Reference	Study location	No. in high-exposure group	No. in reference group	Age range (years)	Fluoride exposure		Outcome measure	Results
					Assessment	Range		
Ren et al. 1989	Shandong, China	160	169	8–14	High-/low-fluoride villages	Not specified	Wechsler Intelligence test[a]	Children in high-fluoride region had lower IQ scores
Chen et al. 1991	Shanxi, China	320	320	7–14	Drinking water	4.55 mg/L (high); 0.89 mg/L (reference)	CRT-RC[b]	The average IQ of children from high-fluoride area were lower than that of the reference area
Guo et al. 1991	Hunan, China	60	61	7–13	Fluoride in coal burning	118.1–1361.7 mg/kg (coal burning area); Control area used wood	Chinese Binet[c]	Average IQ in fluoride coal-burning area was lower than that in the reference area
Lin et al. 1991	Xinjiang, China	33	86	7–14	Drinking water	0.88 mg/L (high); 0.34 mg/L (reference)	CRT-RC[b]	Children in the high-fluoride (low-iodine) area had lower IQ scores compared with the children from the reference fluoride (low-iodine) areas
Sun et al. 1991	Guiyang, China	196	224	6.5–12	Rate of fluorosis	Fluorosis: 98.36% (high); not specified (reference)	Japan IQ test[d]	Mean IQ was lower in all age groups except ≤ 7 years in the area with high fluoride and aluminum (limited to high-fluoride population only)
An et al. 1992	Inner Mongolia, China	121	121	7–16	Drinking water	2.1–7.6 mg/L (high); 0.6–1.0 mg/L (reference)	Wechsler Intelligence test[a]	IQ scores of children in high-fluoride areas were significantly lower than those of children living in reference fluoride area
Li Y et al. 1994	Sichuan, China	106	49	12–13	Burning of high-fluoride coal to cook grain in high-fluoride area	4.7–31.6 mg/kg (high); 0.5 mg/kg (reference)	Child mental work capacity	Early, prolonged high fluoride intake causes a decrease in the child's mental work capacity
Xu et al. 1994	Shandong, China	97	32	8–14	Drinking water	1.8 mg/L (high); 0.8 mg/L (reference)	Binet-Simon[e]	Children had lower IQ scores in high-fluoride area than those who lived in the reference area.
Yang et al. 1994	Shandong, China	30	30	8–14	Well water	2.97 mg/L (high); 0.5 mg/L (reference)	Chinese comparative intelligence test[f]	The average IQ scores was lower in children from high-fluoride and -iodine area than those from the reference area, but the results were not significant
Li XS et al. 1995	Guizhou, China	681	226	8–13	Urine, Dental Fluorosis Index	1.81–2.69 mg/L (high); 1.02 mg/L (reference); DFI 0.8–3.2 (high); DFI < 0.4 (reference)	CRT-RC[b]	Children living in fluorosis areas had lower IQ scores than children living in nonfluorosis areas
Wang G et al. 1996	Xinjiang, China	147	83	4–7	Drinking water	> 1.0–8.6 mg/L (high); 0.58–1.0 mg/L (reference)	Wechsler Intelligence test[a]	Average IQ score was lower in children in the high-fluoride group than those in the reference group
Yao et al. 1996	Liaoning, China	266	270	8–12	Drinking water	2–11mg/L (high); 1 mg/L (reference)	CRT-RC[b]	Average IQ scores of children residing in exposed fluoride areas were lower than those in the reference area
Zhao et al. 1996	Shanxi, China	160	160	7–14	Drinking water	4.12 mg/L (high); 0.91 mg/L (reference)	CRT-RC[b]	Children living in high-fluoride and -arsenic area had significantly lower IQ scores than those living in the reference fluoride (and no arsenic) area
Yao et al. 1997	Liaoning, China	188	314	7–14	Drinking water	2 mg/L (exposed); 0.4 mg/L (reference)	CRT-RC[b]	IQ scores of children in the high-fluoride area were lower than those of children in the reference area

Continued

Although official reports of lead concentrations in the study villages in China were not available, some studies reported high percentage (95–100%) of low lead exposure (less than the standard of 0.01 mg/L) in drinking-water samples in villages from several study provinces (Bi et al. 2010; Peng et al. 2008; Sun 2010).

Publication bias. A Begg's funnel plot with the SE of SMD from each study plotted against its corresponding SMD did not show clear evidence of asymmetry, although two studies with a large SE also reported relatively large effect estimates, which may be consistent with publication bias or heterogeneity (Figure 3). The plot appears symmetrical for studies with larger SE, but with substantial variation in SMD among the more precise studies, consistent with the heterogeneity observed among the studies included in the analysis. Begg ($p = 0.22$) and Egger ($p = 0.11$) tests did not indicate significant ($p < 0.05$) departures from symmetry.

Pooled risk ratios. The relative risk (RR) of a low/marginal score on the CRT-RC test (< 80) among children with high fluoride exposure compared with those with low exposure (16 studies total) was 1.93 (95% CI: 1.46, 2.55; I^2 58.5%). When the model was restricted to 9 studies that used the CRT-RC and included only drinking-water fluoride exposure (Chen et al. 1991; Fan et al. 2007; Li XH et al. 2010; Li XS et al. 1995; Li Y et al. 2003; Lu et al. 2000; Wang ZH et al. 2006; Yao et al. 1996, 1997), the estimate was similar (RR = 1.75; 95% CI: 1.16, 2.65; I^2 70.6%). Although fluoride exposure showed inverse associations with test scores, the available exposure information did not allow a formal dose–response analysis. However, dose-related differences in test scores occurred at a wide range of water-fluoride concentrations.

Discussion

Findings from our meta-analyses of 27 studies published over 22 years suggest an inverse association between high fluoride exposure and children's intelligence. Children who lived in areas with high fluoride exposure had lower IQ scores than those who lived in low-exposure or control areas. Our findings are consistent with an earlier review (Tang et al. 2008), although ours more systematically addressed study selection and exclusion information, and was more comprehensive in *a*) including 9 additional studies, *b*) performing meta-regression to estimate the contribution of study characteristics as sources of heterogeneity, and *c*) estimating pooled risk ratios for the association between fluoride exposure and a low/marginal Raven's test score.

As noted by the NRC committee (NRC 2006), assessments of fluoride safety have relied on incomplete information on potential

Table 1. Continued.

Reference	Study location	No. in high-exposure group	No. in reference group	Age range (years)	Fluoride exposure		Outcome measure	Results
					Assessment	Range		
Zhang JW et al. 1998	Xinjiang, China	51	52	4–10	Drinking water	Not specified	Japan IQ Test[d]	Average IQ scores of children residing in high-fluoride and -arsenic area were lower than those who resided in the reference area
Lu et al. 2000	Tianjin, China	60	58	10–12	Drinking water	3.15 mg/L (high); 0.37 mg/L (reference)	CRT-RC[b]	Children in the high-fluoride area scored significantly lower IQ scores than those in the reference area
Hong et al. 2001	Shandong, China	85	32	8–14	Drinking water	2.90 mg/L (high); 0.75 mg/L (reference)	CRT-RC[b]	Average IQ scores were significantly lower in high-fluoride group (and -iodine) than the reference group
Wang SH et al. 2001	Shandong, China	30	30	8–12	Drinking water	2.97 mg/L (high); 0.5 mg/L (reference)	CRT-RC[b]	No significant difference in IQ scores of children in the high-fluoride/high-iodine and reference fluoride/low-iodine areas
Li Y et al. 2003	Inner Mongolia, China	720	236	6–13	Fluorosis	Endemic vs. control regions defined by the Chinese Geological Office	CRT-RC[b]	Average IQ of children in high-fluorosis area was lower than that in the reference area
Xiang et al. 2003	Jiangsu, China	222	290	8–13	Drinking water	0.57–4.5 mg/L (high); 0.18–0.76 mg/L (reference)	CRT-RC[b]	Mean IQ score was significantly lower in children who lived in the high-fluoride area than that of children in the reference exposure area (both areas also had arsenic exposure)
Seraj et al. 2006	Tehran, Iran	41	85	Not specified	Drinking water	2.5 mg/L (high); 0.4 mg/L (reference)	Raven[g]	The mean IQ of children in the high-fluoride area was significantly lower than that from the reference fluoride area
Wang ZH et al. 2006	Shanxi, China	202	166	8–12	Drinking water	5.54 ± 3.88 mg/L (high); 0.73 ± 0.28 mg/L (reference)	CRT-RC[b]	The IQ scores of children in the high-fluoride group were significantly lower than those in the reference group
Fan et al 2007	Shaanxi, China	42	37	7–14	Drinking water	1.14–6.09 mg/L (high); 1.33–2.35 mg/L (reference)	CRT-RC[b]	The average IQ scores of children residing in the high-fluoride area were lower than those of children residing in the reference area
Wang SX et al. 2007	Shanxi, China	253	196	8–12	Drinking water and urine	3.8–11.5 mg/L (water, high); 1.6–11 mg/L (urine, high); 0.2–1.1 mg/L (water, reference); 0.4–3.9 mg/L (urine, reference)	CRT-RC[b]	Mean IQ scores were significantly lower in the high-fluoride group than from the reference group in the fluoride/arsenic areas
Li et al. 2009	Hunan, China	60	20	8–12	Coal burning	1.24–2.34 mg/L (high); 0.962 mg/L (reference)	CRT-RC[b]	Mean IQ was lower in children in coal-burning areas compared to those in the reference group
Li FH et al. 2010	Henan, China	347	329	7–10	Drinking water	2.47 ± 0.75 mg/L (high)	CRT-RC[b]	No significant difference in IQ scores between children in the exposed and reference groups
Poureslami et al. 2011	Iran	59	60	6–9	Drinking Water	2.38 mg/L (high); 0.41 mg/L (reference)	Raven[g]	Children in the high-fluoride group scored significantly lower than those in reference group

