Fluoride and Environmental Health: A Review

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Abstract

The relationship between environmental fluoride and human health has been studied for over 100 years by researchers from a wide variety of disciplines. Most scientists believe that small amounts of fluoride in the diet can help prevent dental caries and strengthen bones, but there are a number of adverse affects that chronic ingestion at high doses can have on human health, including dental fluorosis, skeletal fluorosis, increased rates of bone fractures, decreased birth rates, increased rates of urolithiasis (kidney stones), impaired thyroid function, and lower intelligence in children. Chronic occupational exposure to fluoride dust and gas is associated with higher rates of bladder cancer and variety of respiratory ailments. Acute fluoride toxicity and even death from the ingestion of sodium fluoride pesticides and dental products have also been reported.

The distribution of fluoride in the natural environment is very uneven, largely a result of the geochemical behavior of this element. Fluorine is preferentially enriched in highly evolved magmas and hydrothermal solutions, which explains why high concentrations are often found in syenites, granitoid plutonic rocks, alkaline volcanics, and hydrothermal deposits. Fluoride can also occur in sedimentary formations that contain fluoride-bearing minerals derived from the parent rock, fluoride-rich clays, or fluorapatite. Dissolved fluoride levels are usually controlled by the solubility of fluorite (CaF$_2$); thus, high concentrations are often associated with soft, alkaline, and calcium-deficient waters.

Although much is known about the occurrence and health effects of fluoride, problems persist in Third World countries, where populations have little choice in the source of their drinking water and food. However, even in developed nations, fluoride ingestion can exceed the recommended dose when sources other than drinking water are ignored.

1. Introduction

The literature pertaining to the occurrence of fluoride in the environment and its relationship to human health is quite extensive and spans a wide variety of disciplines, including the fields of medicine, dentistry, environmental and occupational health, toxicology, environmental geology, petrology, geochemistry, economic geology, hydrogeology, and soil science. There is even an entire journal (Fluoride) devoted to the dissemination of research in this area published by the International Society for Fluoride Research. Consequently, any attempt to summarize the state of knowledge concerning fluoride and environmental health is necessarily limited to a broad overview. Given that limitation, the chief purpose of this paper is to provide a conceptual framework and a bibliography for further study. Nonetheless, this effort is not without bias.
although there are many sources of fluoride in the environment (both natural and anthropogenic) and various exposure pathways, the emphasis here is on the origin and potential health effects of naturally occurring fluoride in drinking water.

2. Fluoride and Human Health

2.1 Background

Most health studies focus on chronic fluoride exposure from drinking water, because that is the easiest pathway to quantify for a community served by a public water supply. However, food provides another potentially important pathway, as do toothpaste and other products used for dental health. In addition, people living in modern societies are increasingly mobile, making studies of chronic exposure to environmental factors nearly impossible. Consequently, part of the problem in studying the link between fluoride and human health is the difficulty in finding study populations with definable fluoride exposure. Whereas such populations existed more commonly in the United States (U.S.) and other European countries when fluoride studies began, research efforts have now shifted largely to Third World developing nations, where people are more likely to remain in one place throughout their lives and to ingest food and water from local sources.

2.2 History

The linkage between fluoride and human health was first postulated during the late 19th Century, when chemists recognized the variable fluoride contents of bones and teeth in humans (Edmunds and Smedley, 2005). During the early 1900s it was observed that residents living in certain areas of the U.S. developed brown stains on their teeth, and the prevalence and severity of this condition were later shown to correlate directly to the fluoride content of drinking water (Smith et al., 1931). As research continued, it was subsequently recognized that the ingestion of fluoride in optimal amounts provided protection against the development of dental caries without staining the teeth (Dean, 1938). Based on these findings and additional studies conducted during the 1940s, it was suggested that public drinking water supplies in the U.S. be fluoridated with an optimal level of 0.7 to 1.2 mg/L depending on the ambient air temperature of the region (Yiming et al., 2001).

The fluoridation of public drinking water supplies in the U.S. has proceeded at a steady rate, reaching 62 percent in 1992, with the goal of 75 percent by the year 2000 (Yiming et al., 2001). Similarly, Canadian government and health organizations have encouraged fluoridation since 1945. However, Western European countries have generally followed a different path, with the majority opting to reject fluoridation from the beginning, and others discontinuing this practice during the last part of the 20th Century. Even in Britain, where some of the earliest studies showing the benefits of fluoride were conducted, only 10 percent of public water supplies are currently fluoridated (Edmunds and Smedley, 2005). Much of the reluctance to fluoridate drinking water by Western European nations stems from studies that show adverse effects from fluoride ingestion. A large number of non-governmental organizations have formed to oppose any fluoridation efforts in Europe and to encourage communities in the U.S. and Canada to stop this practice. One such group, the Fluoride Action Network, reports that over 150 U.S. and
Canadian communities have followed this advice since 1990 alone. In response, Canadian and U.S. governmental agencies have periodically issued reports that re-affirm the benefits of low-level fluoride intake. Thus, fluoridation remains a contentious issue, and this controversy is likely to continue for some time.

2.3 Bioavailability and Absorption

Fluorine is the most electronegative of all elements and occurs primarily as a negatively charged ion in water (Hem, 1985). In most potable waters (TDS < 500 mg/L), the fluoride ion (F\(^-\)) comprises over 95 percent of the total fluoride present, and the magnesium-fluoride complex (MgF\(^2-\)) is typically the next most prevalent form (Edmunds and Smedley 2005; Doull et al., 2006; Edmunds and Smedley, 2005). Fluoride can also form strong complexes with aluminum, boron, beryllium, ferric iron, silica, uranium, and vanadium, but either these constituents are not present or the conditions necessary for their stability are not usually reached in natural waters (Hem, 1985). Even in fluoridated water supplies, the most common additives, sodium hexafluorosilicate (Na\(_4\)SiF\(_6\)) and hexafluorosilicic acid (H\(_2\)SiF\(_6\)), dissociate to form silicic acid (H\(_3\)SiO\(_4\)), HF\(^-\), and F\(^-\) as long as the pH remains above 5 (Urbansky and Schock 2000; Jackson et al. 2002; Urbansky 2002; Morris, 2004; Jackson, Harvey, and Young, 2002; Urbansky, 2002; Urbansky and Schock, 2000). Although there have been epidemiological studies suggesting that the ingestion of fluorosilicates might have different biological effects from those of sodium fluoride or fluoride from natural sources (e.g., Masters and Coplan 1999; Calderon et al. 2000; Masters et al. 2000; Machaliński et al., 2003; Calderon et al., 2000; Masters et al. 2000; Masters and Coplan 1999), this conclusion is not supported by theoretical considerations of fluorosilicate dissociation and hydrolysis equilibria (Urbansky and Schock, 2000).

