

Fluoride and its Antagonists: Implications for Human Health

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Introduction

It is well established that excess consumption of fluoride results in a variety of human health problems. Dental fluorosis, for example, is caused by the impact of too much fluoride on the enamel-producing cells during development. In consequence, necrosis of these cells may occur, interfering with the normal dental calcification process and teeth may be badly stained and pitted. At higher levels fluoride can also result in skeletal fluorosis, which occurs as the result of damage to the normal skeletal metabolic processes. Its major symptoms are osteopetrosis, osteoporosis and osteomalacia (Editorial Board of The Atlas of Endemic Disease, 1989).

Areas of such endemic disease are not rare. Indeed they occur on all continents. As a consequence, dental fluorosis is found as a health issue from England to Japan and from Finland to South Africa (WHO, 1970). Fluoride-related endemic disease is a particular problem in the People's Republic of China where large scale surveys have established its occurrence in 71,413 villages in 991 counties. Some 21 million Chinese, therefore, suffer from dental fluorosis and one million from skeletal fluorosis (Huang Shuze, 1986). A further 51.74 million people live in these high fluoride areas and are threatened by its excess. A 1970 survey established that, even in the United States, one million people living in 524 communities were drinking water that naturally contained more than 2 mg/litre of fluoride (Safe Drinking Water Committee, 1977).

Fluoride Removal

In regions where levels are high enough to cause serious health problems, it is obviously important to lower the fluoride content of drinking water. The conventional procedures for water treatment, such as disinfection, filtration and clarification have little effect, if

any, on the fluoride content of drinking water (Safe Drinking Water Committee, 1977). However, various processes have been developed which are designed to remove excess fluoride from potable water. The two main approaches involve adsorbent filtration and coagulant precipitation. The former defluoridation technique requires the absorption of fluoride on granular media, either activated alumina or bone char (Maier, 1963). To remove fluoride, water is passed through beds of either of these materials, both of which have a strong affinity for this substance. As a result, the fluoride level in the water supply drops. Once the adsorption capacity of the medium begins to fall, it is regenerated with a sodium hydroxide solution, which removes the adsorbed fluoride (Safe Drinking Water Committee, 1977). The Chinese are also experimenting with calcium phosphate in adsorbent filtration in some of their plants. In contrast, coagulant precipitation involves the addition of various aluminum coagulants such as $AlCl_3$ to water containing high levels of fluoride. Such substances react with the fluoride, causing it to precipitate.

Defluoridation is being applied extensively in many regions of China where fluorosis is endemic. To illustrate, by 1983, 9018 projects had been implemented. These involve either water treatment as just described or a change in the source of water supply (Tan et al., 1990). Many of these projects involve the use of community defluoridation plants employing activated alumina, although domestic potable defluoridation units, based on the same principle, are also available (Editorial Board of the Atlas of Endemic Disease, 1989).

Fluoride Antagonists

Aluminum

As just discussed, because of its antagonism aluminum can be used to remove fluoride from drinking water. Conversely, much of the fluoride used in fluoridation plants has been derived from residuals, which remain

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after the processing of aluminum. This environmental antagonism between fluoride and aluminum also occurs during digestion. As Navia (1970) has pointed out "Aluminum and fluoride are mutually antagonistic in competing for absorption in the gut. The more fluoride in the diet, the less aluminum is absorbed. Conversely, feeding aluminum compounds counteracts dental fluorosis, reducing fluoride stores in teeth and bones." This relationship also has been demonstrated in rats (Sharpless, 1936). Ondreicka and colleagues (1971), for example, reported that rats given large doses of aluminum had elevated levels of this element in their brains and other tissues. However, if they were also simultaneously fed fluoride, aluminum levels in urine and feces rose, preventing this element from building up in body tissues. Antagonism between fluoride and aluminum also has been demonstrated in rabbits (Shore et al, 1985). Indeed, human volunteers given both aluminum hydroxide and sodium fluoride showed decreased plasma and urinary fluoride levels, but major increases in fecal fluoride excretion (Spencer et al., 1985).

Calcium

Because of its strong affinity for calcium, most of the fluoride in the earth's crust occurs as a constituent of one of two calcium compounds, fluorite (CaF_2) and fluorapatite ($\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$). The antagonism between calcium and fluoride also influences human health. It has been shown in China, for example, that the prevalence of endemic fluorosis is not simply a reflection of the level of fluoride in drinking water. Prevalence is also affected by other factors including the amount of calcium and vitamins C and D in food and the calcium content of potable water (Editorial Board of the Atlas of Endemic Disease, 1989). Of course, this antagonism between fluoride and calcium is further demonstrated by the use of bone char as an adsorbent medium in defluoridation plants.