[a]Wechsler Intelligence Scale (Lin and Zhang 1986). [b]CRT-RC, Chinese Standardized Raven Test, rural version (Wang G et al. 1989). [c]Chinese Binet Test (Wu 1936). [d]Japan test (Zhang J et al. 1985). [e]Binet-Simon Test (Binet and Simon 1922). [f]Chinese comparative intelligence test (Wu 1983). [g]Raven test (Raven et al. 2003).

risks. In regard to developmental neurotoxicity, much information has in fact been published, although mainly as short reports in Chinese that have not been available to most expert committees. We carried out an extensive review that includes epidemiological studies carried out in China. Although most reports were fairly brief and complete information on covariates was not available, the results tended to support the potential for fluoride-mediated developmental neurotoxicity at relatively high levels of exposure in some studies. We did not find conclusive evidence of publication bias, although there was substantial heterogeneity among studies. Drinking water may contain other neurotoxicants, such as arsenic, but exclusion of studies including arsenic and iodine as co-exposures in a sensitivity analysis resulted in a lower estimate, although the difference was not significant. The exposed groups had access to drinking water with fluoride concentrations up to 11.5 mg/L (Wang SX et al. 2007); thus, in many cases concentrations were above the levels recommended (0.7–1.2 mg/L; DHHS) or allowed in public drinking water (4.0 mg/L; U.S. EPA) in the United States (U.S. EPA 2011). A recent cross-sectional study based on individual-level measure of exposures suggested that low levels of water fluoride (range, 0.24–2.84 mg/L) had significant negative associations with children's intelligence (Ding et al. 2011). This study was not included in our meta-analysis, which focused only on studies with exposed and reference groups, thereby precluding estimation of dose-related effects.

The results suggest that fluoride may be a developmental neurotoxicant that affects brain development at exposures much below those that can cause toxicity in adults (Grandjean 1982). For neurotoxicants such as lead and methylmercury, adverse effects are associated with blood concentrations as low as 10 nmol/L. Serum fluoride concentrations associated with high intakes from drinking water may exceed 1 mg/L, or 50 μmol/L—more than 1,000 times the levels of some other neurotoxicants that cause neurodevelopmental damage. Supporting the plausibility of our findings, rats exposed to 1 ppm (50 μmol/L) of water fluoride for 1 year showed morphological alterations in the brain and increased levels of aluminum in brain tissue compared with controls (Varner et al. 1998).

The estimated decrease in average IQ associated with fluoride exposure based on our analysis may seem small and may be within the measurement error of IQ testing. However, as research on other neurotoxicants has shown, a shift to the left of IQ distributions in a population will have substantial impacts, especially among those in the high and low ranges of the IQ distribution (Bellinger 2007).

Our review cannot be used to derive an exposure limit, because the actual exposures of the individual children are not known. Misclassification of children in both high- and low-exposure groups may have occurred if the children were drinking water from other sources (e.g., at school or in the field).

The published reports clearly represent independent studies and are not the result of duplicate publication of the same studies (we removed two duplicates). Several studies (Hong et al. 2001; Lin et al. 1991; Wang SH et al. 2001; Wang SX et al. 2007; Xiang et al. 2003; Zhao et al. 1996) report other exposures, such as iodine and arsenic, a neurotoxicant, but our sensitivity analyses showed similar associations between high fluoride exposure and the outcomes even after these studies were excluded. Large tracts of China

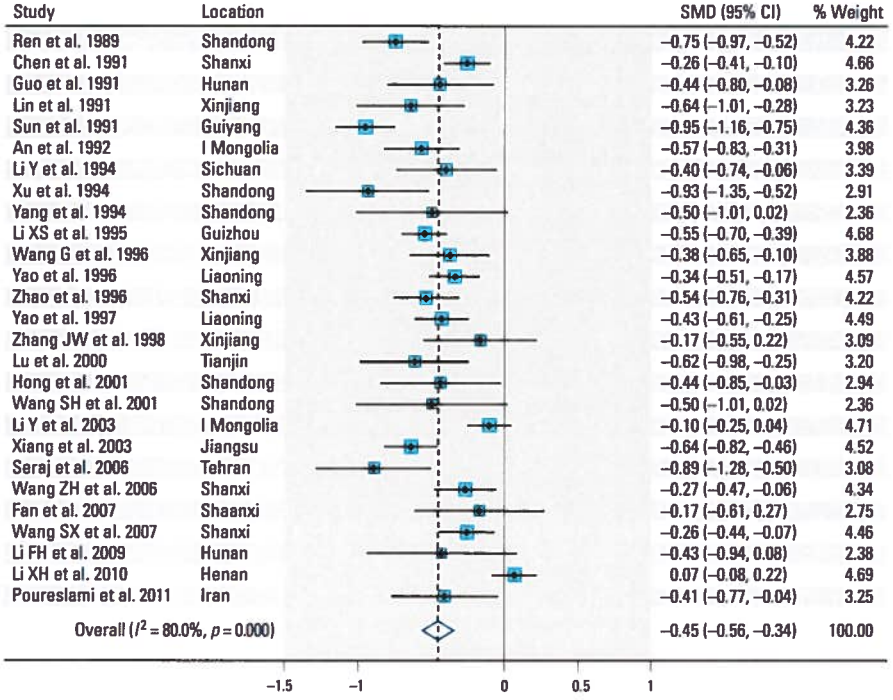

Figure 2. Random-effect standardized weighted mean difference (SMD) estimates and 95% CIs of child's intelligence score associated with high exposure to fluoride. SMs for individual studies are shown as solid diamonds (♦), and the pooled SMD is shown as an open diamond (◊). Horizontal lines represent 95% CIs for the study-specific SMDs.

Table 2. Sensitivity analyses of pooled random-effects standardized weighted mean difference (SMD) estimates of child's intelligence score with high exposure of fluoride.

Model	Available studies for analysis	SMD (95% CI)	I^2	p-Value test of heterogeneity
1. Exclude nonstandardized tests[a]	23	−0.44 (−0.54, −0.33)	77.6%	< 0.001
2. Exclude non–CRT-RC Tests[b]	16	−0.36 (−0.48, −0.25)	77.8%	< 0.001
3. Exclude studies with other exposures (iodine, arsenic)[c] or non-drinking-water fluoride exposure[d]	9	−0.29 (−0.44, −0.14)	81.8%	< 0.001

[a]Mental work capacity (Li Y et al. 1994); Japan IQ (Sun et al. 1991; Zhang JW et al. 1998); Chinese comparative scale of intelligence test (Yang et al. 1994). [b]Wechsler intelligence test (An et al. 1992; Ren et al. 1989; Wang G et al. 1996); Chinese Binet IQ (Guo et al. 1991); Raven (Poureslami et al. 2011; Seraj et al. 2006); Binet-Simon (Xu et al. 1994). [c]Iodine (Hong et al. 2001; Lin et al. 1991; Wang SH et al. 2001); arsenic [Wang SX et al. 2007; Xiang et al. 2003; Zhao et al. 1996; (Zhang JW et al. 1998 was already excluded, see note *a*)]. [d]Fluoride from coal burning [Li FH et al. 2009 (Guo et al. 1991 and Li Y et al. 1994 were already excluded; see notes *a* and *b*)].

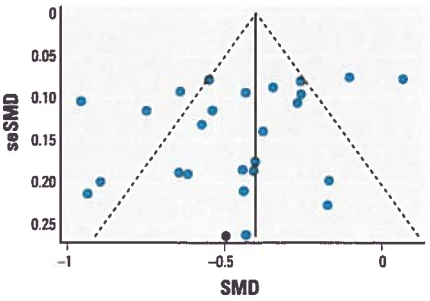

Figure 3. Begg's funnel plot showing individual studies included in the analysis according to random-effect standardized weighted mean difference (SMD) estimates (*x*-axis) and the SE (se) of each study-specific SMD (*y*-axis). The solid vertical line indicates the pooled SMD estimate for all studies combined and the dashed lines indicated pseudo 95% confidence limits around the pooled SMD estimate.

have superficial fluoride-rich minerals with little, if any, likelihood of contamination by other neurotoxicants that would be associated with fluoride concentrations in drinking water. From the geographic distribution of the studies, it seems unlikely that fluoride-attributed neurotoxicity could be attributable to other water contaminants.

Still, each of the articles reviewed had deficiencies, in some cases rather serious ones, that limit the conclusions that can be drawn. However, most deficiencies relate to the reporting of where key information was missing. The fact that some aspects of the study were not reported limits the extent to which the available reports allow a firm conclusion. Some methodological limitations were also noted. Most studies were cross-sectional, but this study design would seem appropriate in a stable population where water supplies and fluoride concentrations have remained unchanged for many years. The current water fluoride level likely also reflects past developmental exposures. In regard to the outcomes, the inverse association persisted between studies using different intelligence tests, although most studies did not report age adjustment of the cognitive test scores.

Fluoride has received much attention in China, where widespread dental fluorosis indicates the prevalence of high exposures. In 2008, the Ministry of Health reported that fluorosis was found in 28 provinces with 92 million residents (China News 2008). Although microbiologically safe, water supplies from small springs or mountain sources created pockets of increased exposures near or within areas of low exposures, thus representing exposure settings close to the ideal, because only the fluoride exposure would differ between nearby neighborhoods. Chinese researchers took advantage of this fact and published their findings, though mainly in Chinese journals and according to the standards of science at the time. This research dates back to the 1980s, but has not been widely cited at least in part because of limited access to Chinese journals.

In its review of fluoride, the NRC (2006) noted that the safety and the risks of fluoride at concentrations of 2–4 mg/L were incompletely documented. Our comprehensive review substantially extends the scope of research available for evaluation and analysis. Although the studies were generally of insufficient quality, the consistency of their findings adds support to existing evidence of fluoride-associated cognitive deficits, and suggests that potential developmental neurotoxicity of fluoride should be a high research priority. Although reports from the World Health Organization and national agencies have generally focused on beneficial effects of fluoride (Centers for Disease Control and Prevention 1999; Petersen and Lennon 2004), the NRC report examined the potential adverse effects of fluoride at 2–4 mg/L in drinking water and not the benefits or potential risks that may occur when fluoride is added to public water supplies at lower concentrations (0.7–1.2 mg/L) (NRC 2006).

