

Second Thoughts about

Fluoride

New research indicates that a cavity-fighting treatment could be risky if overused

By Dan Fagin

KEY CONCEPTS

- Researchers are intensifying their scrutiny of fluoride, which is added to most public water systems in the U.S. Some recent studies suggest that overconsumption of fluoride can raise the risks of disorders affecting teeth, bones, the brain and the thyroid gland.
- A 2006 report by a committee of the National Research Council recommended that the federal government lower its current limit for fluoride in drinking water because of health risks to both children and adults.

—The Editors

Long before the passionate debates over cigarettes, DDT, asbestos or the ozone hole, most Americans had heard of only one environmental health controversy: fluoridation. Starting in the 1950s, hundreds of communities across the U.S. became embroiled in heated battles over whether fluorides—ionic compounds containing the element fluorine—should be added to their water systems. On one side was a broad coalition of scientists from government and industry who argued that adding fluoride to drinking water would protect teeth against decay; on the other side were activists who contended that the risks of fluoridation were inadequately studied and that the practice amounted to compulsory medication and thus was a violation of civil liberties.

The advocates of fluoride eventually carried the day, in part by ridiculing opponents such as the right-wing John Birch Society, which called fluoridation a communist plot to poison America. Today almost 60 percent of the U.S. population drinks fluoridated water, including resi-

dents of 46 of the nation's 50 largest cities. Outside the U.S., fluoridation has spread to Canada, the U.K., Australia, New Zealand and a few other countries. Critics of the practice have generally been dismissed as gadflies or zealots by mainstream researchers and public health agencies in those countries as well as the U.S. (In other nations, however, water fluoridation is rare and controversial.) The U.S. Centers for Disease Control and Prevention even lists water fluoridation as one of the 10 greatest health achievements of the 20th century, alongside vaccines and family planning.

Now, though, scientific attitudes toward fluoridation may be starting to shift in the country where the practice began. After spending more than two years reviewing and debating hundreds of studies, a committee of the National Research Council (NRC) released a report in 2006 that gave a tinge of legitimacy to some longtime assertions made by anti-fluoridation campaigners. The report concluded that the Environmental Protection Agency's current limit

AARON GOODMAN



for fluoride in drinking water—four milligrams per liter (mg/L)—should be lowered because of health risks to both children and adults. In children, consistent exposure to fluoride at that level can discolor and disfigure emerging permanent teeth—a condition called dental fluorosis. In adults, the same fluoride level appears to increase the risk of bone fracture and, possibly, of moderate skeletal fluorosis, a painful stiffening of the joints. Most fluoridated water contains much less fluoride than the EPA limit, but the sit-

uation is worrisome because there is so much uncertainty over how much additional fluoride we ingest from food, beverages and dental products. What is more, the NRC panel noted that fluoride may also trigger more serious health problems, including bone cancer and damage to the brain and thyroid gland. Although these effects are still unproved, the panel argued that they deserve further study.

The largest long-running investigation of the effects of fluoride is the Iowa Fluoride Study, di-

▲ **TOO MUCH OF A GOOD THING:** Fluoride is in many foods, beverages and dental products. The ubiquity of the cavity-fighting chemical can result in overconsumption, particularly among young children.

[TRENDS]