Within the stomach, low pH gastric acid favors the formation of the HF\(^-\) complex, which comprises over 90 percent of the total fluoride at pH 2 (Doull et al., 2006). HF\(^-\) is readily absorbed from both the stomach and small intestine by a process of simple diffusion, and once it enters the less acidic mucosa, it dissociates to release fluoride (Whitford and Pashley, 1984; Whitford, 1994a; Whitford, 1996; 1994a; Whitford and Pashley, 1984). About half of the absorbed fluoride is quickly incorporated into developing bone and teeth, where nearly all of the body’s fluoride is found, and the remainder is excreted in the urine (Cerklewski, 1997). The uptake of fluoride by the skeleton is most efficient in children and decreases with age (Whitford, 1999), but this process can continue up to age 55 (Rao, 2003). Once incorporated into hard tissues, fluoride is retrievable, but this entails an extremely slow process of osteoclastic resorption that occurs over many years (Spencer et al., 1975; Doull et al., 2006; Spencer et al., 1975).

Because the absorption of soluble inorganic fluoride is largely controlled by acidity in the stomach, systemic fluoride absorption from drinking water does not vary with overall water quality (Maguire et al., 2005). However, the absorption of less soluble inorganic and organic fluorides is more complicated, and a variety of dietary factors can either increase or decrease the amount that is absorbed (Cremer and Buttner 1970; Cerklewski, 1997; Cremer and Buttner, 1970).

For example, when calcium, magnesium and aluminum salts are added to the diet, some fluoride is incorporated into less soluble compounds that are eliminated through fecal and urinary excretion (Whitford, 1994b). Similarly, increased absorption of fluoride from the
gastrointestinal tract ensues from the addition of substances like phosphates, sulfates and molybdenum to the diet (Ericsson, 1968).

When considering the effect of diet, it is also important to realize that some foods and beverages are naturally high in fluoride and can thus provide a dietary input beyond that which is accounted for in drinking water. Notable examples include sea foods, certain types of teas and wines, some infant formulas, juices and sodas produced with high-fluoride water, fish harvested from high-fluoride lakes, and certain types of vegetables grown in high-fluoride soils (see Jackson et al. (2002) and Doull et al. (2006) and Jackson et al. (2002) for summaries of the fluoride contents of selected foods and beverages). Studies conducted in high-fluoride districts of Tanzania found that even the choice of weaning foods, food tenderizers, and vegetarian versus non-vegetarian diets can affect the incidence of fluorosis (Awadia et al., 1999; Aminmohamed et al., 2000; Awadia et al., 2000). It should also be noted in this context that acidic beverages produced from fluoridated water could contain SiF6^2- ions, the biological effects of which are not well-known (Doull et al., 2006).

2.4 Beneficial Effects

A preponderance of evidence indicates that moderate levels of fluoride ingestion can reduce the incidence of dental caries and, under certain conditions, promote the development of strong bones (Kaminsky et al., 1990; Heller et al., 1997; Yiming et al., 2001; Rao, 2003; Harrison, 2005; Edmunds and Smedley, 2005; Doull et al., 2006; Edmunds and Smedley, 2005; Harrison, 2005; Rao, 2003; Yiming et al., 2001; Heller et al., 1997; Kaminsky et al., 1990). Hydroxyapatite (Ca10(PO4)6(OH)2) is the mineral deposited in and around the collagen fibrils of skeletal tissues to form bone. When fluoride is present, it can substitute for a column hydroxyl in the hydroxyapatite structure to form fluorapatite (Ca10(PO4)6F2 or Ca10(PO4)6OH,F). This substitution causes a reduction in crystal volume, an increase in structural stability, and a decrease in mineral solubility (Aoba, 1997). Free fluoride ions in the fluid phase may also serve to increase the driving force for apatite mineral growth (Aoba, 1997).

Ever since the beneficial effect of fluoride was recognized during the 1930s, researchers have attempted to identify an optimal fluoride concentration in drinking water to reduce dental caries. This optimal level is obviously dependent upon the amount of water consumed on a daily basis and any additional sources of fluoride in the diet. In the U.S., most studies have shown that the sharpest decline in dental caries occurs as fluoride concentrations are increased from 0 to somewhere between 0.7 and 1.2 mg/L, with little additional benefit as fluoride is increased beyond that range (Keller, 1996; Heller et al., 1997; Doull et al., 2006; Heller et al., 1997; Keller, 1996). Consequently, the U.S. Centers for Disease Control and Prevention (CDC), with support from the American Dental Association (ADA) and American Dental Hygienist’s Association (ADHA), recommends that communities with public water supplies adjust the fluoride content of their drinking water to a value between 0.7 and 1.2 mg/L, depending on the average maximum daily temperature. Health Canada, a Canadian governmental agency, recommends an optimal drinking water concentration of 0.8 to 1.0 mg/L fluoride.

Because of fluoride’s role in the development of strong bones, some medical doctors suggested that fluoride ingestion could help prevent osteoporosis. In fact, a study conducted by Bernstein
et al. (1966) of the occurrence of osteoporosis in regions of North Dakota with variable fluoride content suggested that this might be the case. Clinical research and epidemiological studies have shown that fluoride ingestion supplemented with appropriate doses of calcium and Vitamin D can improve bone mineralization but does not necessarily reduce the number fractures (Rich and Ensinck 1961; Gron et al. 1966; Kleerekoper 1996; Aoba 1997; Cerklewski 1997; Kurtto et al. 1999; Aoba, 1997; Cerklewski, 1997; Kleerekoper, 1996; Gron et al., 1966; Rich and Ensinck, 1964). Rather it appears that the potential for fluoride to reduce bone fractures follows a U-shaped curve, with the maximum benefits achieved at about 1 mg/L (Kurtto et al. 1999; Hillier et al., 2000; Li et al., 2001; Yiming et al., 2001; Hillier et al., 2000; Kurtto et al., 1999). An increase in fracture incidence is especially noticeable when the fluoride content of drinking water equals or exceeds 4 mg/L (Sowers et al., 1986; Sowers et al. 1991; Alarcón-Herrera et al. 2001; Sowers et al. 2005; Alarcón-Herrera et al., 2001; Sowers et al., 1991; Sowers et al., 1986). Therefore, although fluoride may hold promise for the treatment of osteoporosis, much remains to be learned about the optimal levels for maximizing the benefits while minimizing the risks (Aoba, 1997; Schnitzier 1997).

2.5 Adverse Effects

The effects of acute fluoride toxicity from accidental overdoses or the ingestion of sodium fluoride pesticides and dental products are well-documented and include vomiting, hemoptysis, cramping of the arms and legs, bronchospasm, cardiac arrest, ventricular fibrillation, fixed and dilated pupils, hyperkalemia, hypocalcemia, and sometimes death (e.g., Whitford 1992; Shulman and Wells, 1997; Whitford, 1992). The list of maladies attributed to chronic fluoride ingestion is even longer, but in some cases (e.g., genetic mutations, birth defects, hypersensitivity reactions, allergic illnesses, repetitive bone injury, and Alzheimer’s disease) the scientific data are at present inconclusive. This paper focuses on the better studied health problems, with emphasis given to the effects of chronic ingestion by humans rather than the results of laboratory animal studies. The reader is referred to a report issued by Doull et al. (2006) for a more complete treatment of this subject.