In conclusion, our results support the possibility of adverse effects of fluoride exposures on children's neurodevelopment. Future research should formally evaluate dose–response relations based on individual-level measures of exposure over time, including more precise prenatal exposure assessment and more extensive standardized measures of neurobehavioral performance, in addition to improving assessment and control of potential confounders.

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Coalition of U.S. Environmental Protection Agency Unions
Letter to U.S. Congress on Fluoride Regulation

The following letter was sent to the Chairmen and the Ranking Members of these Committees and Subcommittees of the U.S. Senate and House of Representatives, addressed to the Committee/Subcommittee offices. The remaining Members of these Committees/Subcommittees will then each receive a copy of the letter, transmitted by the respective Committee/Subcommittee majority and minority staffs. The letter was sent separately to Speaker of the House Hastert and to Rep. Henry Waxman. The names of chairmen and ranking members are listed below for each committee.

Senate Committees:
Environment and Public Works (Inhofe and Jeffords)
Health, Education, Labor and Pensions (Enzi and Kennedy)
Commerce, Science and Transportation (Stevens and Inouye)
Agriculture, Nutrition and Forestry (Chambliss and Harkin)

House Committees/Subcommittees
Energy and Commerce (Barton and Dingell)
Subcommittee on Environment snd Hazardous Materials (Gillmor and Solis)
Subcommittee on Health (Deal and Brown)
Science (Boehlert and Gordon

August 5, 2005

RE: Bone Cancer-Fluoridation Cover-Up

Hon. Daniel Inouye, Ranking Member
Committee on Science and Transportation
560 Dirksen Senate Office Building
Washington, D.C. 20510-6125

Dear Senator Inouye:

Our unions represent a substantial portion of the nation-wide workforce at the U.S. Environmental Protection Agency, and we are writing to ask for a moratorium on the national program of the U.S. Public Health Service to fluoridate all of America's public water supplies.

One of us (Dr. Hirzy, of NTEU Chapter 280) testified before the Subcommittee on Wildlife, Fisheries and Water of the Senate on June 29, 2000 on this subject on behalf of his headquarters union. At that time the union called for a moratorium based on science indicating a number of adverse health effects and out-of-control, excessive exposures to fluoride.

We now join NTEU Chapter 280 in renewing the call for a moratorium, based on startling and disturbing new information that confirms the worst fears expressed in the earlier testimony.

Work done at Harvard College's School of Dental Medicine by Dr. Elise Bassin, which has been

hidden since 2001, shows that pre-adolescent boys who drink fluoridated water are at a seven-fold increased risk of osteosarcoma, an often fatal bone cancer. We ask that the moratorium take effect immediately and remain in place until a full hearing by the Congress on the wisdom of continuing the practice is concluded. The last such hearing was in 1978.

Dr. Bassin's work, done as her doctoral thesis, was completed and accepted by Harvard in partial fulfillment of the requirements for her Ph.D. in 2001. It is a landmark investigation of age-specific exposure of young people in a case-control epidemiology study of the incidence of osteosarcoma. The thesis remained sequestered until 2004, when her research adviser, Chester Douglass, inexplicably reported to the funding agency, the National Institute of Environmental Health Sciences, that *no* connection was found between fluoride and osteosarcoma. This discrepancy between Chester Douglass' written report and the actual findings of the funded study is under investigation by several entities, and we believe should be looked into by the Congress as well. It appears to be yet another instance of federally funded science gone awry to protect special interests. Chester Douglass edits Colgate Company's *Oral Health Report.*

Chapter three of Dr. Bassin's work (enclosed) cites the impressive weight of convergent evidence for the carcinogenicity of fluoride in young boys (but not girls): fluoride is a mitogen, increasing the rate of cell division; it has been shown to be mutagenic, damaging chromosomal structure; it accumulates primarily in bone, site of the cancer; several previous epidemiology studies have found heretofore unexplained increases in osteosarcoma in young men (but not young women); a National Toxicology Program animal study found statistically significant increases in osteosarcomas in male (but not female) rats. And she discusses why several other epidemiology studies found no association between fluoridation and osteosarcoma; principally, those studies did not consider age-specific exposures and development of the cancer.

It is simply unconscionable that her federally funded work was hidden for four years while millions of young boys continued to be exposed to increased risk of this disease, whose best outcome involves amputation. Several federal statutes express Congressional intent regarding timely warning about such risks. These include, for example, the Toxic Substances Control Act, section 8(e) and the Federal Insecticide, Fungicide and Rodenticide Act section 6(a)(2). We believe another area for Congressional investigation is: who knew about the results of Dr. Bassin's work besides herself and Chester Douglass? and was any federal statute violated by keeping those results hidden for four years?

Another reason for a Congressional review of fluoridation is the recent work of Dr. Richard Maas of the Environmental Quality Institute, University of North Carolina-Ashville, which shows that use of chloramine disinfectant and silicofluoride fluoridating agents with excess ammonia increases lead concentrations in public water supplies. This may explain at least some of the increased lead levels seen in the District of Columbia's water supplies and in the blood of children drinking water fluoridated with silicofluorides. The Centers for Disease Control and Prevention says that ninety four percent of fluoridated water systems use silicofluorides.

Dr. Hirzy is available to meet with your staff to pursue this matter, and we hope that you will find it of sufficient concern to initiate a full investigation of fluoridation, which we believe is long overdue.

Sincerely,

Dwight A. Welch, President
NTEU Chapter 280

J. William Hirzy, Vice-President
NTEU

280

EPA Headquarters

/s/Steve Shapiro, President
AFGE local 3331
EPA Headquarters

/s/Larry Penley. President
NTEU Chapter 279
EPA Cincinnati Laboratory

/s/Wendell Smith, President
ESC/IFPTE Local 20
Region 9 Office, San Francisco

/s/Henry Burrell, President
AFGE Local 3428
Region 1 Office, Boston

/s/Frank Beck, President
AFGE Local 2900
Ada Laboratory

EPA Headquarters

/s/Paul Sacker, President
AFGE Local 3911
Region 2 Office, New York

/s/Nancy Barron, President
NAGE Local R5-55
Region 4 Office, Atlanta

/s/Patrick Chan, President
NTEU Chapter 295
Region 9 Office, San Francisco

/s/Alan Hollis, President
AFGE Local 3611
Region 3 Office, Philadelphia

/s/Mark Coryell, President
AFGE Local 3907
Ann Arbor laboratory

cc: Hon. Stephen L. Johnson, Administrator
U.S. Environmental Protection Agency

REVIEW OF THE 2006 UNITED STATES NATIONAL RESEARCH COUNCIL REPORT: *FLUORIDE IN DRINKING WATER*

Robert J Carton[a]

Averill Park, NY, USA

SUMMARY: The recent report by a 12-member committee of the US National Research Council (NRC) examined the scientific basis for the Maximum Contaminant Level Goal (MCLG) of fluoride in drinking water promulgated in 1985 by the US Environmental Protection Agency (EPA). Due to misdirection by EPA management, who requested the report, the NRC committee identified only health effects known with total certainty. This is contrary to the intent of the Safe Drinking Water Act (SDWA), which requires the EPA to determine "whether any adverse effects can be reasonably anticipated, even though not proved to exist." Further misdirection by EPA consisted of instructing the committee not to identify a new MCLG—in other words, not to determine a safe level of fluoride in drinking water, and not to discuss silicofluorides, phosphate fertilizer manufacturing by-products used in most cities to fluoridate their water. Despite these restrictions, the committee broke new ground declaring severe dental fluorosis and moderate (stage II) skeletal fluorosis adverse health effects, and by noting that the current standard of 4 mg F/L in drinking water does not protect against bone fractures or severe dental fluorosis. Silicofluorides were said to need health effects testing. The NRC review includes extensive information on other possible health effects of fluoride, such as endocrine effects and effects on the brain. On the basis of this information and the proper interpretation of the SDWA, the following are all adverse health effects: moderate dental fluorosis, stage I skeletal fluorosis (arthritis with joint pain and stiffness), decreased thyroid function, and detrimental effects on the brain, especially in conjunction with aluminum. The amount of fluoride necessary to cause these effects to susceptible members of the population is at or below the dose received from current levels of fluoride recommended for water fluoridation. The recommended Maximum Contaminant Level Goal (MCLG) for fluoride in drinking water should be zero.

Keywords: Drinking water; US Environmental Protection Agency (USEPA); Exposure; Fluoride toxicity; Maximum Contaminant Level Goal (MCLG); National Research Council (NRC); Regulations; Risk assessment; Silicofluorides; Toxicity assessment.

