

INVITED REVIEW

What we know and do not know about fluoride*

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Summary

There is much that we know about fluoride as it relates to human health in general and dental health in particular. Some of the information that is known concerning water fluoridation and dental fluorosis is listed. What we do not know about fluoride is discussed in more detail, namely the efficacy of lower levels of fluoride in drinking water, the effect of discontinuing fluoride in drinking water in the absence of additional preventive measures, the prevalence of fluorosis and whether or not this presents a cosmetic problem. Other issues discussed include the actual amount of fluoride ingested from all sources, whether low-fluoride dentifrices are as efficacious as conventional dentifrices in caries protection and reducing enamel fluorosis, the role of socioeconomic factors in determining caries prevalence, and the effects of bottled water use on caries prevalence in fluoridated communities.

Introduction

At the first Herschel S. Horowitz Symposium 5 years ago, I summarized some of the manifold contributions that Hersh made to dental research in the areas of epidemiology, prevention, dental public health, ethical study design, and, of course, fluorides. Hersh first became a proponent of water fluoridation in 1955 as a dental student at the University of Michigan and his support for community water fluoridation was unwavering “because I have seen first-hand the beneficial effects Certainly, I have not changed my mind about the safety and effectiveness of water fluoridation” (1,2). Specifically, as related to this symposium theme, he and colleagues at the National Institute of Dental Research (NIDR) introduced a new method for assessing the prevalence of fluorosis, the Tooth Surface Index of Fluorosis, that was more sensitive with regard to both prevalence and severity of dental fluorosis (3). Hersh also recognized that the level of fluoride in drinking water was not the only contributing factor to dental fluorosis and that, as use of fluoride-containing dentifrices increased, unintentional swallowing of toothpaste had become an

important risk factor. In a paper published in the *Journal of Public Health Dentistry* in 1992, Hersh advocated the introduction in the United States of dentifrices with 400-500 ppm fluoride for preschool-aged children (4). There is much that we know about fluoride as it relates to human health in general and dental health in particular. It has been subject to intense scientific scrutiny and there are many excellent reviews of that literature available (5-9). It would be impossible to cover all we know about the role of fluoride in caries prevention and in enamel fluorosis within the confines of this symposium. Accordingly, I have selected a few points worth noting as they relate to the overall theme of this symposium. The topic “What we know and do not know about fluoride” was assigned to me by the organizers of this symposium, but obviously, knowledge is always incomplete, so that what we know and do not know is relative, rather some things “we know more” and others “we know less.”

Things we know more about fluoride

- Before the widespread availability of topical fluorides, optimal levels of fluoride in the drinking water were designed to maximize its anticaries effect and minimize the levels of enamel fluorosis.
- The difference in caries rates between fluoridated and non-fluoridated communities is less because of the widespread use of fluoride dentifrices and the consumption of foods and beverages manufactured in optimally fluoridated areas (diffusion effect). Yet optimally fluoridated communities consistently have lower caries rates.

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- Excessive amount of fluoride intake, as occurs in some communities with high natural fluoride levels, causes enamel fluorosis and the degree or extent of fluorosis is directly related to the fluoride level in the drinking water.
- Early use of toothpaste (self-reporting), associated with presumed unintentional swallowing of fluoride-containing dentifrices by youngsters, increases the prevalence of enamel fluorosis in later erupting teeth.
- The appropriate dose of fluoride supplement for children in communities with fluoride deficient water supplies provides caries protection similar to that of community water fluoridation, with minimal risk of enamel fluorosis.
- When a fluoride supplement is ingested as a single bolus, fluoride level in the blood peaks and is more likely to cause fluorosis.
- Fluoride acts to prevent caries both pre- and posteruptively, although the relative proportion of benefit has been disputed.
- Fluoride should be ingested systemically (water, salt, milk, or as a supplement) and used topically on a daily basis, for maximum caries prevention.
- With regard to health, at optimal fluoride level in public water supplies, fluoride is safe from a medical perspective.
- In spite of massive evidence with respect to safety and efficacy, water fluoridation continues to engender opposition from a small but vociferous and determined minority.