2.5.1 Dental Effects

Dental fluorosis, the condition which first led to the discovery of a relationship between fluoride ingestion and human health, is characterized by a mottling of the tooth surface, or enamel. As enamel develops, there is increased mineralization within the developing tooth accompanied by a loss of matrix proteins. Exposure to fluoride during this process causes a dose-related disruption of enamel mineralization resulting in anomalously large gaps in its crystalline structure, excessive retention of enamel proteins, and increased porosity (Aoba and Fejerskov 2002). Because fluoride can also accumulate in dentin (Mukai et al. 1994; Kato et al. 1997; Vieira et al., 2004; Kato et al. 1997; Mukai et al. 1994), the mineralized tissue underlying tooth enamel, some researchers have suggested that chronic fluoride exposure could cause aged dentin to crack more easily, but this possibility has not yet been confirmed (Doull et al., 2006).

Mild forms of dental fluorosis are evidenced by the appearance of white horizontal striations on the tooth surface or opaque patches of chalky white discolorations (WHO 1999; Susheela, 2003; Rao, 2003; WHO, 1999). In moderate to severe forms of fluorosis, the opaque patches can
become stained yellow to brown or even black, and eventually the increased tooth porosity leads to structural damages, such as pitting or chipping (Rao, 2003). Table 1 summarizes some of the data linking fluoride concentrations to dental fluorosis based on studies done in the U.S. In the fluoride districts of other countries, it has been reported that dental fluorosis affects at least 60 percent of the population when drinking water contains more than 2 mg/L fluoride (Fordyce et al., 2007) and 100 percent of the population once the fluoride content reaches 6 mg/L (Apambire et al., 1997).

Table 1: Fluoride Content of Drinking Water and the Incidence of Fluorosis in the U.S.¹

<table>
<thead>
<tr>
<th>Fluoride Concentration</th>
<th>Severity of Fluorosis</th>
<th>Percent of Population Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg/L</td>
<td>Mild to Moderate</td>
<td>1 to 2 percent</td>
</tr>
<tr>
<td>2 mg/L</td>
<td>Moderate</td>
<td>10 percent</td>
</tr>
<tr>
<td>2.4 to 4.1 mg/L</td>
<td>Moderate to Severe</td>
<td>33 percent</td>
</tr>
<tr>
<td>2.5 mg/L</td>
<td>Severe</td>
<td>2 percent</td>
</tr>
<tr>
<td>3.5 mg/L</td>
<td></td>
<td>76 percent</td>
</tr>
<tr>
<td>4 to 8 mg/L</td>
<td></td>
<td>1 to 60 percent</td>
</tr>
</tbody>
</table>

¹ Data from Doull et al. (2006), Kaminsky et al. (1990), and Eklund et al. (1987)

2.5.2 Skeletal Effects

Skeletal fluorosis is characterized by increased bone mass and density, accompanied by a range in skeletal and joint symptoms. The mechanism(s) that leads to skeletal fluorosis are poorly understood; however, the stages of development are well-documented (Hileman, 1988; WHO, 1999; Rao, 2003; Susheela, 2003; Edmunds and Smedley, 2005; Rao, 2003; Susheela, 2003; WHO, 1999; Hileman, 1988). In early stages, the symptoms include pain and stiffness in the backbone, hip region, and joints, accompanied by increased bone density (osteosclerosis). The stiffness increases steadily until the entire spine becomes one continuous column of bone, a condition known as “poker back”. As this condition progresses, various ligaments of the spine can also become calcified and ossified. In its most advanced stages, fluorosis produces neurological defects, muscle wasting, paralysis, crippling deformities of the spine and major joints, and compression of the spinal cord.

The threshold level of fluoride ingestion needed to cause skeletal fluorosis varies depending on water intake, water quality, and other dietary factors (Jolly et al., 1969; Raja Reddy, 1985; Jolly et al., 1969). In the U.S. there is no evidence that skeletal fluorosis occurs in the general population if drinking water concentrations are less than 4 mg/L; however, individuals with renal deficiencies who ingest large volumes of water at 2 to 8 mg/L may be at increased risk (Kaminsky et al., 1990; Juncos and Donadio, 1972). Doull et al. (2006) summarized eight cases of skeletal fluorosis that have been documented in the U.S., six of which involved individuals who had sought treatment for renal disease at the Mayo Clinic (Johnson et al., 1979). The remaining two cases included a woman who had ingested well water containing 7.3 to 8.2 mg/L fluoride for a period of seven years (Felsenfeld and Roberts, 1991) and a woman who had consumed large volumes of high-fluoride instant tea made with water that contained 2.8 mg/L fluoride for nearly ten years (Whyte et al., 2005).
2.5.3 Reproductive Effects

A large number of studies have been conducted to explore the relationship between fluoride ingestion and reproductive structure or function, but the majority of these have involved animals that were given high daily doses for short durations, so the application to typical human exposure is uncertain (Doull et al., 2006). Of the studies that involved humans, there are a few results that merit mention, although further study is needed. Perhaps the most conclusive study was that of Freni (1994), who studied a U.S. database from 30 regions within nine states where the fluoride content of drinking water is greater than 3 mg/L. The results showed an association between increasing fluoride concentrations and decreasing birth rates. The reasons for this relationship are not known, but the results of other studies suggest that it might have to do with the effects that high fluoride ingestion has on males, including the morphology and mobility of sperm (Chinoy and Narayanan, 1994), or the levels of testosterone, follicle-stimulating hormones and inhibin-B (Susheela and Jethanandani, 1996; Ortiz-Perez et al., 2003; Susheela and Jethanandani, 1996).

2.5.4 Developmental Effects

Several researchers have found a positive correlation between the fluoride concentrations measured in maternal and umbilical cord blood plasma, which suggests that the placenta allows passive diffusion of fluoride from mother to fetus (Gupta et al., 1993; Malhotra et al., 1993). Studies conducted with laboratory animals indicate that adverse developmental outcomes are possible at very high ingestion rates; but evaluations of developmental defects in human populations have been inconclusive, mostly because the quality of research has been low (Doull et al., 2006). One line of investigation that deserves further study is the possible link between fluoride ingestion and the prevalence of Down’s syndrome (see Whiting et al., 2001), especially for children born to mothers under the age of 30 (Takahashi, 1998). In addition, two small-scale studies conducted in India have raised the possibility that the incidence of spina bifida occulta is abnormally high in fluorosis-prone regions (Gupta et al., 1994; Gupta et al., 1995; Gupta et al., 1994).