INTRODUCTION

In 2002, the US Environmental Protection Agency (USEPA) asked the National Research Council (NRC) to independently evaluate the scientific basis of EPA's

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[a] Robert J. Carton, PhD, is an environmental scientist who has worked for over 30 years in the US federal government writing regulations, managing risk assessments on high priority toxic chemicals, and providing environmental oversight of medical research conducted by the government. From 1972–1992 he worked at the headquarters of the US Environmental Protection Agency in Washington, DC, and wrote the first regulations for controlling asbestos discharges from manufacturing plants. In 1985, as an official in the union for professionals at EPA, he became aware of possible scientific fraud in the development of the EPA standard for fluoride in drinking water and convinced the union to challenge EPA in court. From 1992–2002, he was Chief of Environmental Compliance for the US Army Medical Research and Materiel Command, Fort Detrick, MD. He successfully opposed attempts to put fluoride in the post's drinking water. Since retiring from government service he has continued to work on exposing the unethical nature of government claims about fluoridation.
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Maximum Contaminant Level Goal (MCLG) of 4 mg/L and the Secondary Maximum Contaminant Level (SMCL) of 2 mg/L of fluoride in drinking water. On March 22, 2006, NRC released its report in which it is clearly stated that the current MCLG does not prevent adverse health effects, and that the regulatory Maximum Contaminant Level (MCL) should be lowered.[1] Although the NRC committee was appointed to provide a balance of views on the safety of water fluoridation, it did not determine a fluoride level in drinking water that would protect against known or suspected adverse health effects with an adequate margin of safety. Instead, the committee deferred this analysis to EPA, which is required by the 1974 Safe Drinking Water Act (SDWA) to periodically review its standards. Indeed, according to Dr Hardy Limeback, one of the members of the committee, "We were clearly instructed to avoid trying to figure out a new MCLG."[2] Instead, according to another member of the committee, Dr Kathleen Thiessen, "We endeavored to provide a solid information basis for the conclusions that need to be drawn by EPA and others."[3]

This review analyzes whether or not the committee fully utilized its mandate and provided sufficient information to allow EPA to come to conclusions required by law.

EPA CHARGE TO THE COMMITTEE

The mandate of the committee, as explained by a representative of EPA at a public meeting held with NRC in August 2003, was to reevaluate the scientific basis of the 1986 MCL (Maximum Contaminant Level), and the SMCL (Secondary Maximum Contaminant Level—the guideline used to protect against adverse cosmetic dental effects).[4] The request to focus on the MCL was identical to the requirement for the previous 1993 report by NRC. However, transcripts of this meeting show that the committee requested and obtained a change in its mission from evaluating the enforceable MCL to the unenforceable MCLG (Maximum Contaminant Level Goal). This change removed the committee from evaluating an essentially political decision that requires judgments about feasibility and cost, to the more reasonable and possibly more satisfying evaluation of the scientific basis for the 1985 health goal.

In this connection it should be noted that the current MCL and MCLG for fluoride are both 4 mg/L. There is no requirement that they be the same. Other inorganic chemicals, such as arsenic and lead, have higher MCLs than MCLGs due to the difficulty and expense of treatment. The MCLGs for arsenic and lead are zero, while their MCLs are 0.010 mg/L and 0.015 mg/L, respectively.

Specifically excluded from the charge was the issue of artificial water fluoridation. EPA claimed this was a CDC (Centers for Disease Control) program, not under its jurisdiction. This view was clearly stated by another representative of EPA at a subsequent presentation in November 2003.[5] Similarly, silicofluorides, the chemicals used to achieve 1 mg/L of fluoride in 92% of all fluoridated drinking water supplies, were identified as off limits for analysis in this report. The EPA representative suggested that these chemicals would be better addressed as separate contaminants, presumably by a different committee. He noted that the dissociation of silicofluorides in water is under investigation at the University of Michigan (study now published).[6]

The committee discovered, however, that it was not possible to exclude discussion of these issues. The chapter on sources of fluoride exposure states: "The major dietary source of fluoride for most people in the United States is fluoridated municipal (community) drinking water."[7] In the chapter on the immune system, the report notes that "Machalinski et al. (2003) reported that four different human leukemic cell lines were more susceptible to the effects of sodium hexafluorosilicate, the compound most often used in fluoridation, than to NaF." The report also states: "The possibility of biological effects of SiF_6^{2-} [silicohexafluoride ion], as opposed to free fluoride ion, should be examined." There are numerous other references to fluoridation and silicofluorides, and even an entire page in the section on neurotoxicity is devoted to the neurotoxic effects of silicofluorides.

SCIENTIFIC REQUIREMENTS OF MCLG

In the August 2003 meeting, EPA explained in a general way the differences between the MCL and MCLG. The MCLG was discussed as the health goal that protects against adverse health effects and provides an adequate margin of safety. An important distinction, however, was left out of the discussion, namely, the amount of certainty necessary to establish the existence of an adverse health effect. According to Congress, Recommended MCLs (or MCLGs as they are now called) "are to represent non-enforceable health goals which are to be set at a level which assures 'that the health of persons will be protected against *known or anticipated* adverse effects [of the substance], allowing an adequate margin of safety'."[8] (Emphasis added in reference)

This means Congress intended that the administrator of EPA could determine that an adverse health effect existed without having to show total certainty. As discussed in the *amicus curiae* brief submitted by the EPA professionals union to a US District Court in 1986: "Moreover, the legislative history makes clear that 'the Administrator must decide whether any adverse effects *can be reasonably anticipated, even though not proved to exist*'."[9] (Emphasis added).

This distinction was not explained to the committee. The committee had much broader leeway in determining health effects than they apparently knew. If they had known, their discussions could have indicated possible adverse health effects to sensitive members of the population at fluoride levels well below 1 mg/L. Moreover, contrary to the conclusions of the committee, no new research is necessary to make this determination. More research is necessary of course to understand more fully the chronic effects of fluorides, silicofluorides, and their interactions with other chemicals in and out of the body. Here, however, we are not limited and can therefore draw conclusions based on the Precautionary Principle as embodied in the requirements of the Safe Drinking Water Act as stated above.

If the committee had looked at the existing MCLG of 4 mg/L in light of the proper legal requirement, they might have asked the following questions:

1 What health effects can reasonably be anticipated to occur, although not proved to exist, to the most sensitive members of the population?

2 What is the lowest level at which these effects occur?

3 What margin of safety would be adequate given the level of certainty of the data?

A proper review of the scientific basis of the 1985 standard would answer these questions and compare them with the current standard.

FOCUS OF COMMITTEE

The committee apparently believed that it was their mission to identify only health effects known with total certainty. They also apparently believed that they should not identify the Lowest Observed Adverse Effect Level (LOAEL) at which these health effects can be found. Instead, they focused mainly on the safety of the numerical level of the current MCLG of 4 mg/L, and the SMCL of 2 mg/L.

To demonstrate the conclusions that are possible using the proper interpretation of the law, this review addresses the adverse health effect identified by the committee (severe dental fluorosis and bone fractures), and a number of other health effects discussed by them (skeletal fluorosis, endocrine effects, and effects on the brain).

DENTAL FLUOROSIS

The committee agreed that enamel fluorosis is a dose-related mottling of enamel, which is permanent once a child's teeth are formed. It is described as a toxic effect caused by fluoride interfering with ameloblasts in the developing tooth, resulting in a disruption of the process of enamel formation making it ever more porous. What is new in this analysis is the agreement by the committee that the most severe form of dental fluorosis is an adverse health effect, contradicting the official position of the Surgeon General and EPA in 1985, which claimed it is only cosmetic. While breaking new ground in this regard, the committee balked at including moderate dental fluorosis as an adverse health effect because of the lack of absolute certainty of the damage.

The committee stated that the available data are not adequate to categorize moderate enamel fluorosis as an adverse health effect on the basis of structural or psychological effects.[10] However, the weight of evidence of the possible adverse nature of this health effect appears to be sufficient to include it in the list of adverse health effects. The following statements from the report justify this assessment.

First: "In *moderate to severe* forms of fluorosis, porosity increases and lesions extend toward the inner enamel. After the tooth erupts, its porous areas may flake off, leaving enamel defects where debris and bacteria can be trapped. The opaque areas can become stained yellow to brown, with more severe structural damage possible, primarily in the form of pitting of the tooth surface."[11] (Emphasis added)

This statement suggests quite strongly that moderate dental fluorosis includes structural damage to tooth enamel, although not to the degree seen in severe dental fluorosis. As the report states: "One of the functions of tooth enamel is to protect the dentin and, ultimately, the pulp from decay and infection."[12] Thus the definite possibility exists of a detrimental effect on the tooth, which should be prevented.

Second: "It is reasonable to assume that some individuals will find moderate enamel fluorosis on front teeth to be detrimental to their appearance."[13]

One possible explanation for ignoring moderate fluorosis as an adverse health effect is that the level at which it may occur coincides with the level of artificial water fluoridation, 0.7–1.2 mg/L. Selecting severe fluorosis as an adverse health effect was a concession but not one the committee thought would occur at water fluoridation levels. In the report they give assurances that the occurrence of severe

fluorosis would be near zero below 2 mg F/L. The unspoken assumption here is that "near zero" is not sufficient to trigger a protective MCLG. This is contrary to the Safe Drinking Water Act, which does not allow for damage to occur to any fraction of the population.

The 1993 NAS review reported an incidence of severe dental fluorosis in 4 cities of approximately 0.1% at the levels of water fluoridation If this low incidence was found in only these 4 cities, irrespective of the incidence found in any other city or cities, this should be determined as the LOAEL and then a safety factor applied to allow for missing data and the wide variation in fluoride intake from sources other than drinking water. Taking moderate dental fluorosis into account, the MCLG would be lower than 0.7 mg/L.

Missing from the report is any indication of the minimal dosage necessary to cause moderate or severe dental fluorosis. There exists a determination by EPA in its Integrated Risk Information System (IRIS) database that the reference dosage, which would prevent objectionable dental fluorosis (moderate and severe), is 0.06 mg/kg/day.[14] This is slightly lower than what the Institute of Medicine (IOM) determined in 1997, or 0.10 mg/kg/day, which was pointed out in the NRC report. Interestingly the committee also noted that "infants (nursing and non-nursing) and children 1–2 years old would be at or above the IOM limits at a fluoride concentration of 1 mg/L."[15] These numbers are for the average child and do not represent the 99th percentile of exposure. Consequently, a recommendation should have been made to establish moderate fluorosis as an adverse health effect and an attempt made to calculate a fluoride concentration in water that would prevent children from getting that effect, using the 99th percentile as the target group. This was done by a consulting firm, Pacific Western Technologies, Ltd (PWT), for the US Army as part of an environmental assessment evaluating the possibility of fluoridating the water supply of Fort Detrick in Frederick, MD. PWT found that over 50% of children, between the ages of one and three-years-old, exceeded the EPA reference dosage of 0.06 mg/kg/day at the naturally occurring concentration in the Fort Detrick source water of 0.2 mg/L.[16] With only 0.2 mg/L in the drinking water, fluoride from all other sources consumed by a small child exceeded the EPA reference dose for a large fraction of that sub-population. This brought into question the wisdom of adding even more fluoride to their diet through water fluoridation at 1.0 mg/L.