Things we know less about fluoride

- If the level of fluoride in water supplies is reduced from currently accepted optimal levels, how effective is the caries reduction and is the prevalence of enamel fluorosis reduced?
- Several observational surveys of communities that ceased altogether fluoridation of their water supplies found no subsequent rise in caries rates. What would have been the caries rates if water fluoridation had continued? Could this be explained by improved oral health behavior and increased application of preventive measures such as topical fluoride and sealants?
- Has the prevalence of dental fluorosis really increased in the United States and is it of aesthetic/cosmetic concern?
- We are not sure of the exact amount of fluoride ingested from all sources (water and other beverages, food, topical fluoride agents especially dentifrices) by an individual, particularly by young children whose teeth are mineralizing. Although we have a pretty good idea of the average fluoride intake, we need to know the amount that will trigger enamel fluorosis.
- Whether the prevalence of enamel fluorosis is less in countries that market low-level fluoride dentifrices (250-500 ppm F instead of 1,000-1,100 ppm F) for young children and have extensive communal water fluoridation than in the United States.

- Have socioeconomic factors played an increasing role in determining the efficacy of communal water fluoridation?
- Has the rise in consumption of bottled water in lieu of fluoridated tap water resulted in an increase in caries prevalence or a decrease in fluorosis?

Discussion

Clearly, there is much more that we know well about fluorides than what we know less about it. Having listed some of the issues to which we still do not have all the answers, let me discuss them further item-by-item.

Efficacy of lower levels of fluoride in drinking water

As of July 1, 2007, the level of fluoride in drinking water in Ireland has been set at between 0.6 and 0.8 ppm (down from 1.00 ppm); thus, it is too soon to determine if this lower level has changed either the prevalence of caries or fluorosis. In Hong Kong, Ho Chi Minh City, and Singapore, fluoridation when first introduced was probably set at too high a level considering ambient temperatures and humidity. In Hong Kong, fluorosis has decreased since the level of fluoride in its drinking water was lowered from 1.0 to 0.7 ppm (10).

Effect of discontinuing fluoride in drinking water

A study in Antigo, Wisconsin showed 112 percent increase in caries prevalence (2.5 def to 5.3 def) from 1960 to 1966 (11). Similar adverse trends resulting from ending water fluoridation have been reported in Anglesey, Wales (12), Wick, Scotland (13), Wigtownshire, Scotland (14). In Prague, Czech Republic in 1995, 7 years after fluoridation had stopped, caries in 6-year-olds had risen markedly by 40 percent (15). A systematic review of the effect of stopping water fluoridation found a median increase of 18 percent in dental caries during 6-10 years of follow-up (16).

After communal water fluoridation was discontinued in several communities in the former East Germany (Chemnitz, Spremberg, Zittau) (17), in Cuba (La Salud) (18), and Finland (Kuopio) (19), caries prevalence remained stable or continued to fall and did not rise as had been anticipated. Several preventive measures were instituted in Cuba, Germany, and Finland after the cessation of water fluoridation, primarily involving the use of topical fluorides, which account for the stability of the caries prevalence.

In La Salud, Cuba, starting in 1990 all children received supervised fluoride mouthrinses biweekly throughout the school year (15 times/year) using 0.2 percent NaF solution. Furthermore, children between the ages of 2 and 5 years old received one or two applications of fluoride varnish annually.

In the former East Germany, very little fluoride toothpaste was used (15 percent of all dentifrice sales during 1985-1989) before reunification of Germany, whereas use of fluoride toothpaste rose rapidly to 90 percent of the market share afterwards (1990-1994). In Germany, systemic fluoride use also changed from fluoridated drinking water ingestion to widespread use of vitamin D plus fluoride (0.25 mg) supplements. Additionally, fluoridated salt (250 mg F/kg) increased from 10 percent of market share in 1992 to 40-50 percent in 1999, a sizeable increase (20).