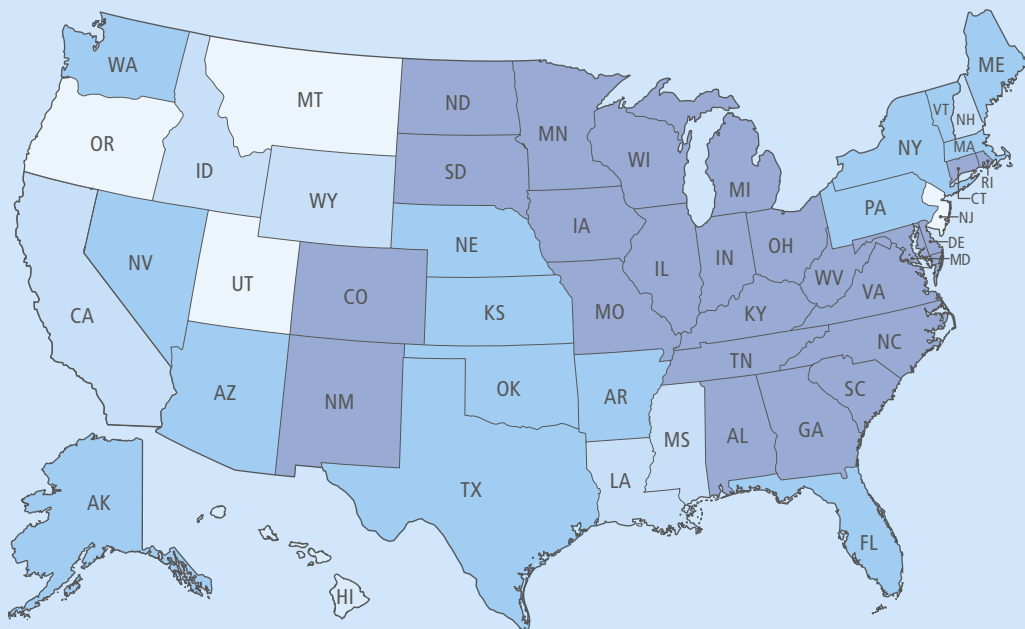
FLUORIDATION ACROSS AMERICA

59% of the U.S. population received fluoridated water in 2002

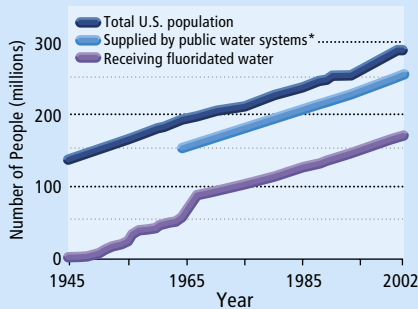
Water fluoridation has spread across the U.S. since its introduction in 1945. In 2002, the latest year for which data are available, Americans receiving fluoridated water represented 67 percent of all people supplied by public water systems and 59 percent of the total population. Fluoridation is most prevalent in the District of Columbia (100 percent) and Kentucky (99.6 percent) and least common in Hawaii (8.6 percent) and Utah (2.2 percent).

PERCENTAGE OF STATE POPULATIONS RECEIVING FLUORIDATED WATER, 2002

☐ < 25% ☐ 25%–49% ☐ 50%–75% ☐ >75%



FLUORIDATION RISING IN THE U.S.



*Data on public water systems not available before 1964

rected by Steven M. Levy of the University of Iowa College of Dentistry. For the past 16 years Levy’s research team has closely tracked about 700 Iowa children to try to tease out subtle effects of fluoridation that may have been overlooked by previous studies. At the same time, Levy is also leading one of the most extensive efforts ever to measure fluoride concentrations in thousands of products—including foods, drinks and toothpastes—to develop credible estimates of typical fluoride intake.

It is a maddeningly complex area of research because diets, toothbrushing habits and water fluoridation levels vary so much and also because genetic, environmental and even cultural factors appear to leave some people much more susceptible to the effects of fluoride—both positive and negative—than others. Despite all the uncertainties, however, Levy and some other fluoride researchers have come around to the view that some children, especially very young ones, are probably getting more fluoride than they should. Most of those scientists, including Levy, still support water fluoridation as a proved method of controlling tooth decay, especially in populations where oral hygiene is poor. But the researchers also believe that in communities with good dental care the case for fluoridation

is not as strong as it used to be. “Instead of just pushing for more fluoride, we need to find the right balance,” Levy says.

The Advent of Fluoride

Framed toothpaste advertisements from more than half a century ago hang on the walls of Levy’s conference room. One touting Pebecco Toothpaste reads: “Do you want your teeth to ache and get ugly?” Another asserts that “Colgate Chlorophyll Toothpaste Destroys Bad Breath.” They are artifacts of the prefluoride era, when tooth decay—called caries in the parlance of dentistry—was pervasive and toothpastes were marketed with questionable medical claims.

The introduction of fluoride changed all that. In 1945 Grand Rapids, Mich., became the first city to fluoridate its water supply. Ten years later Procter & Gamble introduced Crest, the first fluoridated toothpaste, which contained stannous fluoride (a compound with one atom of tin and two of fluorine). Colgate-Palmolive followed in 1967 by modifying its Colgate brand with what has become one of the dominant cavity-fighting ingredients in toothpastes: sodium monofluorophosphate. Instead of sticking with the fluoride salts found in toothpastes and fa-

[THE AUTHOR]