BONE FRACTURES

The entire committee agreed, "Fluoride can weaken bone and increase the risk of fractures."[17] A majority of the committee believed that people exposed to 4 mg/L in their drinking water over their lifetime are likely to have an increase in bone fractures over those exposed to 1 mg/L. The summary of the report explains that the best study they reviewed actually found a risk of hip fracture above 1.5 mg/L, but this "study alone is not sufficient to judge fracture risk for people exposed to fluoride at 2 mg/L."[18]

This is not a necessary analysis, however, for the purposes of determining a new MCLG and for carrying out the purposes of the Safe Drinking Water Act. The biological certainty of fluoride weakening bone is demonstrated in clinical studies in humans and with animals. The report also says that there appears to be a gradient of effect between 1 and 4 mg/L, and that at 2 mg/L the evidence suggests

an increased risk of bone fracture. These statements could be used as a basis for setting an MCLG taking into account the need to protect susceptible individuals, such as those with high water intakes due to occupational necessity or medical condition. The report explains these exposure extremes in detail. What is not discussed is the magnitude of the safety factors necessary to insure protection from anticipated adverse health effects.

SKELETAL FLUOROSIS

The existing MCLG of 4 mg/L is based on the prevention of severe skeletal fluorosis, or Stage III skeletal fluorosis, as it is also known. The NRC committee expanded concerns for skeletal effects by including Stage II as an adverse health effect, declaring that: " . . . mobility is not *significantly* affected, but it is characterized by *sporadic pain*, *stiffness of joints*, and osteosclerosis of the pelvis and spine."[19] (Emphasis added)

Curiously, the reference to sporadic pain and stiffness of joints avoids the word "arthritis" used in describing the same clinical signs in Stage III. Nevertheless, arthritis could be used as a term to describe these symptoms. Rather than implying a specific etiology, arthritis is a general term for the presence in a joint of inflammation, the classical features of which are heat, swelling, redness and pain. Thus within the broad category of arthritis, in which it is implied that some but not necessarily all of the symptoms and signs of inflammation are present, the condition of Stage I skeletal fluorosis, due to exposure to fluoride, with the symptoms of joint pain and stiffness, may be placed alongside approximately 100 other forms of arthritis, with different etiologies, such as gout, osteoarthritis, rheumatoid arthritis, psoriatic arthropathy, ankylosing spondylitis, and postinfectious arthritis. Previously, only the effect of actual crippling was regarded by the NRC as an adverse health effect. Fluoride exposure, then, can now be officially listed as one of the causes of arthritis.

The committee had insufficient information to determine if Stage II or Stage III skeletal fluorosis was occurring in the US, and they failed to speculate on the possibility of the very large historical increase in cases of arthritis in the US being due to the ever-increasing amounts of fluoride exposure. Instead, they used a model they developed to estimate the possibility of Stage II occurring based on studies with known concentrations of fluoride in the drinking water and fluoride levels in bone. The model found that at 2 mg/L of fluoride in drinking water, the amounts of fluoride in bone ash from subjects exposed to these levels "fall within or exceed the ranges historically associated with Stage II and Stage III skeletal fluorosis . . ."[20] This indicates the likelihood that some individuals in the US *may* be experiencing Stage II and Stage III skeletal fluorosis at less than 2 mg/L despite the following statement by the committee: " . . . this comparison alone is insufficient for determining whether Stage II or Stage III skeletal fluorosis *is* a risk for populations exposed to fluoride at 4 mg/L."[21] (Emphasis added)

The key to understanding how the data should be evaluated goes back to the original legal mandate from Congress in setting standards (see above). Absolute proof is not needed to act when there are data showing possible harm. The possibility that harm may be occurring is more than justified based on the following additional analysis of the fluoride dose used to derive the current EPA standard of 4 mg/L.

According to EPA representatives at the August 2003 meeting with NRC, EPA claimed that the MCLG is based on the LOAEL of 20 mg/day for 20 years "from case studies in a limited number of kid [= child] studies of crippling clinical skeletal fluorosis." While differing substantially from previous assertions by EPA that the 1985 MCLG is based on a statement by Dr Harold C Hodge, this calculation does serve as a useful point of departure for looking at its implications for earlier stages of fluorosis. First, however, the actual lifetime dose needs to be calculated for Stage III skeletal fluorosis in order to deal with real life exposures. Thus, the 20 mg/day for 20 years should be multiplied by 20/70, where 70 is the average life expectancy. This results in a dose of 5.7 mg/day. Using the only in-depth study ever done on human exposure by Dr Kaj Roholm,[22] one can evaluate the possible doses necessary to cause the early stage of skeletal fluorosis as follows: Stage II occurred in Danish cryolite workers in approximately 1/2 of the time it took for workers to reach Stage III. Stage 1 occurred in 1/4 of the time. Thus we have the possibility of Stage I and Stage II occurring with a daily dose over a lifetime of 1.42 mg and 2.86 mg, respectively. These are both within the range of current fluoride exposures from all sources documented in the NRC report.

ENDOCRINE EFFECTS

The NRC report cites many endocrine effects of fluoride exposure, including decreased thyroid function, impaired glucose tolerance (Type II diabetes), and earlier sexual maturity. The Executive Summary of the report merely states that these effects are achievable with fluoride concentrations in drinking water of 4 mg/L or less.

Many details, however, can be found in the chapter on effects on the endocrine system. The summary at the end of the chapter explains the dosage necessary to affect thyroid function: "In humans effects on thyroid function were associated with fluoride exposures of 0.05–0.13 mg/kg/day when iodine intake was adequate and 0.01–0.03 mg/kg/day when iodine intake was inadequate . . ." [23] This simply means that for a 70-kg person (often called the "standard man"), fluoride doses as low as 3.5 mg/day for those with an adequate intake of iodine, and 0.7 mg/day for those with an inadequate intake of iodine may have an affect on the thyroid. The report also notes: "The recent decline in iodine intake in the United States could contribute to increased toxicity of fluoride for some individuals." Impaired glucose tolerance was identified as occurring in humans at levels as low as 0.07 mg/kg/day or 4.9 mg/day for a 70-kg man. Either of these effects could occur at water fluoridation levels of 1 mg/L to some people with the high water intakes identified in the report.

Moreover, the committee noted that some of the identified endocrine effects may not be adverse but are nonetheless grounds for concern because apparently even minor endocrine disruption may still cause adverse health effects. Given these possibilities, it is logical to base the MCLG on the lowest endocrine effects found for the most susceptible populations. If thyroid effects were used, this would mean that the total dose of fluoride from all sources should be less than 0.7 mg/day. This intake level covers susceptible people with iodine deficiency. Since the average American already exceeds this dose in the diet, the MCLG for fluoride in drinking water should be zero.

NEUROTOXICITY AND NEUROBEHAVIORAL EFFECTS

The committee also cited research indicating adverse health effects such as lower IQ in children, behavioral, and histopathological changes in the brains of laboratory animals (some of these resembling the brains of Alzheimer's patients), cerebral impairment of humans, and enhancement of effects in the presence of aluminum. The report concludes: "fluorides have the ability to interfere with the functions of the brain and the body by direct and indirect means." It also noted that many of the adverse effects of fluoride can be attributed to the formation of aluminum-fluoride complexes. The report provides a wealth of information showing the negative effects of fluoride on the brain but is often unduly cautious in drawing the appropriate conclusions. The summary[24] states: "A few epidemiological studies of Chinese populations have reported IQ deficits in children exposed to fluoride at 2.5 to 4 mg/L in drinking water." This information is said to "lack sufficient detail to fully assess their quality and relevance to US populations." However, the results are significant enough to "warrant additional study."

The report goes on to identify "a few animal studies" reporting alterations in the behavior of rodents. Limiting the impact of this statement, the committee concluded that the changes were not "substantial." They list "molecular, cellular, and anatomical changes in the nervous system . . . suggesting that functional changes could occur." More research is urged to "clarify the effects . . . on brain chemistry and function." Of particular concern is their statement: " . . . histopathological changes similar to those traditionally associated with Alzheimer's disease in people have been seen in rats chronically exposed to AlF [sic] (Varner et al. 1998)."[25]

Given these and many other examples, there is little doubt that fluoride affects the brain and that it enhances the uptake of aluminum in the brain. Human observations support the conclusion of brain effects, and animal studies allow dose levels causing these effects to be estimated for the purposes of developing an MCLG.

Exposure figures mentioned in this and other sections of the report often give only animal data. However, the committee suggested a way to convert such data to human exposures.[26] Apparently rats require 5 times the daily dose required by humans to arrive at the same serum concentrations. Thus, rats exposed to fluoride at 5 mg/L would achieve the same serum fluoride concentrations as humans exposed to 1 mg/L.

As noted in the report,[27] rats administered AlF_3 in drinking water at 0.5, 5.0, and 50 mg/L for 45 weeks (approximately 60% of AlF_3 is fluoride), all had significant damage in the hippocampus. An unusual number of deaths occurred at the lowest dose tested. A repeat of the test comparing AlF_3 at 0.5 mg/L and NaF at 2.1 mg/L for a test period of one year found that 6 out of 9 animals died in the AlF_3 group, 3 out of 9 of the NaF group died, and only 1 out of 9 control animals died. Both treated groups had twice as much aluminum in their brains as control animals. Leaving aside the unexplained deaths, there was a proven increase of AlF_3 in the brain with both AlF_3 and NaF, and significant damage to the brain at the low dose of 0.5 mg AlF_3/L, or approximately 0.3 mg F/L.