Furthermore, because of restructuring in the provision of dental services in the former East Germany, private practitioners were compensated for each restoration or fissure sealant on a fee-for-service basis, not capitation. Consequently, a high proportion of the children (40 percent) had fissure sealants, on average 3.6 molars were sealed (21). Since most caries in children is fissure caries, the widespread use of sealants must have had a profound effect in helping to reduce caries prevalence. Currently about 33 percent of US children have had occlusal fissures sealed (22).

In none of these studies on caries prevalence in communities following the cessation of water fluoridation is there a control population that continued to receive both fluoridated water and also received the preventive measures discussed above, namely topical fluorides and fissure sealants. Based on extensive epidemiological data from Ireland where communities with or without water fluoridation were compared in the 1980s, caries prevalence declined in both as a result of the introduction of fluoride dentifrices. However, caries prevalence was consistently less in populations that enjoyed the benefits of both water fluoridation and fluoride dentifrices (23). In Tamworth, N.S.W. Australia, a community that began fluoridation in 1963 and has been studied for caries prevalence for over 25 years, caries rates continued to decrease long after the maximum benefits attributable to water fluoridation would have been reached. Presumably, this can be attributed to topical fluoride from dentifrices, rinses, and office applications, as well as the introduction of occlusal sealants (24).

One study in Canada has used a control community that continued water fluoridation. In Comox/Courtenay & Campbell River, B.C., Canada, water fluoridation ceased in 1992, while Kamloops, B.C. continued to fluoridate (25). The sites where fluoridation had ended and fluoridation continued were surveyed in 1993-1994 and only 3 years later in 1996-1997. The prevalence of caries decreased in the fluoridation-ended site while remaining unchanged in the fluoridated site. The authors concluded that multiple sources of fluoride, generally low caries experience and affluence with widely accessible dental services, make it difficult to detect changes. Detailed statistical analyses, including socioeconomic status (SES), could not explain their findings. Maupomé wrote the following to an anti-fluoridation Web site:

“The most common distortion of the findings is that we concluded that communities served by fluoridated water and those without fluoridated water have the same experience of tooth decay. This simplistic assertion is a misrepresentation of the research reported in the publications. The important conclusion from these analyses is that even in a low disease activity population such as these Canadian children, and even over a relatively short time interval such as three years, water fluoridation still had a noticeable effect in reducing tooth decay incidence.”

In other words, the systemic ingestion of fluoride during tooth formation had a prolonged benefit for the “fluoride-ended” children in grades 5, 6, 11, and 12 (ages 11, 12, 17, and 18).

For political or legal reasons, some European countries have not succeeded in achieving or maintaining communal water fluoridation.

Because of declining caries prevalence, some of these countries had a surplus of dentists, many of whom were kept employed delivering preventive treatments such as topical fluoride applications and sealants. By a combination of intensive fluoride therapies (supervised rinses, fluoride dentifrice, fluoride varnishes, sealants), caries prevalence has been lowered. When European colleagues in academia or public health tell me that they no longer need communal water fluoridation, I am reminded of Aesop’s fable of the fox and the grapes!

Prevalence of fluorosis: cosmetic problem or not?

Several reviewers (26-28) have also concluded that the prevalence of fluorosis has risen in North America. A nine percentage point increase in the prevalence of very mild or greater fluorosis was observed among children and adolescents aged 6-19 years when data from 1999 to 2002 were compared with those from the NIDR 1986-87 survey of school children (from 22.8 percent in 1986-87 to 32 percent in 1999-2002) (29,30). These were national studies of diverse populations, using multiple examiners. In a community study, using narrower standardization of examiners, Selwitz *et al.* (31) found no change in the prevalence of fluorosis when comparing the same Illinois population from 1980 to 1990. Both at above-optimal (2-4 ppm F) and optimal fluoride levels, dental fluorosis remained stable or demonstrated no sustained increase over a decade.