2.5.5 Renal Effects

The renal system is responsible for excreting most of the body’s excess fluoride and is exposed to higher concentrations of fluoride than are other organs (Whitford, 1996). This suggests that it might be at higher risk of fluoride toxicity than most soft tissues. However, at present there are only two published studies which suggest that the chronic ingestion of fluoride can have non-carcinogenic effects on the kidney, and both pertain to the incidence of kidney stones (Doull et al., 2006). Juuti and Heinonen (1980) found that residents living in high fluoride districts of Finland (i.e., where groundwater concentrations exceed 1.5 mg/L) experienced higher hospital admission rates for urolithiasis (kidney stones) than did residents living in other areas, although the rates differed only by 16 percent. A more convincing study by Singh et al. (2001) examined more than 18,700 people living in a region of India where fluoride concentrations in the drinking water ranged from 3.5 to 4.9 mg/L and found that patients with clear signs of skeletal fluorosis were 4.6 times more likely to develop kidney stones. However, because the subjects of this
study were probably at greater risk of kidney stone formation because of malnutrition, it is difficult to draw firm conclusions.

2.5.6 Neurological Effects

A number of studies conducted in China have suggested that dietary fluoride ingestion has an effect on the intelligence of children (e.g., Li et al. 1995; Zhao et al. 1996; Lu et al. 2000; Xiang et al. 2003; Wang et al., 2007; Xiang et al., 2003; Lu et al., 2000; Zhao et al., 1996; Li et al., 1995). Children in these studies who ingested high levels of fluoride (in each case, > 2 mg/L) scored more poorly on intelligence tests than did children who ingested lower levels of fluoride (in each case, < 1 mg/L). Working in India, Trivedi et al. (2007) found a statistically significant inverse relationship between the intelligence quotient (IQ) and urinary fluoride levels of school-aged children. The Indian researchers compared populations living in two different high-fluoride districts, where the average fluoride contents of drinking water were 5.6 mg/L and 2.0 mg/L, respectively. Based on these studies, it appears that the threshold fluoride level required for a neurotoxicity response is between 2 and 4 mg/L (Spittle et al., 1998). The reason for this response has not been identified, but Spittle (1994) described several types of biochemical changes that fluoride might cause in proteins and enzymatic systems which could interfere with normal brain function and cause impaired cognition and memory. A study by Calderon et al. (2000) suggests that fluoride could affect reaction times and visuospatial abilities, which would then be manifested as lower IQ scores in time-sensitive tests.

Several authors have reported an association between the use of fluorosilicates (i.e., Na₂SiF₆ and H₂SiF₆) to fluoridate community drinking water and elevated concentrations of lead (a known neurotoxicant) in the blood of children (e.g., Masters and Coplan 1999; Masters et al. 2000; Coplan et al., 2007; Masters et al., 2000; Masters and Coplan, 1999). This association has been attributed to both the effect that incompletely dissociated fluorosilicates in drinking water have on the cellular absorption of lead (Masters and Coplan 1999; Masters et al., 2000; Masters and Coplan, 1999) and to increased corrosion of lead-bearing plumbing by fluorosilicates (Coplan et al., 2007), especially in systems that use chloramines as a disinfectant (Maas et al., 2005a; Maas et al., 2007a; Maas et al., 2005b). However, Urbansky and Schock (2000) have questioned the scientific rigor of these studies and the validity of their conclusions. They argue that fluorosilicates are completely hydrolyzed before reaching the consumer’s tap and that there is no credible evidence that fluorideation has any measurable effect on the solubility, bioavailability, or bioaccumulation of lead. Macek et al. (2006) also examined blood lead concentrations in children who were exposed to different types of fluoridation additives. Their analysis did not support an association between blood lead concentrations and the use of fluorosilicates, but neither could they disprove this possibility, especially for children living in older homes with plumbing that contains lead.

2.5.7 Endocrine Effects

Studies of laboratory animals and human populations indicate that fluoride can affect normal endocrine function and response, but there is considerable ambiguity involved in interpreting the results of this research. Doull et al. (2006) summarized this body of research and concluded that the primary effects of fluoride exposure on the endocrine system are decreased thyroid function,
increased calcitonin activity, increased parathyroid activity, secondary hyperparathyroidism, and impaired glucose tolerance (Type II diabetes). However, these effects vary in degree and kind in different individuals, and many could be classified as subclinical, meaning that they are not considered adverse health effects.

Perhaps the best example of the complexity involved in understanding the effects of fluoride on the endocrine system is the association found by several researchers between endemic goiter and fluoride exposure in human populations (e.g., Steyn 1948, Day and Powell-Jackson 1972; Obel 1982; Desai et al. 1993; Jooste et al., 1999; Desai et al., 1993; Obel, 1982; Day and Powell-Jackson, 1972; Steyn, 1948). Although these spatial correlations are suggestive of a cause and effect relationship, the exact causal mechanism for fluoride’s effect on the thyroid has not been established (Doull et al., 2006). Thus, the prevalence of goiter in some epidemiological studies might not be directly caused by fluoride, but could be due to some other substance that either is associated with the fluoride (Day and Powell-Jackson, 1972) or that enhances the effect fluoride has on thyroid function (Steyn, 1948). Even if a specific role for fluoride in the onset of goiter could be defined, it is unlikely that a simple dose-response relationship would exist, because thyroid function is sensitive to a number of factors, including dietary deficiencies in iodine and selenium (see Larsen et al., 2002). This might explain why some studies have found no correlation between fluoride ingestion and goiter (e.g., Gedalia and Brand 1963; Leone et al., 1964; Teotia et al. 1978, Leone et al. 1964; Gedalia and Brand 1963).

2.5.8 Gastrointestinal Effects

A variety of gastrointestinal effects, including nausea, vomiting, diarrhea, and abdominal pain, have been reported in cases of acute fluoride toxicity (e.g., Gessner et al. 1994; Penman et al. 1997; Sidhu and Kimmer, 2002; Penman et al., 1997; Gessner et al., 1994). Animal studies reveal that fluoride can stimulate the secretion of stomach acid, reduce blood flow away from the stomach lining, and even cause the death of gastrointestinal tract epithelium cells (Doull et al., 2006). The level of chronic fluoride ingestion required to cause these types of responses in humans is not established, and it is likely that this threshold varies with other factors. For example, adverse gastrointestinal symptoms are common in areas of endemic fluorosis where nutrition is generally poor (e.g., Gupta et al. 1992; Susheela et al. 1993; Dasarathy et al., 1996; Susheela et al. 1993; Gupta et al. 1992); but similar levels of fluoride exposure in the U.S. and Britain do not necessarily produce the same response (e.g., Leone et al. 1955; Jenkins, 1991; Leone et al., 1955). Another important factor appears to be peak concentration rather than duration of exposure, because in clinical trials where fluoride is administered through tablets, the gastric side effects can be minimized by using slow-release fluorides and calcium supplements (Kleerekoper and Mendlovic, 1993; Das et al. 1994; Hagenauer et al., 2000; Das et al., 1994; Kleerekoper and Mendlovic, 1993). The weight of evidence suggests that if fluoride exposure is slight to moderate (e.g., drinking water concentrations less than 4 mg/L), less than one percent of the population will experience gastrointestinal symptoms, and these individuals are likely to have gastrointestinal hypersensitivities (Doull et al., 2006).