Two other studies were noted to have found the same pattern of neuronal degeneration. Thus, there exists a lowest observed effect level of 0.06 mg/L of

fluoride to develop an MCLG using the preventative approach of the Safe Drinking Water Act as mentioned earlier. (This figure of 0.06 mg/L is derived from the above 0.3 mg/L concentration of fluoride divided by the conversion factor for rats to humans of 5.) An appropriate safety factor does not have to be mentioned to see clearly that fluoridation at 1 mg/L cannot be considered acceptable for an MCLG.

CONCLUSIONS

The NRC committee's reevaluation of EPA's MCLG for fluoride in drinking water failed to identify a safe level of fluoride in drinking water. This failure can be attributed to misdirection by EPA of the intended goal of the effort. When the committee requested and received a change in its mandate from evaluating the MCL to the MCLG, EPA strangely omitted the key scientific criteria necessary for evaluating this standard. The committee should have been told to look for health effects that "can be reasonably anticipated, even though not proved to exist." As a result of this omission, the NRC panel focused only on end points that were totally certain and concluded that the current standard of 4 mg/L did not protect against bone fractures and severe dental fluorosis. For the first time in history, a committee of the NRC removed severe dental fluorosis from the benign category of cosmetic effects and added it to the list of adverse health effects. In addition, Stage II skeletal fluorosis was added to the list, but the committee was unable to state with absolute certainty that this was occurring at the current EPA standards.

This review applied the necessary criteria to some but not all of the adverse health effects discussed in the NRC report. The results are as follows:

1 Moderate dental fluorosis is an adverse health effect occurring at fluoride levels of 0.7–1.2 mg/L, the levels of water fluoridation.

2 The Lowest Observed Adverse Effect Level (LOAEL) for bone fractures is at least as low as 1.5 mg/L and may be lower than this figure.

3 Stage II and Stage III skeletal fluorosis may be occurring at levels less than 2 mg/L.

4 Stage I skeletal fluorosis, (arthritis, clinically manifested as pain and stiffness in joints) is an adverse health effect which may be occurring with a daily fluoride intake of 1.42 mg/day, which is less than the amount the average person already obtains in their diet in non-fluoridated areas. The Maximum Contaminant Level Goal (MCLG) should be zero.

5 Decreased thyroid function is an adverse health effect, particularly to individuals with inadequate dietary iodine. These individuals could be affected with a daily fluoride dose of 0.7 mg/day (for a "standard man"). Since this is less than the amount already in the diet, the MCLG should be zero.

6 Fluoride has adverse effects on the brain, especially in combination with aluminum. Seriously detrimental effects are known to occur in animals at a fluoride level of 0.3 mg/L in conjunction with aluminum. The goal for this effect should also be zero.

The committee should be applauded for their efforts in general and in particular for ignoring directives not to include discussions of water fluoridation and silicofluorides. Their recommendations for research should be taken seriously. EPA has sufficient information in this report to act immediately, using the appropriate criteria set forth in the Safe Drinking Water Act. Using the preventive public health intent of the law, the Maximum Contaminant Level Goal for fluoride in drinking water should be zero.

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13 Ibid. p. 4.
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16 Rasmussen GP. Personal communication, Environmental Assessment for Proposed Water Fluoridation—Fort Detrick, MD., from Rasmussen GP, Pacific Western Technologies, Ltd, to Gonzalez G, U.S. Army Medical Command [letter]; 2001 Jun 1.
17 Doull J, et al. op cit., p. 6.
18 Ibid. p. 5.
19 Ibid. p. 139.
20 Ibid. p. 5.
21 Ibid. p. 146.
22 Roholm K. Fluorine intoxication: a clinical-hygienic study with a review of the literature and some experimental investigations. London: HK Lewis; 1937.
23 Doull J, et al. op cit., p. 218.
24 Ibid. p. 6.
25 Ibid. p. 178.
26 Ibid. p. 80.
27 Ibid. p. 182.

FLUORIDE: TOPICAL VS. SYSTEMIC

The premise underlying water fluoridation was that ingesting fluoride increased the fluoride content of the teeth, the teeth would be more resistant to decay for life.

It is now common knowledge that if fluoride does help prevent tooth decay, it is topical use and not systemic (through ingestion).

Primary Sources

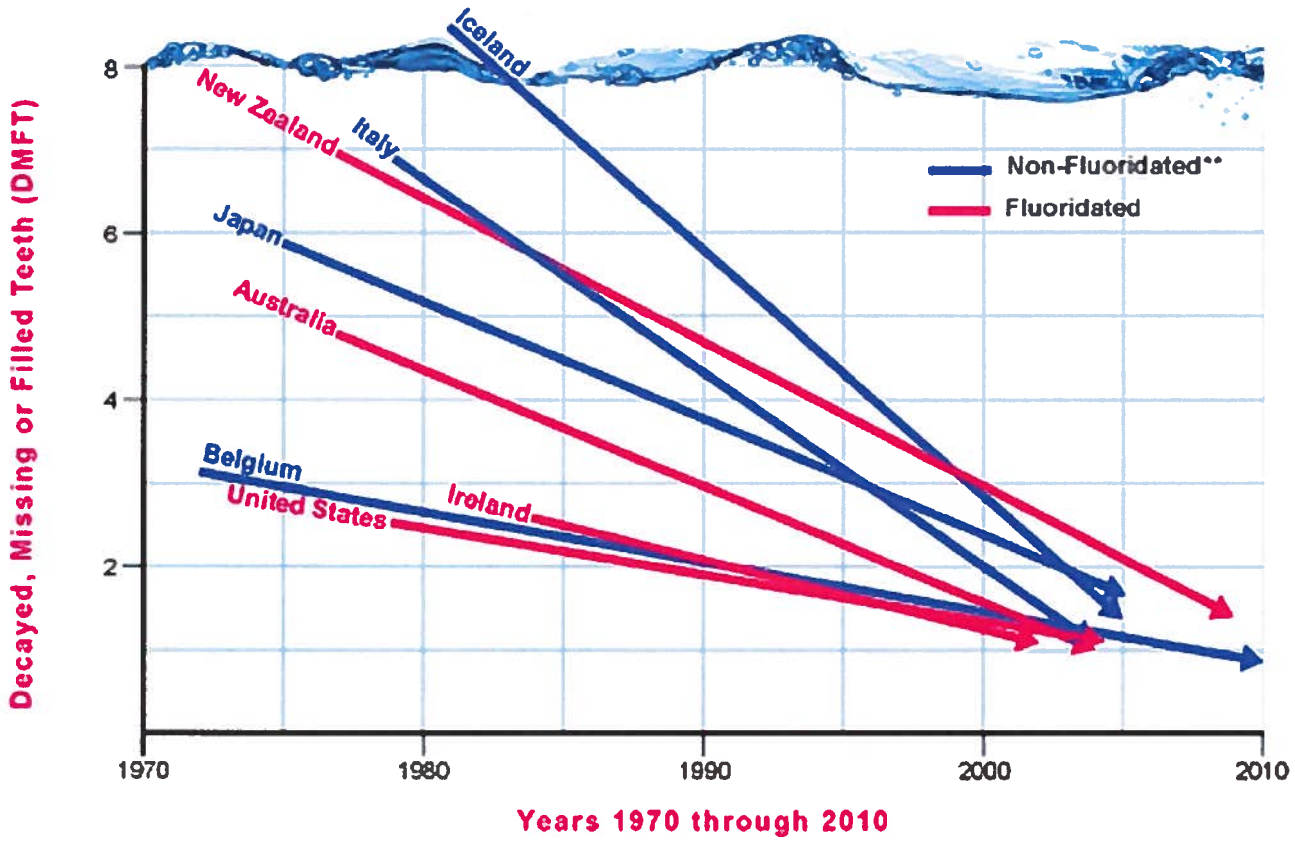
"the major anticaries benefit of fluoride is topical and not systemic."
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 13.

"Fluoride is most effective when used topically, after the teeth have erupted."
SOURCE: Cheng KK, et al. (2007). Adding fluoride to water supplies. British Medical Journal 335(7622):699-702.

"[F]luoride's predominant effect is posteruptive and topical."
SOURCE: Centers for Disease Control and Prevention. (2001). Recommendations for Using Fluoride to Prevent and Control Dental Caries in the United States. Morbidity and Mortality Weekly Report 50(RR14): 1-42.

"Fluoride, the key agent in battling caries, works primarily via topical mechanisms: inhibition of demineralization, enhancement of remineralization, and inhibition of bacterial enzymes."
SOURCE: Featherstone, JDB. (2000). The Science and Practice of Caries Prevention. Journal of the American Dental Association 131: 887-899.