Opponents of community water fluoridation have made a big fuss about enamel fluorosis, claiming it is an early warning sign of systemic excess fluoride, yet enamel fluorosis occurs at fluoride levels (1.8-2.2 mg/L) much lower than that at which crippling skeletal fluorosis becomes clinically evident, namely 20-80 mg per day (32).

Numerous studies have addressed the issue of the public perception of enamel fluorosis as an aesthetic problem (33-37). Although these studies were conducted in various countries (Australia, Canada, UK, USA) using different indices of enamel fluorosis, the findings generally from all these studies are that both parents and children are less concerned about low levels of fluorosis than dentists, that children with such low-level fluorosis are less likely to have experienced decay and that everyone, lay and dental professionals, considers high levels of fluorosis cosmetically objectionable. However, aesthetically objectionable fluorosis is a rare outcome, observed in only about 2 percent of children (36). A clear population threshold exists for severe enamel fluorosis, such that the occurrence of the advanced form of fluorosis is close to zero in areas where the fluoride level in drinking water is below 2 mg/L (38).

Amount of fluoride ingested

What is the exact amount of fluoride ingested at optimal fluoride levels, does it matter and, more importantly, what amount will trigger enamel fluorosis? There have been numerous studies using market basket surveys analyzing fluoride content of different foods and beverages and extrapolating what might be the average fluoride ingested in different age groups. Levy (39) has shown that some of the claims by opponents of fluoridation (Citizens for Safe Drinking Water) of high amounts of fluoride ingested from breakfast cereals and milk are erroneous by a factor as much as 10-fold. This is nothing new; similar false claims were made by Lee (40) that children in a nonfluoridated area were already getting optimal fluoride in their diets, yet when such children's urine was analyzed, the fluoride content was significantly less than that of children from an optimally fluoridated community (41).

While sample food analyses are useful when correctly performed, the only really accurate way to determine fluoride intake is to measure the amount of each food or beverage at each meal and set aside a duplicate sample for analyses. Such methods are, of course, impracticable on a public health scale and have therefore not been widely used. The question remains what amount of ingested fluoride will cause fluorosis, is it just the total amount, the rapidity with which it is absorbed causing high peak blood plasma levels, and why do some children in the same family, presumably eating and drinking the same foods and beverages, exhibit fluorosis and other siblings not?

Low-fluoride dentifrices: efficacy in caries protection and reducing enamel fluorosis

Many countries (Australia, Austria, Czech Republic, Belgium, Finland, France, Germany, Israel, Luxembourg, Netherlands,

New Zealand, Portugal, Sweden, Switzerland, UK) market children's dentifrices containing 250, 400, 500, or 550 ppm fluoride in order to reduce unintentional fluoride ingestion (42). In the early 1990s, all the major manufacturers introduced low-fluoride toothpastes to the Australian market with fluoride concentrations in the range 400-550 mg/L (43). In Ireland, low-fluoride toothpastes are marketed for children, and appear to be widely used. One cross-sectional study showed that 51 percent of 1.5-2.5-year-olds and 59 percent of 2.5-3.5-year-olds in Cork use low-fluoride toothpaste containing <800 ppm F (44). Nevertheless, The Irish Expert Body on Fluorides and Health (<http://www.fluoridesandhealth.ie>) does not recommend the use of low-fluoride toothpastes due to the inconsistent evidence of effectiveness in primary teeth (C. Parnell, personal communication, 2009).