A comparable process also seems to occur in the human body where fluoride is rapidly removed from serum and deposited in bones and teeth. As a consequence, under steady-state conditions, 99 percent of the fluoride in the body is sequestered in calcified tissues. Most of the rest occurs in the plasma and is available for excretion (Safe Drinking Water

Committee, 1977).

Implications for Human Health

Aluminum

Numerous publications, including one by this author, have examined the adverse effects of aluminum on human health (Houeland, 1990; Doll, 1993; Foster, 1993). It is not necessary, therefore, to review the evidence in detail. Suffice it to say that, in a variety of disciplines, evidence is building which strongly suggests an etiologic role for aluminum in both Alzheimer's disease and osteoporosis. Since fluoride is antagonistic with aluminum and reduces its absorption by the gut (Navia, 1970), it follows that if aluminum is a primary cause of Alzheimer's disease, this health problem should be less common in communities drinking water enriched with fluoride.

Evidence is accumulating that this is indeed the case. Still and Kelley (1980), for example, studied first admissions of dementia patients, over the age of 55, in three South Carolina hospitals during the period July 1971 to June 1979. Horry County was studied because its water had the highest fluoride content (4.2 mg/litre) of any in the state. In contrast, the water of the other two counties, Anderson and York had the state's lowest fluoride contents, 0.5 and 0.6 mg/litre, respectively. Only patients with ten or more years of continuous residence in one of these three counties, prior to hospital admission, were included in the survey. Still and Kelley (1980) established that although the annual hospital admission rates for vascular dementia were similar for all three counties, that for Alzheimer's disease in Horry, the high fluoride county, was only one-fifth the average rate of the other two low fluoride counties. This difference was significant at the 0.01 level (Still and Kelley, 1980; Kraus and Forbes, 1992).

Similarly, in 1986, Liss and Thornton reported on a double-blinded randomized trial in which an experimental group of Alzheimer's patients received either a placebo or 40 to 60 mg of sodium fluoride daily. Twelve patients who had been study participants were 'decoded' after 30-36 months. In 11 of 12 cases the researchers were correctly able to identify whether the patient had been receiving fluoride or the placebo. This was possible be-

cause, it was claimed, there had been an observable difference in the rate of progression of the symptoms between the two groups, with those receiving fluoride deteriorating more slowly.

In 1991, Forbes and coworkers interviewed surviving members of the Ontario Longitudinal Study of Aging and identified 285 who were displaying evidence of mental impairment. A further 280 individuals were selected from the same cohort who were matched for both age and sex but showed no sign of mental impairment. Water quality information was then collected about the places of residence of all participants in the study. Forbes and colleagues (1991a) identified high and low aluminum and fluoride drinking water, divided according to concentrations below or above the 50th percentile. It was found, for example, that in men the relative risk of mental impairment varied with the aluminum and fluoride content of the drinking water traditionally drunk by the study participant. Mental impairment was greatest in high aluminum-low fluoride areas (odds ratio 2.7) and lowest in high fluoride areas (odds ratio 0.7). Indeed the level of fluoride in drinking water seemed more important than the level of aluminum as an indication of the risk of developing mental impairment. In a later paper about the same study, Forbes and coworkers (1991b) provided new data for 'impaired mental functioning'. These had been derived from a logistic regression model, in which the odds ratios for high aluminum and high fluoride were 1.86 and 0.58 respectively.

In this author's view, the available evidence seems consistent with the position that high aluminum is a significant risk factor in Alzheimer's disease and that because fluoride reduces the body's absorption of aluminum, it therefore reduces the risk of developing this form of dementia.

In addition to its possible etiologic role in Alzheimer's disease, there is also some evidence that high levels of aluminum may increase the risk of developing osteoporosis. To illustrate, zoologists have shown birds eating insects containing elevated aluminum lay eggs with very fragile shells (Nyholm and Myhrberg, 1977). Furthermore, during the 1970s, many patients undergoing dialysis with aluminum-enriched tap water developed osteomalacia, a softening of the bone result-

ing from impaired mineralization (Parkinson et al, 1979). In addition, Mjoberg (1988) has shown a significant tendency towards higher aluminum levels in the bones of younger hip fracture patients. Mjoberg's results seem to support the hypothesis that aluminum impairs bone mineralization and increases fracture rates in the general population. This may be why in British Columbia, at the local health area scale, initial research appears to suggest a strong positive correlation between hospitalization rates for osteoporosis and the aluminum content of drinking water (Zhang, 1993).