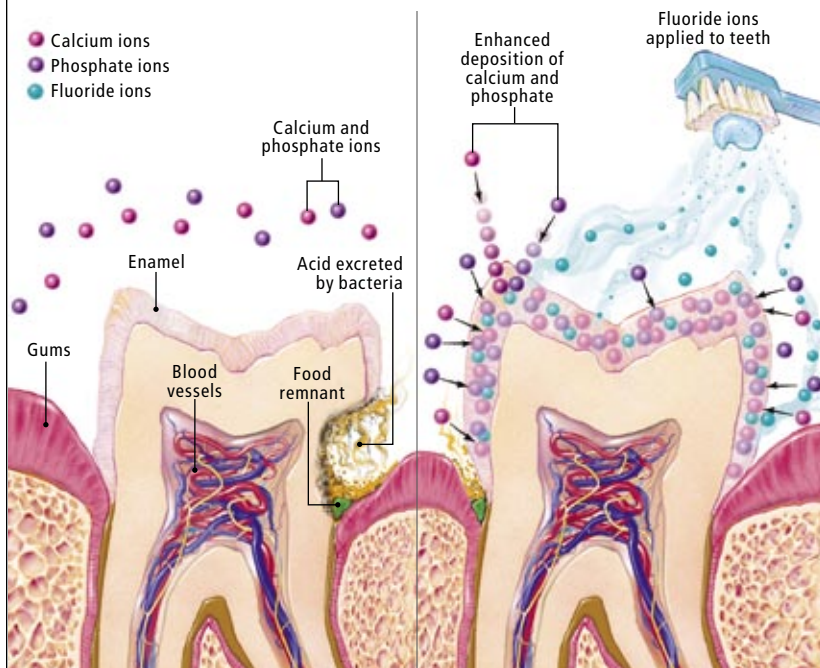
Dan Fagin is an associate professor of journalism and director of the Science, Health and Environmental Reporting Program at New York University. A former environmental and science writer for *Newsday*, his articles on cancer epidemiology won the AAAS Science Journalism Award in 2003. Fagin is co-author of *Toxic Deception* (Common Courage Press, 1999) and is working on a book about gene-environment interactions and the childhood cancer cluster in Toms River, N.J.

COURTESY OF ANNA FAGIN (Fagin); LUCY READING-IKKANDA (map and graph); MOOBOARD/CORBIS (paper clip)

[FOCUS ON TEETH]

FIGHTING CAVITIES

Fluoride's role in combating tooth decay is rooted in the ion's powerful attraction to enamel, the hard, white outer layer of the teeth.



▲ Without Fluoride

The primary mineral in enamel is hydroxylapatite, a crystal composed of calcium, phosphorus, hydrogen and oxygen. When food remnants become lodged between teeth, bacteria consume the sugars and excrete lactic acid, which can lower the pH of the mouth enough to dissolve the hydroxylapatite. If the rate of dissolution is higher than the rate of remineralization—the deposition of calcium and phosphate ions from saliva onto the enamel—then cavities will form in the teeth.

▲ With Fluoride

The topical application of fluoride to the teeth has two effects. First, the fluoride ions replace some of the hydroxyl groups in the hydroxylapatite molecules, creating fluorapatite crystals that are slightly more resistant to the enamel-dissolving acid excreted by the bacteria. Second, the fluoride on the surface of teeth serves as a catalyst that enhances the deposition of calcium and phosphate, thus remineralizing damaged enamel and combating decay.

vored by dentists in office treatments, most water suppliers eventually switched to the cheaper option of fluoridating with silicofluorides such as hexafluorosilicic acid, a by-product of a fertilizer manufacturing process in which phosphate ores are treated with sulfuric acid.

By the 1970s and 1980s America was awash in various forms of fluoride, and fluoridation had become the cornerstone of preventative dentistry in most English-speaking countries. Exactly why and how much caries incidence decreased during the same period is a matter of fierce debate, but the consensus among dental researchers is that the decline was steep and that fluoride deserved much of the credit.

That was the culture in which Levy got his start in public health dentistry in the mid-1980s. Colgate-Palmolive funded his early research, which had the effect of encouraging more fluoride use in dental offices. But as American dentists began to see fewer cavities and more fluorosis on the teeth of their young patients, Levy started to wonder whether children were getting too much of a good thing. “There was a transition in my own thinking from ‘more fluoride is definitely our goal’ to making sure we understand where the right balance is between caries and fluorosis.”