TOOTH DECAY TRENDS IN FLUORIDATED VS. UNFLUORIDATED COUNTRIES

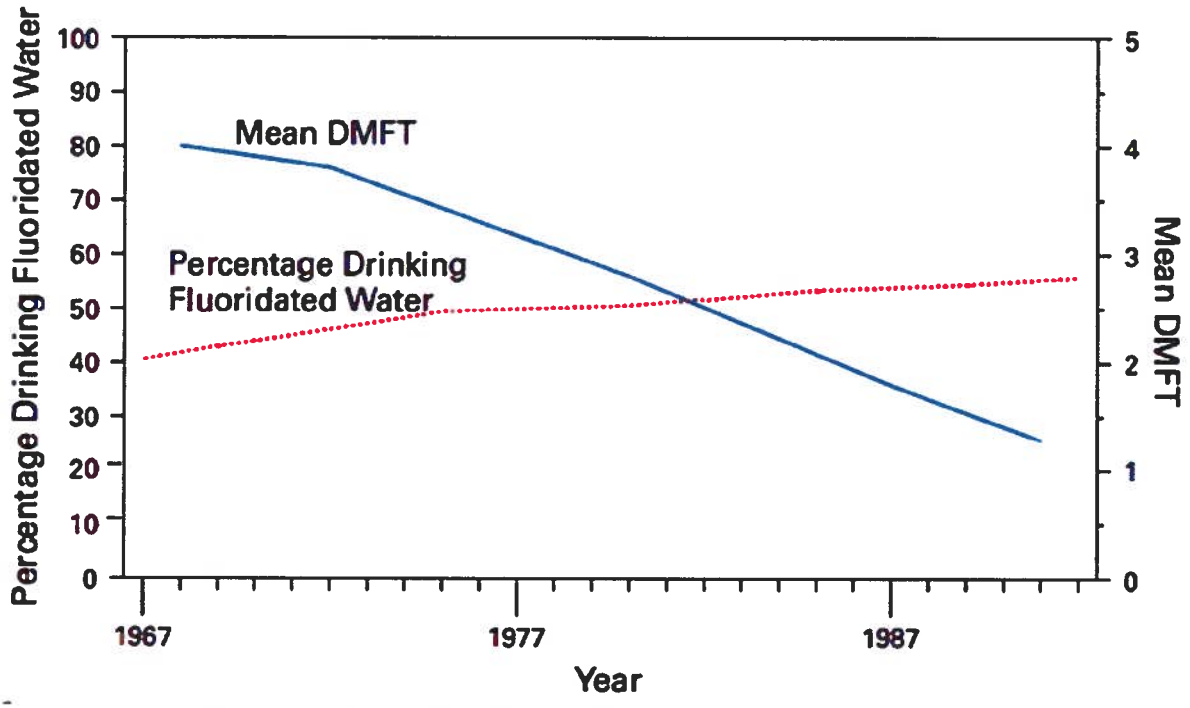


* World Health Organization (WHO). Collaborating Centre for Education, Training, and Research in Oral Health, Malmö University, Sweden. http://www.mah.se/CAPP/ (accessed June 10, 2012).

** No water or salt fluoridation.

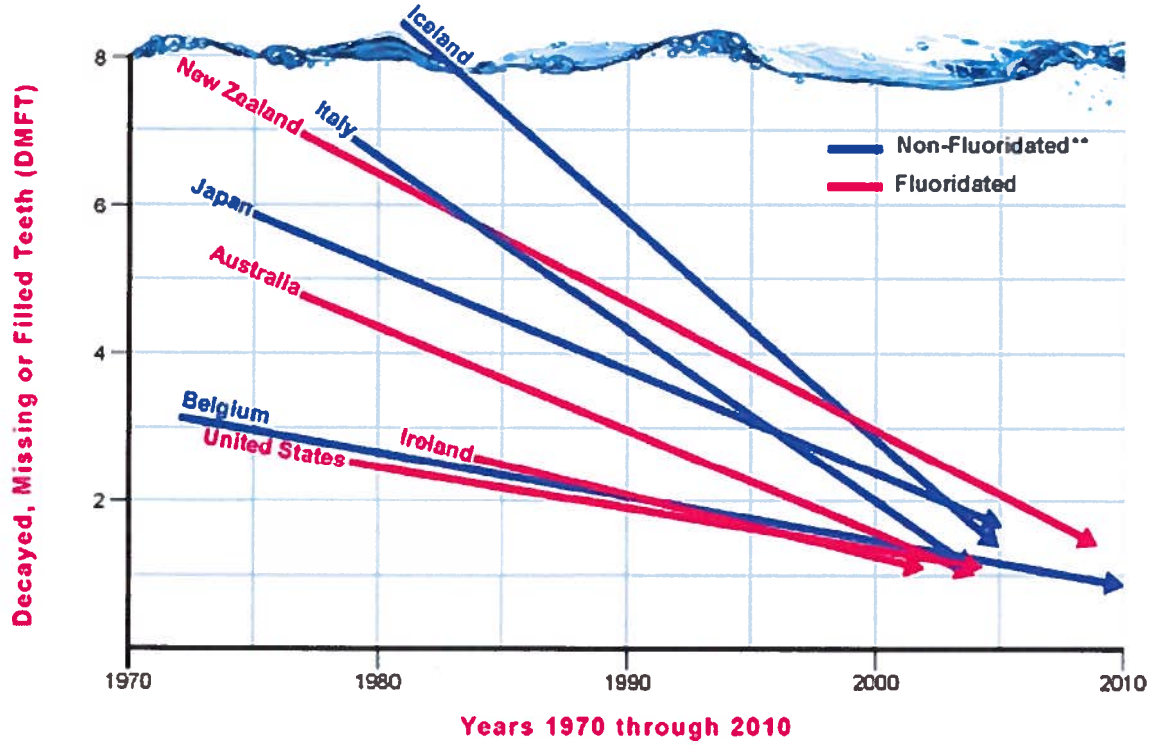
Tooth decay rates have "precipitously declined" in all western countries, irrespective of whether the country ever fluoridated its water. Indeed, most western countries do not fluoridate their water and yet their tooth decay rates have declined at the same rate as the U.S..

(CDC) ATTRIBUTES DECLINE IN TOOTH DECAY TO FLUORIDATION.



SOURCE: Centers for Disease Control (1999). Achievements in Public Health, 1900-1999: Fluoridation of Drinking Water to Prevent Dental Caries. MMWR 48:933-40

(WHO) DATA SHOWS SAME DECLINE IN UNFLUORIDATED COUNTRIES



CONFIRMATION OF AND EXPLANATIONS FOR ELEVATED BLOOD LEAD AND OTHER DISORDERS IN CHILDREN EXPOSED TO WATER DISINFECTION AND FLUORIDATION CHEMICALS.

Neurotoxicology. 2007 Sep;28(5):1032-42. Epub 2007 Mar 1
Coplan MJ, Patch SC, Masters RD, Bachman MS.

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>10microg/dL) is about double that in non-fluoridated communities (Risk Ratio 2, chi2p<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.

EFFECTS OF FLUORIDATION AND DISINFECTION AGENT COMBINATIONS ON LEAD LEACHING FROM LEADED-BRASS PARTS.

Neurotoxicology. 2007 Sep;28(5):1023-31. Epub 2007 Jun 30.
Maas RP1, Patch SC, Christian AM, Coplan MJ.

Abstract

This study concerns effects on water-borne lead from combinations of chlorine (CL) or chloramines (CA) with fluosilicic acid (FSA) or sodium fluoride (NaF). CL is known to corrode brass, releasing lead from plumbing devices. It is known that CA and CL in different ratios with ammonia (NH) mobilize copper from brass, which we have found also enhances elution of lead from leaded brass alloys. Phase I involved leaded-brass 1/4 in. elbows pre-conditioned in DI water and soaked in static solutions containing various combinations of CL, CA, FSA, NaF, and ammonium fluosilicate. In Phase II 20 leaded-brass alloy water meters were installed in pipe loops. After pre-conditioning the meters with 200 flushings with 1.0 ppm CL water, seven different solutions were pumped for a period of 6 weeks. Water samples were taken for lead analysis three times per week after a 16-h stagnation period. In the static testing with brass elbows, exposure to the waters with CA+50% excess NH3+FSA, with CA and ammonium fluosilicate, and with CA+FSA resulted in the highest estimated lead concentrations. In the flow-through brass meter tests, waters with CL+FSA, with CL+NaF, and with CL alone produced the highest average lead concentration for the first 3-week period. Over the last 3 weeks the highest lead concentrations were produced by CL+NaF, followed by CL alone and CA+NH3+FSA. Over the first test week (after CL flushing concentrations were increased from 1.0 to 2.0 ppm) lead concentrations nearly doubled (from about 100 to nearly 200 ppb), but when FSA was also included, lead concentrations spiked to over 900 ppb. Lead concentrations from the CL-based waters appeared to be decreasing over the study period, while for the CA+NH3+FSA combination, lead concentrations seemed to be increasing with time.

SECTION I	PRODUCT AND COMPANY IDENTIFICATION
TRADE NAME:	Hydrofluosilicic Acid
CHEMICAL NAME:	Hydrofluosilicic Acid
CAS NUMBER:	16961 - 83 – 4
CHEMICAL FAMILY:	Inorganic Fluorides
SYNONYMS:	Fluorosilicic Acid Hexafluosilicic Acid HFS FSA
PRIMARY USE:	Industrial Chemical
COMPANY INFORMATION:	Mosaic Crop Nutrition, LLC 13830 Circa Crossing Drive Lithia, Florida 33547 www.mosaicco.com 866-928-7901 or 306-523-2800, 8 AM to 5 PM Central Time US
EMERGENCY TELEPHONE:	CHEMTREC 1-800-424-9300

SECTION II	HAZARD IDENTIFICATION	
EMERGENCY OVERVIEW :	Health Hazards:	Corrosive to the skin, eyes and mucous membranes through direct contact, inhalation or ingestion. May cause severe irritation and burns, which may not be immediately apparent. Handle with extreme care.
	Physical Hazards:	Not applicable
	Physical Form:	Liquid
	Appearance:	Water white to amber liquid
	Odor:	Pungent

NFPA HAZARD CLASS	
Health:	3
Flammability:	0
Instability:	1
Special Hazard:	Corrosive

HMIS HAZARD CLASS	
Health:	3
Flammability:	0
Physical Hazard:	0
PPE:	Section 8

WHMIS HAZARD CLASS	
Symbol	
Classification	E
Sub Class	

POTENTIAL HEALTH EFFECTS:	**Eye:**	Corrosive. Contact may cause severe irritation, eye burns, and permanent eye damage.
	Skin:	Corrosive. Contact may cause severe irritation, skin burns, and permanent skin damage.
	Inhalation (Breathing)	Corrosive. Harmful if inhaled. May cause severe irritation and burns of the nose, throat, and respiratory tract.