2.5.9 Carcinogenic Effects
Epidemiological studies designed to identify the carcinogenic potential of chronic fluoride exposure face a number of inherently difficult challenges. One of the biggest problems is that cancer diagnosis typically occurs years to perhaps decades after exposure to the causal factors, during which time individuals migrate both into and out of the study area. This often leads to an incorrect estimation of the study group’s exposure. Another difficulty is the large diversity of cancers and potential causal factors, which necessitates that each type of cancer be evaluated separately. Thus, it is not surprising that efforts to find a correlation between fluoridated water and overall cancer rates have not been fruitful (e.g., NRC 1993; McDonagh et al. 2000; Steiner 2002; Harrison 2005; Steiner 2002; McDonagh et al., 2000; NRC, 1993).

Because fluoride is deposited in the skeleton, the possibility that it might contribute to bone cancer has received considerable attention by researchers. Some laboratory studies of animals have shown evidence of increased osteosarcoma (bone cancer) and osteoma (noncancerous bone tumors), although there is uncertainty in the application of these findings to humans (Doull et al., 2006). Studies conducted of human populations have yielded mixed results, including those that suggest a positive association between fluoride ingestion and osteosarcoma (e.g., Hoover et al. 1991; Cohn 1992; Yang et al. 2000; Bassin, 2001; Takahashi et al. 2001; Yang et al. 2000; Cohn, 1992; Hoover et al., 1991), those that show no relationship (e.g., Hrudey 1990; Mahoney et al. 1991; Freni and Gaylor 1992; Grandjean et al. 1992; Moss et al. 1995; Gelberg et al. 1995; Freni and Gaylor, 1992; Grandjean et al., 1992; Mahoney et al., 1991; Hrudey, 1990), and even some that found negative correlations (e.g., McGuire et al. 1991; Gelberg et al., 1995; McGuire et al., 1991). Recent work suggests that certain subgroups (e.g., boys aged 6 to 8) might be more susceptible to the carcinogenic effects of fluoride than the overall population (Bassin et al., 2006), but more research is needed to confirm these conclusions (Douglass and Joshipura, 2006).

There is also a possibility that fluoride ingestion might increase kidney and bladder cancer rates based on the tendency for hydrogen fluoride, a caustic and potentially toxic substance, to form under the acid conditions found in urine. Strong evidence for this comes from studies conducted by Grandjean and Olsen (2004), Grandjean et al. (1990), Grandjean et al. (1992), and Grandjean and Olsen (2004), who examined the effects of chronic occupational exposure to fluoride dust by workers at a cryolite processing plant. They found that the inhalation of cryolite dust can result in skeletal fluorosis and is associated with higher rates of bladder cancer. However, because the cryolite workers were exposed to roughly the equivalent of ingesting water that contains 16 mg/L fluoride, it is not clear how these study results might apply to more typical fluoride exposures. Although there is some evidence of an association between fluoridated drinking water and the incidence of kidney and bladder cancer (e.g., Hoover et al. 1991; Yang et al. 2000; Takahashi et al., 2001; Yang et al., 2000; Hoover et al., 1991), more robust studies are needed to establish this link (Doull et al., 2006).

Several studies have found evidence for a relationship between fluoride exposure and specific cancers for which no biological causal mechanism is known. These include possible associations between fluoride in drinking water and the prevalence of uterine cancer (Grandjean et al. 1992; Yang et al., 2000; Tohyama, 1996) and colon cancer (Yang et al., 2000; Takahashi et al., 2001; Yang et al., 2000). The studies by Grandjean et al. (1990), Grandjean et al. (1992) and Grandjean and Olsen (2004)Grandjean and Olsen (2004), Grandjean et al. (1992), and Grandjean et al. (1990) cited previously found that cryolite workers also face an increased risk of lung cancer. Related
studies conducted in aluminum manufacturing plants, where cryolite is used as an electrolyte to facilitate aluminum oxide reduction, have found that workers exposed to both gaseous fluoride (HF) and fluoride dust in aluminum “potrooms” experience higher rates of chronic bronchitis, emphysema and asthma, although the underlying causal mechanism is not established (Soyseth et al. 1994; Romundstad et al. 2000; Shahtaheri et al. 2004; Romundstad et al., 2000; Soyseth et al., 1994).

2.6 Drinking Water Standards

Given the variety of fluoride sources (both natural and anthropogenic) and exposure pathways, it is very difficult to ensure that total fluoride intake will not exceed safe limits for every individual in a particular region. Instead, governmental health agencies have focused on the pathways that are easiest to quantify, one of which is drinking water. However, even in this, it is only public water supplies that are regulated, so many homeowners with private wells are unaware of how much fluoride they ingest from their drinking water.

Drinking water standards for fluoride should obviously reflect the results of studies undertaken to establish the links between fluoride and human health. But as the literature review presented in previous sections has shown, there is some uncertainty in the results of such studies and how they should be interpreted. Although nearly everyone involved in this research agrees that the chronic ingestion of high levels of fluoride (generally more than 2 mg/L) is detrimental to human health, there is considerable disagreement on the value of ingesting fluoride in lower doses. For example, proponents of fluoridation point to the documented benefits of fluoride in developing strong bones and teeth and assert that there is little evidence of important health problems caused by drinking water with less than 1 mg/L fluoride (Yiming et al., 2001). Others are skeptical of studies that show beneficial effects (e.g., Marshall 1990; Hamilton 1992; Burgstahler, 2004; Hamilton, 1992; Marshall, 1990) and argue that the risks to fluoride ingestion outweigh whatever advantages might exist (Diesendorf et al. 1997; Limebeck, 2000; Diesendorf et al., 1992). Despite the continuing debate, most environmental health scientists believe that fluoride is both beneficial and potentially detrimental to human health. Table 2 summarizes the health effects typically associated with long-term ingestion of fluoride-bearing waters as described by Dissanayake (1991).

Table 2: Effects of Fluoride Ingestion on Human Health

<table>
<thead>
<tr>
<th>Fluoride Concentrations</th>
<th>Effect on Human Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5 mg/L</td>
<td>Conducive to dental caries</td>
</tr>
<tr>
<td>0.5 - 1.5 mg/L</td>
<td>Promotes development of strong bones and teeth</td>
</tr>
<tr>
<td>1.5 - 4.0 mg/L</td>
<td>Promotes dental fluorosis in children</td>
</tr>
<tr>
<td>&gt; 4.0 mg/L</td>
<td>Promotes dental and skeletal fluorosis</td>
</tr>
<tr>
<td>&gt; 10 mg/L</td>
<td>Crippling skeletal fluorosis, possibly cancer</td>
</tr>
</tbody>
</table>

It is evident that the establishment of appropriate drinking water standards for fluoride (i.e., maximum allowable concentrations) is dependent upon many factors, including climate, diet, and
characteristics of the target population (and even within a given region, different subsets of the population may respond differently to the same dose). Because fluoride intake includes food sources and the volumes of water ingested vary, it is difficult to establish ubiquitous standards for drinking water.