Fluoride's role in causing one disease and deterring another is rooted in the fluorine ion's powerful attraction to calcium-bearing tissues in the body. In fact, more than 99 percent of ingested fluoride that is not quickly excreted ends up in bones and teeth. Fluoride inhibits cavities through two separate mechanisms. First, fluoride that touches the enamel—the hard, white outer layer of the teeth—becomes embedded in the crystalline structures of hydroxylapatite, the main mineral component of teeth and bones. The fluorine ions replace some of the hydroxyl groups in the hydroxylapatite molecules of the enamel, and this substitution makes teeth slightly more resistant to the enamel-dissolving acid excreted by bacteria in the mouth as they consume food remnants. Second, the fluoride on the surface of teeth serves as a catalyst that enhances the deposition of calcium and phosphate, making it easier for the body to continually rebuild the enamel crystals that the bacteria are dissolving.

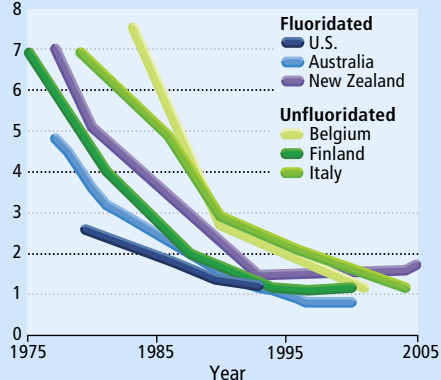
Fluoride has a very different effect, however, when large doses are ingested by young children whose permanent teeth are still developing and have not yet erupted. The key proteins in early tooth formation are called amelogenins, which regulate the formation of hydroxylapatite crys-

Debating the Effects

The U.S. Centers for Disease Control and Prevention has hailed fluoridation as one of the 10 greatest public health achievements of the 20th century, claiming that the addition of the chemical to drinking water has been one of the main reasons for the decline in tooth decay over the past three decades (measured here by the number of decayed, missing or filled teeth in 12-year-olds). Rates of tooth decay have also plunged, however, in many countries where public water systems are not fluoridated. In some of these nations, fluoride added to foods, beverages and dental products may account for part of the decline.

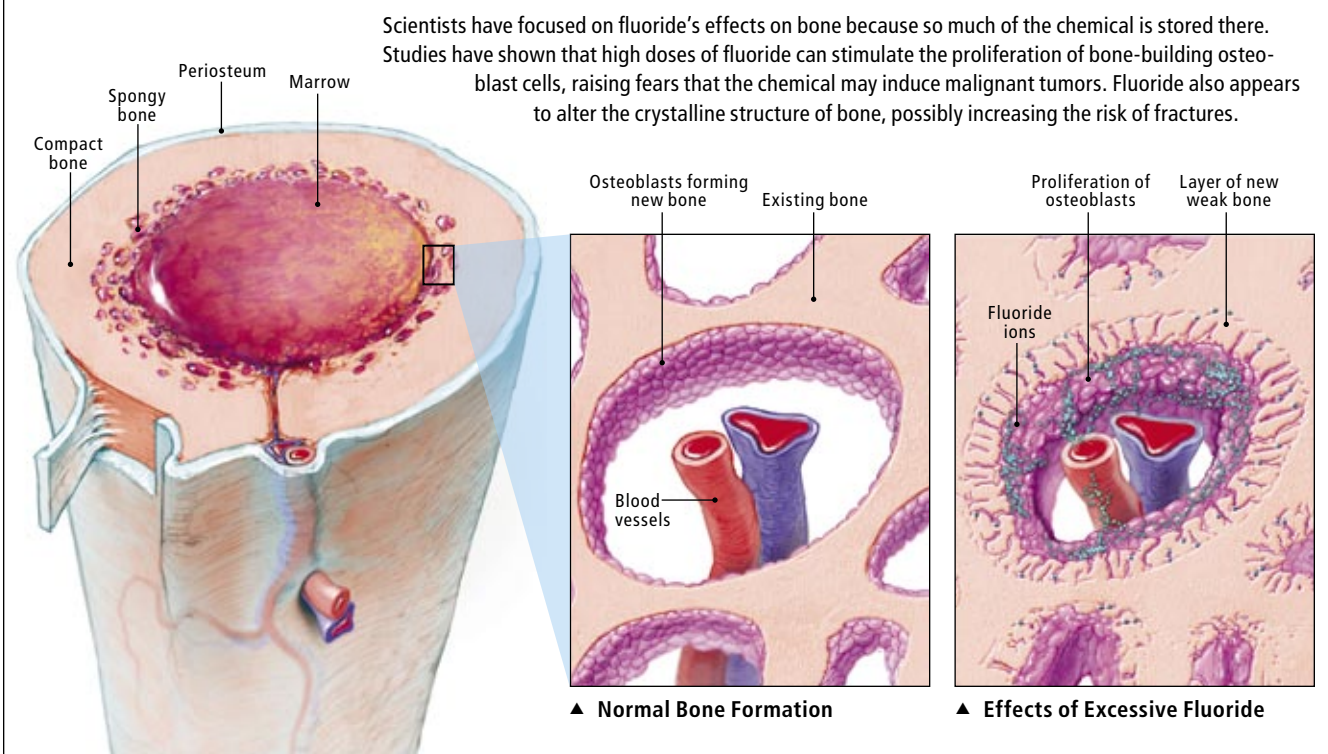
TOOTH DECAY INDEX

(number of decayed, missing or filled teeth in 12-year-olds)