	Ingestion (Swallowing)	Corrosive. Harmful or fatal if swallowed. May cause severe irritation and burns of the mouth, throat and digestive tract.
	Signs and Symptoms:	Effects of overexposure may include severe irritation and burns of the mouth, nose, throat, respiratory and digestive tract. Symptoms of overexposure may include ulceration of the nose and throat, coughing, salivation, headache, fatigue, dizziness, nausea, shock, and pulmonary edema (accumulation of fluid around the lungs). May lead to coma or death. Onset of symptoms may be delayed.
	Cancer:	The ingredient(s) of this product is (are) not classified as carcinogenic by NTP, IARC, or OSHA
	Target Organs:	No data available for this material (see Other Comments below).
	Developmental:	No data available for this material
	Other Comments:	Prolonged or repeated overexposure to fluoride compounds may cause fluorosis. Fluorosis is characterized by skeletal changes, consisting of osteosclerosis (hardening or abnormal density of bone) and osteomalacia (softening of bones) and by mottled discoloration of the enamel of teeth (if exposure occurs during enamel formation). Symptoms may include bone and joint pain and limited range of motion. Conditions aggravated by exposure may include skin and respiratory (asthma-like) disorders.
	Pre-Existing Medical Conditions:	Conditions aggravated by exposure may include skin and respiratory (asthma-like) disorders.
POTENTIAL ENVIRONMENTAL EFFECTS:		
SECTION III	**COMPOSITION / INFORMATION ON INGREDIENTS**	
FORMULA:	H_2SiF_6	
COMPOSITION:	Hydrofluosilicic Acid	20-25%
	Fluoride	19%
	Water	75-80%
SECTION IV	**FIRST AID MEASURES**	
FIRST AID PROCEDURES:	Eyes:	Immediately flush with plenty of water for at least 15 minutes. Get medical attention immediately.
	Skin:	Immediately flush with plenty of water. Remove contaminated clothing. Discard contaminated clothing properly. Get medical attention if irritation occurs or persists.

	Inhaled:	Move to fresh air. Administer oxygen. Treat symptomatically. Get medical attention promptly. Observe for possible delayed reaction.
	Ingestion:	Do Not induce vomiting. Give large quantities of milk or water to patient if conscious. Seek medical attention promptly.
NOTE TO PHYSICIAN:		
SECTION V	**FIRE FIGHTING MEASURES**	
Flammable Properties:	Flash Point:	Not applicable
	OSHA Flammability Class:	Not applicable
	LEL/UEL:	Not applicable
	Auto-Ignition Temperature:	Not applicable
Extinguishing Media:	Small fires: Water spray, foam, dry chemical or CO_2 Large fires: Water spray, fog or foam.	
Protection of Firefighters:	Wear self-contained breathing apparatus with full protective clothing. Fluorosilicic Acid is not flammable, however when heated to decomposition, highly toxic and corrosive fumes of fluorides are emitted. May generate flammable and explosive hydrogen gas in contact with some metals.	
SECTION VI	**ACCIDENTAL RELEASE MEASURES**	
RESPONSE TECHNIQUES:	Small spills: Contain spill and stop leak if it can be done without risk. Neutralize acid spill using sodium carbonate or a mixture of soda ash and slaked lime. Absorb material with sand o vermiculite or inert absorbent material. Place in DOT-approved poly container and dispose of properly. Large spills: Isolate spill area and deny entry. Prevent discharge into waterways and sewers. If possible transfer material to appropriate containers for reclamation or disposal. Remaining spill may be neutralized with sodium carbonate or a mixture of soda ash and slaked lime. Contact proper local, state, or federal regulatory agencies to ascertain proper disposal techniques and procedures. All waste to be collected in a DOT-approved poly drum for disposal.	
SECTION VII	**HANDLING AND STORAGE**	
HANDLING:	Avoid contact with eyes, skin, and clothing. Wash thoroughly after handling. Maintain proper hygiene practices when handling this product.	
STORAGE:	Store in tightly closed containers, in a well ventilated area. Keep away from heat, combustible materials, strong bases and metals. Large storage tanks should be bermed. Avoid using glass, metal or ceramic containers.	
SECTION VIII	**EXPOSURE CONTROLS / PERSONAL PROTECTION**	
ENGINEERING CONTROLS:	Assure that ventilation is adequate to control airborne levels.	
PERSONAL	Eye/Face:	Splash proof goggles and full-face shield should be worn at all times.

PROTECTIVE EQUIPMENT (PPE):	Skin:	Acid proof gloves, headgear, protective shoes and clothing should be worn to prevent contact.
	Respiratory:	Wear NIOSH approved respiratory protective equipment when vapor or mists may exceed applicable concentration limits.
	Other:	Facilities utilizing or storing this material should be equipped with an eyewash station and a safety shower.
GENERAL HYGIENE CONSIDERATIONS:	Avoid breathing fumes. Avoid ingestion Wash thoroughly after handling Avoid contact with eyes or skin Use with adequate ventilation	
EXPOSURE GUIDELINES:	OSHA Permissible Exposure Limits (PEL):	2.5 mg/m^3 as Fluoride
	ACGIH Threshold Limit Value (TLV): TLV-TWA	2.5 mg/m^3 as Fluoride
	BIOLOGICAL EXPOSURE INDEX (BEI) Index Timing BEI Fluoride in urine Prior to shift 3 mg/L; End of shift 10 mg/L ACGIH 2004	

SECTION IX — PHYSICAL AND CHEMICAL PROPERTIES

Note: Unless otherwise stated, values in this section are determined at 20°C (68°F) and 760 mm Hg (1 atm).

Flash Point:	Not applicable
Flammability/Explosive Limits (%):	Not applicable
Auto-Ignition Temperature:	Not applicable
Appearance:	Water white to amber liquid
Physical State:	Liquid
Odor:	Pungent
Molecular Weight of Pure Material:	144.11
pH:	1.2
Vapor Pressure(mm Hg):	Not applicable
Vapor Density(air=1):	Not applicable
Boiling Point:	222 – 223 °F
Freezing/Melting Point:	Not applicable
Solubility in Water:	100% Soluble in water
Specific Gravity:	1.2
Volatility:	Not applicable

Bulk Density:	9.7 – 10.1 lb/gallon at 25% Sol. @ 77°F
SECTION X	**STABILITY AND REACTIVITY**
Chemical Stability:	Stable under recommended conditions of storage, handling and proper use.
Conditions to Avoid:	Avoid all heat sources.
Incompatible Materials:	Avoid contact with metals, stoneware, strong acids and alkalies, explosives, toxicants, readily oxidizable materials, alkali metals, combustible solids, and organic peroxides.
Hazardous Decomposition Products:	Extreme temperatures such as a fire cause formation of highly toxic and corrosive fumes of fluorides such as SiF_4 and HF. Hydrogen gas may be formed at temperatures above 227°F.
Corrosiveness:	Attacks silica bearing materials, metals, and stoneware
Hazardous Polymerization:	Will not occur.
SECTION XI	**TOXICOLOGICAL INFORMATION**
Acute Oral Toxicity	LD50 = 200 mg/Kg (guinea pig)
Acute Inhalation Toxicity	LC50 850 – 1070 ppm / 1 hour (Rat)
Acute Dermal Toxicity	140 mg/kg LDLo (Frog)
Mutagenesis	No data available
Target Organ	No data available
Developmental Toxicity	No data available
Carcinogenicity	No data available
SECTION XII	**ECOLOGICAL INFORMATION**
Ecotoxicology	No data available
SECTION XIII	**DISPOSAL CONSIDERATIONS**
	This material, if discarded in the same state as it was delivered, meets RCRA Hazardous Waste characteristic for Corrosivity (D002) See 40CFR261.22. Keep in covered DOT-approved container pending disposal. Handle and dispose in full compliance with all applicable International, Federal, State and Local regulations.
SECTION XIV	**TRANSPORT INFO**
Regulatory Status	Regulated by US DOT, Canada TDG, IATA, IMO/IMDG
Proper Shipping Name	Fluorosilicic Acid

Hazard Class	Class 8 (Corrosive)
Packing Group	II
Identification Number	UN1778
DOT ERG Number	154
SECTION XV	**REGULATORY INFORMATION**
CERCLA:	Not Regulated
RCRA 261.33:	Not Regulated
SARA TITLE III: (Exemptions at 40 CFR, Part 370 may apply for agricultural use, or for quantities of less than 10,000 pounds on-site.)	Section 302: Not Regulated
	Section 304: Not Regulated
	Section 311/312: Acute and Chronic Section 313: Not Regulated
NTP, IARC, OSHA:	The ingredient(s) of this product is (are) not classified as carcinogenic by NTP, IARC, or OSHA
Canada DSL and NDSL:	On Inventory
TSCA:	On Inventory
CA Proposition 65: (Health & Safety Code Section 25249.5)	Not listed
WHMIS:	Fluorosilicic acid is listed as a Class E - Corrosive Material. This MSDS has been prepared according to the hazard criteria of the Controlled Product Regulations (CPR) and the MSDS contains all of the information required by the CPR
CBSA:	N/A
SECTION XVI	**OTHER INFORMATION**
Disclaimer:	The information in this document is believed to be correct as of the date issued. **HOWEVER, NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR ANY OTHER WARRANTY IS EXPRESSED OR IS TO BE IMPLIED REGARDING THE ACCURACY OR COMPLETENESS OF THIS INFORMATION, THE RESULTS TO BE OBTAINED FROM THE USE OF THIS INFORMATION OR THE PRODUCT, THE SAFETY OF THIS PRODUCT, OR THE HAZARDS RELATED TO ITS USE.** This information and product are furnished on the condition that the person receiving them shall make their own determination as to suitability of the product for their particular purpose and on the condition that they assume the risk of their use thereof. The conditions and use of this product are beyond the control of Mosaic, and Mosaic disclaims any liability for loss or damage incurred in connection with the use or misuse of this substance.
Preparation:	The preparation of this MSDS was in accordance with ANSI Z400.1-2004.
Note to ____ (*if applicable*):	