The U.S. Environmental Protection Agency (EPA) has set 4 mg/L as the maximum contaminant level (MCL) for fluoride in drinking water and 2 mg/L as the secondary maximum contaminant level (SMCL). The MCL, which is enforceable, is intended to prevent acute and chronic illness, although some studies have suggested that concentrations up to 10 mg/L have no harmful effects. The SMCL is not enforceable but indicates the level at which long-term ingestion could cause dental fluorosis. The World Health Organization (WHO) recommends that drinking water have less than 1.5 mg/L fluoride, a more appropriate standard in countries where people drink more water than the average U.S. citizen (WHO guidelines are based on an adult water consumption of 2 liters per day, assuming that food provides 0.2 to 0.5 mg of fluoride per day). However, some researchers have argued for even more stringent standards for countries with hot, dry climates (e.g., Brouwer et al., 1988) or where the fluoride content of food is higher than assumed by WHO (e.g., Apambire et al., 1997). India and China, each of which is known for its naturally high fluoride districts, have 1 mg/L as their national standard.

3. Fluoride in the Natural Environment

3.1 Atmospheric Sources

The natural sources of fluorine in precipitation include marine aerosols, volcanic gas emissions, and air-borne soil dust (Angelis and Legrand 1994; Saether et al. 1995; Tavener and Clark, 2006; Saether et al., 1995; Angelis and Legrand, 1994). Efforts to measure fluoride concentrations in pristine rainfall have been hampered by the nearly ubiquitous presence of anthropogenic fluoride, but several studies have found that values are typically less than 0.08 mg/L unless the precipitation is directly affected by volcanic emissions (Barnard and Nordstrom 1982; Neal 1989; Saether and Andreassen 1989; Cook et al. 1991; Edmunds and Smedley 2005; Tavener and Clark, 2006; Edmunds and Smedley, 2005; Cook et al., 1991; Neal, 1989; Saether and Andreassen, 1989; Barnard and Nordstrom, 1982). Even during volcanic eruptions, the resulting plume of HF gas is quickly depleted from the troposphere through both dry and wet deposition, having only localized and transient effects on atmospheric chemistry (Angelis and Legrand 1994; Rubin et al., 1994; Aiuppa et al., 2006; Sawyer and Oppenheimer, 2006; Angelis and Legrand, 1994; Rubin et al. 1994). Consequently, natural inputs of fluoride into the environment from the atmosphere have not been directly linked to human health problems in the scientific literature. However, there have been cases of acute and chronic fluorosis occurring in animals that grazed on pastures covered by ash and other particulates from recent volcanic eruptions (Cronin et al., 2003; Sawyer and Oppenheimer, 2006; Cronin et al., 2003) or by dust derived from phosphate rocks (Cronin et al., 2000).

The primary anthropogenic sources of fluorine are industrial aerosols, which include emissions from brickworks, aluminum smelters, iron and steel production, fossil fuel burning, ceramic industries and phosphate fertilizers plants (Fuge and Andrews 1988; Cronin et al., 2000; Feng et
These pollution sources release fluoride to the environment in both gaseous (e.g., HF, SiF₄, F₂, and H₂SiF₄) and particulate forms (e.g., CaF₂, NaF, and Na₃SiF₆). Atmospheric chlorofluorocarbons also contribute fluoride to rainwater, but the concentrations (< 0.001 mg/L) are insignificant when compared to natural background levels (Sidebottom and Franklin, 1996). Rainfall contaminated by industrial emissions can contain fluoride concentrations that are an order of magnitude greater than background levels, even exceeding 1 mg/L (Neal 1989; Saether and Andreassen 1989; Feng et al. 2003; Walna et al., 2007; Feng et al., 2003; Neal, 1989; Saether and Andreassen, 1989), and these concentrations can persist up to 2 km from the source (Mirlean and Roisenberg, 2007). In one notable case, the atmospheric fluoride pollution from brickworks in the UK was apparently responsible for fluorosis in nearby farm animals (Fuge and Andrews, 1988). There have also been studies that showed elevated fluoride levels in the bones and antlers of deer living in industrialized regions of continental Europe (e.g., Machoy et al., 1991; Kierdorf and Kierdorf, 2000; Machoy et al., 1994). Therefore, although governmental regulatory agencies (such as the U.S. EPA) maintain that current air quality emission standards are protective of human health, environmental advocacy groups argue that people living near an industrial source of fluoride emissions face significant health risks (Griffith, 1992).

3.2 Mineral Sources

With an average concentration of 625 mg/kg, fluoride is one of the more abundant trace elements in the Earth’s crust (Edmunds and Smedley, 2005; Tavener and Clark, 2006; Edmunds and Smedley, 2008); however, its occurrence varies greatly from one rock type to another. Fluoride contents typically range from 100 mg/kg in ultramafic rocks and some limestones to 1,000 mg/kg in alkaline igneous rocks and 1,300 mg/kg in marine shales (Hem 1985; Faure 1991; IGRAC, 2003; Faure, 1991; Hem, 1985), although values as high as 2,000 mg/kg have been measured in volcanic rocks produced at a subduction zone boundary (Anazawa, 2006). The reasons for differential partitioning within the Earth’s crust are important to an understanding of how fluoride occurs in the environment.

The most common fluoride-bearing minerals in the natural environment are fluorite (CaF₂), fluorapatite (Ca₅(PO₄)₃F), micas and amphiboles (where F substitutes for OH within the mineral structures), cryolite (Na₃AlF₆), villiaumite (NaF), topaz (Al₆(SiO₄)F₂), and certain clays (Hem 1985; Apambire et al. 1997; Cronin et al. 2000; Rao 2003; Saxena and Ahmed 2003; Edmunds and Smedley 2005; Chae et al., 2007; Edmunds and Smedley, 2005; Rao, 2003; Saxena and Ahmed, 2003; Cronin et al., 2000; Apambire et al., 1997; Hem, 1985). These minerals are found primarily in certain igneous and metamorphic rocks and, to a lesser extent, the sedimentary deposits derived from such rocks. However, sedimentary formations may also contain fluorine-enriched clays and fluorapatite that precipitated from phosphate-rich waters (Edmunds and Walton 1983; Edmunds and Smedley, 2005; Edmunds and Walton, 1983).