ANDREW SWIFT (teeth); LUCY READING-IKKANDA (graph)

IS FLUORIDE WEAKENING BONE?



Scientific attitudes toward fluoridation may be starting to shift in the country where the practice began.

tals. As a crystal matrix forms, the amelogenins break down and are removed from the maturing enamel. But when some children consume high doses of fluoride, which is absorbed through the digestive tract and delivered by the bloodstream to the developing teeth, the biochemical signaling goes awry and the proteins remain inside the budding tooth longer than usual, thereby creating gaps in the crystalline enamel structure. As a result, when a fluorosed tooth finally erupts it is often unevenly colored, with some portions whiter than others—a visual effect caused by light refracting off the porous enamel. In more severe cases, the surface of the tooth is pitted and the stains are brown. Nutrition and genetics can influence the risk of fluorosis, but the most important factor by far is the amount of fluoride ingested.

With grant money from the National Institute of Dental and Craniofacial Research, Levy set out to determine how much fluoride children consume and how it affects their teeth and bones. There is no universally accepted optimal level for daily intake of fluoride—that is, a level that maximizes protection against tooth decay while minimizing other risks—but the range most often cited by researchers is 0.05 to 0.07 milligram of fluoride per kilogram of body

weight per day. In the early 1990s, when the children in Levy's study were infants, he found that more than a third of them were ingesting enough fluoride—mostly via water-based infant formula, baby foods and juice drinks—to put them at a high risk of developing mild fluorosis in their permanent teeth. That fraction dropped only slightly as their diet changed during their toddler years—a critical period for enamel formation in preemergent teeth. Typical fluoride ingestion stayed high during the toddler years, in part because toothpaste replaced formula as a key source. Although both children and adults are supposed to spit out their toothpaste after brushing, Levy had found in an earlier study that toddlers on average actually swallowed more than half of their toothpaste.

By the time the Iowa children were nine years old and their permanent front teeth had emerged, it was obvious that the earlier exposures to fluoride had literally left their mark. The front teeth of children who had been in the high-intake group as infants and toddlers were more than twice as likely to show the telltale staining of fluorosis than the teeth of children who had ingested less fluoride when they were younger. And as their diet broadened, so did their sources of fluoride. Tests performed in

Levy's lab found, for example, that many kinds of juice drinks and soda pop contain enough fluoride (generally about 0.6 mg/L) so that drinking a little more than a liter a day would put a typical three-year-old at the optimal intake level, without counting any other daily sources.

Dozens of food items tested by Levy's team contained even higher concentrations of fluoride: an average of 0.73 mg/L in cranberry-juice cocktail, 0.71 mg/L in ice pops, 0.99 mg/L in beef gravy and 2.10 mg/L in canned crabmeat, for example. In most cases, the fluoride came from water added during processing, although higher levels also got into grapes and raisins via pesticides, into processed chicken products via ground-up bone, and into tea leaves via absorption from soil and water.

Levy found that exposure to fluoridated drinking water was an even more important risk factor for fluorosis. Iowa children who lived in communities where the water was fluoridated were 50 percent more likely to have mild fluorosis on at least two of their eight permanent front teeth at nine years of age than children living in nonfluoridated areas of the state (there was a 33 percent prevalence in the former versus 22 percent in the latter). Similar results appeared in the NRC report, which found that infants and toddlers in fluoridated communities ingest about twice as much fluoride as they should. Furthermore, the committee noted that adults who drink above-average amounts of water, including athletes and laborers, are also exceeding the optimal level for fluoride intake.

But enamel fluorosis, except in the severest cases, has no health impact beyond lowered self-esteem: the tooth marks are unattractive and do not go away (although there are masking treatments). The much more important question is whether fluoride's effects extend beyond altering the biochemistry of tooth enamel formation. Says longtime fluoride researcher Pamela DenBesten of the University of California, San Francisco, School of Dentistry: "We certainly can see that fluoride impacts the way proteins interact with mineralized tissue, so what effect is it having elsewhere at the cellular level? Fluoride is very powerful, and it needs to be treated respectfully."