Calcium

In high fluoride environments the antagonism of this substance with calcium results in numerous bone-related diseases, including osteoporosis (Editorial Board of the Atlas of Endemic Disease, 1989). However, evidence is accumulating that suggests that, at lower concentrations, fluoride itself may be protective against this disorder. In numerous studies, for example, patients with osteoporosis have been treated with substantial amounts of sodium fluoride (Laitinen et al., 1980; Riggs et al., 1980; Rich et al., 1964; Cass et al., 1966). There have been reports of recalcification of the skeleton, initiation of a positive calcium balance and declines in urinary calcium levels as a consequence of such fluoride supplementation.

The geographical and epidemiological evidence also appears to suggest that, at moderate levels, fluoride may reduce the prevalence of osteoporosis. To illustrate, Leone and coworkers (1955, 1960) described how roentgenograms of the vertebrae of inhabitants of Bartlett County, Texas, who drank water which naturally contained 8 mg/litre of fluoride, showed substantially less osteoporosis than those of the residents of Framingham, Massachusetts. The latter, in contrast, drank water with a fluoride content of only 0.09 mg/ litre. Similarly, Bernstein and collaborators (1966) compared roentgenograms of the lateral lumbar area of the spine from 300 inhabitants of North Dakota, who drank water containing 4 to 5.8 mg/litre of fluoride, with those of 715 individuals from the same state, but with a water supply that had fluoride levels of only 0.15 to 0.3 mg/litre. Evidence of osteoporosis, reduced bone density and col-

lapsed vertebrae was found to be substantially greater in the low fluoride areas of Dakota, especially in women. Also of interest was the observation that visible calcification of the aorta, that is evidence of arteriosclerosis, was also much more obvious in residents of the low fluoride areas, especially men.

In 1985 Simonen and Laitinen published a comparison of the incidence of hip fractures in two Finnish towns of similar economic structure, Kuopio and Jyvaskyla. The former had been fluoridating its water (1 mg/litre) since 1959, while in contrast, Jyvaskyla had very low (0-0.1 mg/litre) naturally occurring levels of fluoride in its drinking water. The water hardness (calcium and magnesium) of both towns was virtually identical. An analysis of femoral-neck fracture data showed that hip fractures were far less common in Kuopio, the town that fluoridated its water than in Jyvaskyla, the town that did not. The differences in incidence were greatest in men in the 50 to 59 age group, where the K/J ratio was 0.20, and smallest in the over 80 age group at 0.56. All differences in men were statistically significant at the $p < 0.001$ level. In women a statistically significant difference in hip fracture incidence only began to occur after age 69, with the K/J ratio reaching 0.68 in the 70 to 79 age group and 0.59 in those aged 80 or older. Overall, in Jyvaskyla the relative risk of hip fracture was 2.5 higher in men and 1.5 higher in women than in Kuopio.

Conclusion

In his book *Fluoridation: The Great Dilemma*, Waldbott writes of fluoridation that "No other procedure in the history of medicine has been praised so highly nor at the same time condemned so thoroughly." As Coffel (1992) points out these extremes are highlighted by two comments, one by an analyst in a dental journal who wrote "If fluoride presents any risk to the public at the level to which most of us are exposed, these risks are so small that they are impossible to detect." In contrast, Yiamouyiannis, a fluoride researcher concluded that his study "provide[d] clear evidence that fluoride is a carcinogen". Indeed, it is argued by opponents of fluoridation that even at levels of 1 mg/litre of drinking water fluoride may interfere with enzymes in the body, injure the developing fetus, and play a role in gastric ulcers, arthritis, atheroscler-

osis, kidney disorders and migraine headaches (Coffel, 1992). If the only significant gain from water fluoridation is reduced tooth decay in children, risks from fluoridation would seem to outweigh gains (Foulkes, 1992). However, if as suggested by the evidence presented in this article, because of its antagonism with both aluminum and calcium, moderate levels of drinking water fluoride are protective against Alzheimer's disease, osteoporosis and calcification of the arterial system, then the reverse may be true. Obviously, the great fluoridation debate can be expected to continue in earnest (Rifat, 1992; Kraus and Forbes, 1992; Foulkes, 1992).

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