Many of the world’s high-fluoride districts are underlain by crystalline igneous and metamorphic rocks (e.g., parts of India, Sri Lanka, Senegal, Ghana, South Africa, and Scandinavia) or occur in areas of volcanic and associated hydrothermal activity. The explanation for this pertains to the geochemical behavior of fluorine in magma. Because fluorine has a higher affinity for silicate
melts than solid phases (Anazawa, 2006; Sawyer and Oppenheimer, 2006), it is progressively enriched in magmas and hydrothermal solutions through time as magmatic differentiation takes place (Fuge 1977; Hyndman 1985; Taylor and Fallick 1997; Li et al., 2003; Dolejs and Baker, 2004; Scalliet and Macdonald, 2004; Li et al., 2003; Taylor and Fallick, 1997; Hyndman, 1985; Fuge, 1977). As a result, hydrothermal vein deposits and rocks that crystallize from highly evolved magmas often contain fluorite, fluorapatite, and fluoride-enriched micas and/or amphiboles. Cryolite, villiaumite, and/or topaz can also occur depending on the percentages of silica and calcium present in the magma (Stormer and Carmichael 1970; Hyndman 1985; Taylor and Fallick 1997; Dolejs and Baker, 2004; Taylor and Fallick, 1997; Hyndman, 1985; Stormer and Carmichael, 1970).—Studies conducted in regions underlain by crystalline igneous and metamorphic rocks have found that the highest fluoride levels are associated with syenites, granites, quartz monzonites, granodiorites, felsic and biotite gneisses, and alkaline volcanics (e.g., Stormer and Carmichael 1970; Handa 1975; Jones et al., 1977; Nanyaro et al., 1984; Hyndman 1985; Dissanayake 1991; Taylor and Fallick 1997; Apambire et al., 1997; Rosi et al., 2003; Robinson and Kapo 2003; Moore 2004; Chae et al. 2006a; Ozsvath 2006; Chae et al., 2007; Chae et al., 2006a; Ozsvath, 2006; Moore, 2004; Rosi et al., 2003; Robinson and Kapo, 2003; Apambire et al., 1997; Taylor and Fallick, 1997; Dissanayake, 1991; Hyndman, 1985; Nanyaro et al., 1984; Jones et al., 1977; Handa, 1975; Stormer and Carmichael, 1970).—Although these rock types can contain a variety of fluoride-rich accessory minerals, laboratory experiments and field studies have shown that the presence of biotite alone is sufficient to produce dissolved fluoride concentrations above 4 mg/L (Chae et al., 2006a; Chae et al., 2006b; Chae et al., 2007; Chae et al., 2006a; Chae et al., 2006b).

Most of the world’s other high-fluoride districts occur over sedimentary aquifers, especially in arid and semi-arid environments. —Some notable examples include the La Pampa Province of central Argentina (Smedley et al., 2002), the Sahara region of northern Africa (Edmunds 1994), and parts of northern China (Fuhong and Shuquin 1988; Woo et al., 2000; Fuhong and Shuquin, 1988).—The sources of fluorine in sediments and sedimentary rocks include fluoride-bearing minerals derived from the parent rock, volcanic ash, fluoride-rich clays (mostly in marine sediments and shales), and fluorapatite (in some carbonate rocks, phosphate beds, and argillaceous deposits).—Often the occurrences of high dissolved fluoride are associated with high pH in sodium-bicarbonate waters (Chae et al., 2007).

Sometimes even low-fluoride rocks can be a cause of fluoride-related health problems. —In a case that illustrates the importance of both culture and exposure pathways other than drinking water, Li et al. (2007) describe how the indoor burning of coal has led to high rates of fluorosis in parts of southwest China (see also Ando et al., 1998).—Inhabitants of this region have long practiced a method of cooking that involves drying food over coal-fired stoves with no chimneys. Although the coal contains less than 300 mg/kg fluoride, indoor combustion in rooms without chimneys contaminates the air and food with sufficient fluoride to create health problems from chronic exposure.

3.3 Geothermal Sources

Some of the highest dissolved fluoride concentrations measured near the earth’s surface occur in areas affected by geothermal activity, such as the East African Rift Valley, New Zealand, France,
Iceland, China, and parts of the western U.S. - For reasons described above (Section 3.2), highly evolved magmas and their associated hydrothermal solutions are typically enriched in fluorine. As meteoric waters come in contact with these types of magma bodies or solutions, they can acquire fluoride up to the limit imposed by fluorite solubility (Mahon 1964; Nordstrom and Jenne 1977; Ashley and Burley 1994; Ayenew, 2007; Lottermoser and Cleverley, 2007; Ashley and Burley, 1994; Nordstrom and Jenne, 1977; Mahon, 1964). - Thus, geothermal hot springs, long purported to have medicinal value, often contain fluoride concentrations above 1 mg/L (Ellis and Mahon, 1977).

In the East African Rift Valley, where the incidence of dental and skeletal fluorosis is very high (Nanyaro et al. 1984; Gaciri and Davies 1993; Ayenew, 2007; Gaciri and Davies, 1993; Nanyaro et al., 1984), the occurrence of hyperalkaline volcanic rocks and geothermal activity combine to produce fluoride concentrations that can sometimes exceed 1,000 mg/L in closed-basin alkaline lakes (Jones et al., 1977). - Weathering of the bedrock and the inflow of geothermal waters produce lakes that are characterized by high sodium and bicarbonate concentrations, near-neutral to alkaline pH values, and undersaturation with respect to fluorite (Gizaw, 1996). - These conditions are conducive to high fluoride concentrations, which are further increased through evaporation.

Acidic geothermal waters can also contain high fluoride concentrations (Ellis and Mahon 1977; Nordstrom et al., 2005; Ellis and Mahon, 1977) but for a different reason. - Under low pH conditions, fluoride solubility is enhanced by the formation of complexes with hydrogen (HF° and HF₂⁻), silicon (SiF₆²⁻), and aluminum (AlF₆³⁻), which prevent fluorite from forming. - Low pH values (especially less than 4) also inhibit the precipitation of silicate sinter when geothermal waters reach the earth’s surface (Nordstrom et al., 2005). - This increases the likelihood that fluoride will remain in the dissolved phase as it is released to the surface environment. - Although human health is not often affected by these types of waters, Heikens et al. (2005) document a case of endemic dental fluorosis in Indonesia that has resulted from the ingestion of fluoride derived from a hyperacid volcanic lake.

3.4 Mobility in Soils

Whereas the fluorine content of most rocks ranges from 100 to 1,300 mg/kg (Faure, 1991), soil concentrations typically vary between 20 and 500 mg/kg (Edmunds and Smedley, 2005). However, much higher concentrations (> 1,000 mg/kg) can occur in soils that are derived from rocks with high fluorine contents (Cronin et al., 2000) or in soils affected by anthropogenic inputs, such as phosphate fertilizers (Kabata-Pendias and Pendias, 2001), sewage sludge (Rea, 1979) and industrial pollution (Cronin et al., 2000). - Most of the fluorine found in soils occurs within minerals or is adsorbed to clays and oxyhydroxides, with only a few percent or less dissolved in the soil solution (Pickering, 1985; Cronin et al., 2000; Pickering, 1985).

Fluoride mobility in soil is highly dependent on the soil’s sorption capacity, which varies with pH, the types of sorbents present, and soil salinity (Pickering 1985; Fuhong and Shuquin 1988; Cronin et al., 2000; Fuhong and Shuquin, 1988; Pickering, 1985). - In general, fine-grained soils have higher clay and oxyhydroxide contents than do sandy soils and therefore retain more fluoride. - One study showed that up to half of the dissolved fluoride may pass through a coarse-
grained soil that contains little clay, iron, or aluminum (Pickering, 1985). The minimum fluoride mobility occurs in fine-grained soils at a pH of 6.0 to 6.5 (Larsen and Widdowson 1971; Gilpin and Johnson 1980; Wenzel and Blum, 1992; Gilpin and Johnson, 1980; Larsen and Widdowson, 1971). As pH rises above that range, colloid surfaces release adsorbed F⁻ as it is displaced by increasing OH⁻ concentrations (Larsen and Widdowson, 1971). At pH values less than 6, the formation of cationic AlF³⁺ and AlF₂⁻ complexes inhibit adsorption (Barrow and Ellis 1986: Anderson et al., 1991; Wenzel and Blum, 1992; Anderson et al., 1991; Barrow and Ellis, 1986). High salinity (ion strength) affects fluoride mobility by enhancing the potential for fluoride complexes to form and by increasing the number of ions that compete for soil sorption sites. Edmunds and Smedley (2005) suggest that the effect of evapotranspiration, which raises the salinity of soil solutions, can increase the concentrations of fluoride reaching groundwater.