Fluoride and Bone

Bone is an obvious place to look for fluoride's fingerprints because so much fluoride is stored there. What is more, studies of patients with

osteoporosis—a bone disease that increases the risk of fractures—have shown that high doses of fluoride can stimulate the proliferation of bone-building osteoblast cells, even in elderly patients. The exact mechanism is still unknown, but fluoride appears to achieve this by increasing the concentrations of tyrosine-phosphorylated proteins, which are involved in biochemical signaling to osteoblasts. As with tooth enamel, however, fluoride not only stimulates bone mineralization, it also appears to alter the crystalline structure of bone—and in this case, the effects are not merely aesthetic. Although fluoride may increase bone volume, the strength of the bone apparently declines. Epidemiological studies and tests on lab animals suggest that high fluoride exposure increases the risk of bone fracture, especially in vulnerable populations such as the elderly and diabetics. Although those studies are still somewhat controversial, nine of the 12 members of the NRC panel concluded that a lifetime of exposure to drinking water fluoridated at 4 mg/L or higher does indeed raise the risk of fracture. The committee noted that lower fluoridation levels may also increase the risk, but the evidence is murkier.

As the Iowa children in his study enter adolescence, Levy hopes that analyses of the strength of their spine, hips and overall skeleton will point to possible connections between fluoride intake and bone health. He presented some preliminary data in 2007, finding little difference in the mineral content of the bones of 11-year-olds based on how much fluoride they had ingested as young children. As they go through adolescence, however, Levy thinks that trends may emerge.

The even bigger question looming over the fluoride debate is whether these known cellular effects in bones and teeth are clues that fluoride is affecting other organs and triggering other diseases besides fluorosis. The biggest current debate is over osteosarcoma—the most common form of bone cancer and the sixth most prevalent cancer in children. Because fluoride stimulates the production of osteoblasts, several researchers have suggested that it might induce malignant tumors in the expanding cell population. A 1990 study conducted by the U.S. government's National Toxicology Program found a positive dose-response relation for osteosarcoma incidence in male rats exposed to different amounts of fluoride in drinking water (all those amounts, as is typical for ani-

SIGNS OF FLUOROSIS

When young children consume large amounts of fluoride, the chemical can disrupt the development of their permanent teeth. When the teeth emerge, their enamel may be discolored (top) or, in more severe cases, disfigured (bottom). Researchers have found that this condition, called dental fluorosis, is more common in communities where the drinking water is fluoridated.





A FLUORIDE DIET

The optimal range for daily intake of fluoride—the level that maximizes protection against tooth decay but minimizes other risks—is generally considered to be 0.05 to 0.07 milligram for each kilogram of body weight. Consuming foods and beverages with large amounts of fluoride can put a diet above this range. Below are typical trace levels of fluoride, measured in parts per million (ppm), found in foods and drinks tested at the University of Iowa College of Dentistry.

3.73 ppm Brewed black tea

2.34 ppm Raisins ▶

2.02 ppm White wine

1.09 ppm Apple-flavored juice drink

0.91 ppm Brewed coffee

0.71 ppm Tap water (U.S.-wide average)

0.61 ppm Chicken soup broth

0.60 ppm Diet Coke (U.S.-wide average)

0.48 ppm Hot dog

0.46 ppm Grapefruit juice

0.45 ppm Beer ▶

0.45 ppm Baked russet potatoes

0.35 ppm Cheddar cheese

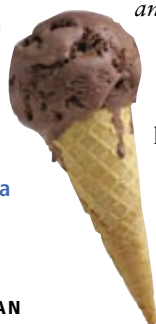
0.33 ppm Flour tortillas

0.32 ppm Creamed corn (baby food)

0.23 ppm Chocolate ice cream ▶

0.13 ppm Brewed chamomile tea

0.03 ppm Milk (2%)



mal studies, were far above the actual exposures found in fluoridated communities). But other animal studies as well as most epidemiological studies in human populations have been ambiguous at best.