Many studies (45,46) have shown that high-fluoride dentifrices significantly increase caries protection compared to standard fluoride dentifrices (~1,100 ppm). There is positive dose-response between fluoride concentrations in dentifrices and caries reductions (42). There were fewer studies using low-fluoride dentifrices (<1,100 ppm); some have shown less efficacy in caries protection compared to standard fluoride toothpastes (47-50), while others have found no statistical difference (51-54). On the basis of a meta-analysis, it was concluded that 250 ppm fluoride dentifrices were not as effective in caries prevention as standard fluoride dentifrices containing 1,000 ppm fluoride or more (55,56). One study has reported significantly less enamel opacities using the Thylstrup-Fejerskov classification or Tooth Fluorosis (TF) index of fluorosis for children using low-fluoride (550 ppm) compared with standard fluoride (1,050 ppm) dentifrices; however, "the differences were numerically very small despite being statistically significant" (57). In addition to controlled prospective studies comparing low- and standard fluoride dentifrices, there are also data from a retrospective "recall" study of use of such dentifrices. Surprisingly, in optimally fluoridated Perth, Australia, fluorosis was almost halved, from 40 percent to 22 percent prevalence, after low-fluoride dentifrices became available for children. Only 22 percent of children were using the low-fluoride dentifrice, while 67 percent continued to use regular fluoridated toothpaste (43). Introduction of low-fluoride dentifrices was not the only variable; use and dosage of fluoride supplements had also changed, which points out the limitation of observational, noninterventional studies. Similarly, use of 400-550 ppm F dentifrices by children from age 2 to 7 years did not significantly increase caries rates but significantly lowered fluorosis prevalence. The prevalence of fluorosis by TF1+ case definition declined from 34.7 percent to 22.1 percent, and by TF2+ case definition from 17.9 percent to 8.3 percent. (37,58). Additional controlled studies are needed comparing concentrations of 500 and 1,000 ppm fluoride, both with regard to efficacy in caries protection and especially to determine if enamel fluorosis is reduced.

Role of socioeconomic factors

Social class is a potent discriminator of health inequalities and caries is no exception. As had been found in earlier studies in the United States, English studies have shown that implementation of water fluoridation reduced decay and that socioeconomic dental inequalities are reduced (59,60). When the original studies of Newburg and Kingston (both were similar socioeconomically) were conducted, there was a clear difference between caries rates in fluoridated Newburg and nonfluoridated Kingston. This difference only holds when similar socioeconomic groups are compared (61). It is more likely that these differences are due to use of self-applied preventive agents such as fluoride dentifrices than due to differences in diet and widespread consumption of junk food, soft drinks, and sugar snacks (62). Because of socioeconomic differences, low SES children are less likely to have toothbrushes and fluoride dentifrices, early diagnosis of caries, more likely to have extractions, all of which would account for disparities in apparent benefits from communal water fluoridation. Whether fluoridation reduces disparities in caries is a continuing research question.

Effects of bottled water use

The final answer is still not in on the effects of drinking bottled water (most contain below 0.3 fluoride parts per million), although it is assumed that this leads to decreased fluoride intake. Whether this is clinically significant is not known. The American Dental Association (ADA) makes no conclusion, simply recommending that “consumers should seek the advice from their dentist about specific fluoride needs” (63). Presumably, persons living in a water-fluoridated community would still consume other beverages made from fluoridated water and have their food cooked in optimally fluoridated water. So the question remains, does it affect caries prevalence and fluorosis rates? The only scientifically acceptable way would be to conduct a double-blind study with half the sample population using nonfluoridated bottled water and the other half using fluoride containing bottled water. It would require a long-term study and that is why it probably will never be done!

Conclusions

The randomized, controlled, double-blind clinical trial is the gold standard for answering many of the questions that remain concerning fluoride therapy in relation to preventing dental caries and minimizing enamel fluorosis. Given the length, cost, and difficulty of conducting such clinical trials, some of the issues raised in this symposium will never be properly investigated. Some clues can be derived from retrospective “recall” studies, but they cannot substitute for long-

term prospective investigations. A public health measure like communal water fluoridation exposes the entire population; it must be undertaken only after the most thorough inquiries into its safety, cost, and efficacy. A few scientifically valid questions for further study have been identified. As stated by Harold Hodge over 20 years ago: “Inspired surveillance must continue with unabated zeal to detect injury if it occurs” (64). Similarly, Kumar recommends, “surveillance and research activities should continue to assess the effect of total fluoride exposure.” (65).

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