The latest dustup over fluoride and osteosarcoma was instigated by a young researcher named Elise B. Bassin of the Harvard School of Dental Medicine. Bassin collected information about fluoride exposures among 103 osteosarcoma patients and 215 matched control subjects and concluded that fluoride is a risk factor for the cancer among boys (the results were ambiguous for girls). Bassin's report appeared in 2006 in the journal *Cancer Causes and Control*; in the same issue, however, her dissertation adviser at Harvard, Chester Douglass, wrote a commentary warning readers to be "especially cautious" in interpreting her findings because, he said, better data, still unpublished, contradict them. Antifluoridationists and some environmental groups quickly rushed to

Bassin's defense, demanding that Harvard investigate Douglass, professor and chair of epidemiology at the dental school, for allegedly misrepresenting Bassin's work and for having a conflict of interest because he is editor in chief of a newsletter for dentists funded by Colgate. The university's investigation of Douglass, completed in 2006, concluded that there was no misconduct or conflict of interest.

Clashes over the possible neurological effects of fluoride have been just as intense. Phyllis Mullenix, then at the Forsyth Institute in Boston, set off a firestorm in the early 1990s when she reported that experiments on lab rats showed that sodium fluoride can accumulate in brain tissue and affect animal behavior. Prenatal exposures, she reported, correlated with hyperactivity in young rats, especially males, whereas exposures after birth had the opposite effect, turning female rats into what Mullenix later described as "couch potatoes." Although her research was eventually published in *Neurotoxicology and Teratology*, it was attacked by other scientists who said that her methodology was flawed and that she had used unrealistically high dosages. Since then, however, a series of epidemiological studies in China have associated high fluoride exposures with lower IQ, and research has also suggested a possible

mechanism: the formation of aluminum fluoride complexes—small inorganic molecules that mimic the structure of phosphates and thus influence enzyme activity in the brain. There is also some evidence that the silicofluorides used in water fluoridation may enhance the uptake of lead into the brain.

The endocrine system is yet another area where some evidence exists that fluoride can have an impact. The NRC committee concluded that fluoride can subtly alter endocrine function, especially in the thyroid—the gland that produces hormones regulating growth and metabolism. Although researchers do not know how fluoride consumption can influence the thyroid, the effects appear to be strongly influenced by diet and genetics. Says John Doull, professor emeritus of pharmacology and toxicology at the University of Kansas Medical Center, who chaired the NRC committee: "The thyroid changes do worry me. There are some things there that need to be explored."

The Controversy Continues

The release of the NRC report has not triggered a public stampede against fluoridation, nor has it prompted the EPA to quickly lower its fluoride limit of 4 mg/L (the agency says it is still studying the issue). Water suppliers who add fluoride typically keep levels between 0.7 to 1.2 mg/L, far below the EPA limit. About 200,000 Americans—and several million people in China, India, the Middle East, Africa and Southeast Asia—drink concentrations higher than the limit, but their excess fluoride comes from naturally occurring runoff from fluoride-containing rocks and soils near water sources.

The report is, however, prompting some researchers to wonder whether even 1 mg/L is too much in drinking water, in light of the growing recognition that food, beverages and dental products are also major sources of fluoride, especially for young children. The NRC committee did not formally address the question, but its analyses suggest that lower water fluoridation levels may pose risks, too. "What the committee found is that we've gone with the status quo regarding fluoride for many years—for too long, really—and now we need to take a fresh look," Doull says. "In the scientific community, people tend to think this is settled. I mean, when the U.S. surgeon general comes out and says this is one of the 10 greatest achievements of the 20th century, that's a hard hurdle to get over. But when we looked at the studies that have

FLUORIDE HISTORY

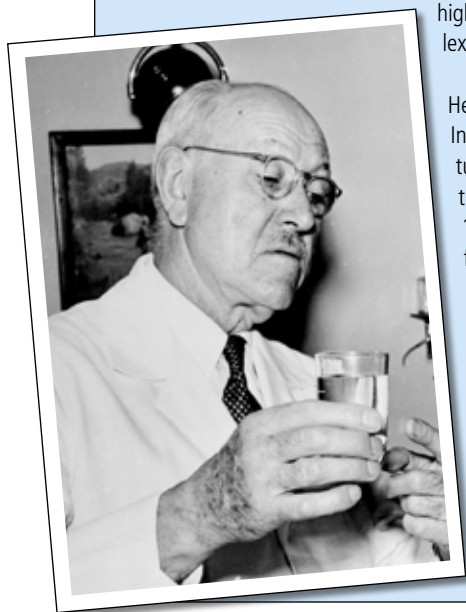
The risks of fluoride were known long before its benefits. Starting in the first decade of the 20th century, a dentist named Frederick McKay traveled the American West investigating reports of what was then known as Colorado Brown Stain. With a collaborator, G. V. Black, dean of the Northwestern University Dental School, McKay discovered that children born in Colorado Springs, Colo., had stained teeth, but adults who moved there did not. They hypothesized that young children whose permanent teeth had not yet erupted or developed enamel faced the highest risk of developing the stain. McKay, who guessed that the stain was caused by some unknown compound in the local drinking water, also noticed a curious fact: the mottled teeth were surprisingly resistant to decay.

The cause remained a mystery until 1930, when McKay went to Arkansas to investigate reports of tooth staining in Bauxite, a company town owned by the Aluminum Company of America (Alcoa). Worried that aluminum might be blamed, Alcoa's chief chemist, H. V. Churchill, tested the local water and discovered something McKay had never suspected: high levels of naturally occurring fluoride. McKay quickly tested other suspect water supplies and found that wherever fluoride levels were high—typically 2.5 milligrams per liter or higher—Colorado Brown Stain was prevalent. A new disease entered the lexicon: fluorosis.

Spurred by Churchill's and McKay's discoveries, a researcher named Henry Trendley Dean, head of the dental hygiene unit at the National Institute of Health (which later changed its name to the National Institutes of Health), tried to determine how much fluoride was enough to trigger fluorosis. By the late 1930s he had concluded that levels below 1 mg/L would pose little risk. Dean remembered that McKay had found that fluorosed teeth were resistant to decay, and so he began pushing for a citywide test of a revolutionary idea: deliberately adding fluoride to water at levels that would deter cavities without triggering fluorosis. He got his wish in 1945 in Grand Rapids, Mich., and Dean went on to become fluoridation's leading advocate as the first director of the newly formed National Institute of Dental Research from 1948 until his retirement in 1953.

—D.F.

◀ COLORADO DENTIST Frederick McKay, whose investigations led to the discovery of fluoride's effects on teeth.



been done, we found that many of these questions are unsettled and we have much less information than we should, considering how long this [fluoridation] has been going on. I think that's why fluoridation is still being challenged so many years after it began. In the face of ignorance, controversy is rampant."

Some longtime fluoride researchers, however, remain unimpressed by the evidence of effects beyond teeth and bones, and they continue to push for an expansion of water fluoridation in the U.S. and elsewhere. Their view remains the official position of the American Dental Association and the U.S. Public Health Service. "We feel there are enough communities out there with high caries rates to justify additional fluoridation," says Jayanth V. Kumar, director of oral health surveillance and research at the New York State Department of Health and a member of the NRC panel who dissented from some of

its findings. He acknowledges, however, that the argument for water fluoridation is not as strong in affluent areas with good nutrition and dental care. "Today it depends on what the caries level is in the community. If the disease is low, the return on investment [for fluoridation] may not be all that great."

Opponents of fluoridation, meanwhile, have been emboldened by the NRC report. "What the committee did was very, very important, because it's the first time a truly balanced panel has looked at this and raised important questions," says Paul Connett, a chemistry professor at St. Lawrence University and the executive director of the Fluoride Action Network, one of the most active anti-fluoridation groups worldwide. "I absolutely believe it's a scientific turning point because now everything's on the table. Fluoride is the most consumed drug in the U.S., and it's time we talked about it." ■

➔ MORE TO EXPLORE

Patterns of Fluoride Intake from Birth to 36 Months. Steven M. Levy, John J. Warren, Charles S. Davis, H. Lester Kirchner, Michael J. Kanellis and James S. Wefel in *Journal of Public Health Dentistry*, Vol. 61, No. 2, pages 70–77; June 2001.

Patterns of Fluoride Intake from 36 to 72 Months of Age. Steven M. Levy, John J. Warren and Barbara Broffitt in *Journal of Public Health Dentistry*, Vol. 63, No. 4, pages 211–220; December 2003.

Timing of Fluoride Intake in Relation to Development of Fluorosis on Maxillary Central Incisors. Liang Hong, Steven M. Levy, Barbara Broffitt, John J. Warren, Michael J. Kanellis, James S. Wefel and Deborah V. Dawson in *Community Dentistry and Oral Epidemiology*, Vol. 34, No. 4, pages 299–309; August 2006.

Age-Specific Fluoride Exposure in Drinking Water and Osteosarcoma. Elise B. Bassin, David Wypij, Roger B. Davis and Murray A. Mittleman in *Cancer Causes and Control*, Vol. 17, No. 4, pages 421–428; May 2006.

Caution Needed in Fluoride and Osteosarcoma Study. Chester W. Douglass and Kaumudi Joshipura in *Cancer Causes and Control*, Vol. 17, No. 4, pages 481–482; May 2006.

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