3.5 Mobility in Groundwater

Fluoride occurs in almost all groundwater, but the concentration found in most potable waters is less than 1 mg/L (Hemm, 1985). The primary controls on dissolved fluoride concentrations include the types of source minerals, residence time, and climate. However, the overall water quality (e.g., pH, hardness and ionic strength) also has an important role through its influence on mineral solubility, complexation, and sorption/exchange reactions (Apambire et al., 1997).

With the exception of villiaumite, the common fluoride-bearing minerals are only sparingly soluble and release fluoride to water slowly (Nordstrom and Jenne 1977; Cronin et al., 2000; Gaus et al., 2002; Saxena and Ahmed, 2003; Gaus et al., 2002; Cronin et al., 2000; Nordstrom and Jenne, 1977). Therefore, in the absence of villiaumite, it might be expected that fluoride concentrations in groundwater will be relatively low unless the percentage of fluoride-bearing minerals is high, but there are many exceptions to this rule. For example, despite the slow rates of mica and amphibole weathering, there is evidence that fluoride is preferentially released from its hydroxyl position in these minerals, which effectively increases their influence on dissolved fluoride levels (Li et al., 2003; Edmunds and Smedley 2005; Chae et al., 2006b; Chae et al., 2007; Chae et al., 2006a; Edmunds and Smedley, 2005; Li et al., 2003). Environmental conditions may also play a role, as illustrated by the fact that fluorapatite dissolution can be enhanced in the presence of microbes seeking to separate phosphorus from the solid phase (Allen-Long, 2001). Similarly, the rate of fluoride dissolution may be faster in sodium-bicarbonate waters, and the release of fluoride from clay minerals depends strongly on pH (Apambire et al., 1997; Saxena and Ahmed, 2003; Apambire et al., 1997). Even when environmental conditions are held constant in laboratory experiments, the percentage of total fluoride that is leachable varies widely from one rock type to another (Lirong et al., 2006). Consequently, the concentration of fluoride in groundwater is not correlated to the percentage of fluoride-bearing minerals in the geologic substrate in a simple, linear fashion.

The maximum concentration of fluoride in groundwater is usually controlled by the solubility of fluorite (Handa 1975; Nordstrom and Jenne 1977; Pekdeger et al., 1992; Apambire et al., 1997; Reardon and Wang 2000; Cronin et al., 2000; Saxena and Ahmed 2003; Edmunds and Smedley 2005; Chae et al., 2007; Edmunds and Smedley, 2005; Saxena and Ahmed, 2003; Reardon and Wang, 2000; Cronin et al., 2000; Apambire et al., 1997; Pekdeger et al., 1992; Nordstrom and Jenne, 1977; Handa, 1975), although in the presence of dissolved phosphate it is possible for
fluorapatite to precipitate instead of fluorite (Elihu Stauffer 1982; Somasundaran et al. 1985; Pekdeger et al. 1992; Cronin et al. 2000; Pekdeger et al., 1992; Somasundaran et al., 1985; Elihu Stauffer, 1982). Once the solubility limit for fluorite (CaF$_2$) is reached, an inverse relationship will exist between fluoride and calcium concentrations (see Figure 1), and many studies have found a strong association between high fluoride and soft, alkaline (i.e., sodium-bicarbonate) groundwater that is depleted in calcium (e.g., Handa 1975; Robertson 1986; Pekdeger et al., 1992; Whittemore et al. 1993; Bardsen et al., 1995; Conrad et al. 1999; Gupta et al. 1999; Kohut et al., 2001; IGRAC 2003; Earle and Krogh 2004; Chae et al., 2007; Chae et al., 2006a; Dhiman and Keshari 2006; Chae et al., 2007). As a result, the groundwater in contact with these rocks is often soft and calcium-deficient, which allows for higher fluoride concentrations when equilibrium with fluorite is attained (Ozsvath, 2006).

Figure 1: Fluorite (CaF$_2$) solubility curve in water at 10°C, ignoring the effects of ionic strength and complexes on mineral solubility.

High fluoride concentrations (up to 30 mg/L) can also result from anion exchange (OH$^-$ for F$^-$) on certain clay minerals, weathered micas, and oxyhydroxides that are typically found in residual soils and sedimentary deposits (Whittemore et al. 1993; Apambire et al. 1997; Kohut et al. 2001; Smedley et al. 2002; Earle and Krogh 2004; Warren et al. 2005; Earle and Krogh 2004).
Smedley et al., 2002; Kohut et al., 2001; Apambire et al., 1997; Whitemore et al., 1993). Laboratory studies have shown that aluminum-hydroxides have an especially high fluoride exchange capacity (Cronin et al., 2000). This mechanism is favored by and/or produces high pH values (usually above 8.0) under conditions that can lead to the base-exchange softening of groundwater (Ca\(^{2+}\) and Mg\(^{2+}\) for Na\(^{+}\)) and low calcium concentrations. Thus, the release of fluoride through anion exchange often occurs in an environment that is conducive to high fluoride concentrations. The effectiveness of this process is illustrated in a study conducted by Earle and Krogh (2004). These authors found a direct relationship between pH and fluoride concentrations within their study area as a result of base-exchange softening. Groundwater pH values were measured as high as 9.3, and fluoride concentrations reached 9.5 mg/L, even though the source formation (sandstone) has relatively low fluoride content (350 mg/kg).

The degree of water-mineral interaction as measured by groundwater residence time is often positively correlated to dissolved ion concentrations until the limit imposed by mineral solubility is reached. This is an especially important control on fluoride concentrations because the dissolution rates of most fluoride-bearing minerals are slow (Nordstrom and Jenne, 1977; Gaus et al., 2002; Nordstrom and Jenne, 1977) and the maximum concentrations allowed by fluoride solubility are not always attained in groundwater (Robertson, 1986). A number of field studies have demonstrated the influence that residence time can have on dissolved fluoride levels, especially in crystalline rocks where groundwater moves primarily through fractures (e.g., Bardsen et al., 1996; Conrad et al., 1999; Goodwin et al., 1999; Frengstad et al., 2001; Saxena and Ahmed, 2003; Kim and Jeong, 2005; Chae et al., 2006a; Chae et al., 2007; Chae et al., 2006a; Kim and Jeong, 2005; Frengstad et al., 2001; Saxena and Ahmed, 2003; Conrad et al., 1999; Goodwin et al., 1999; Bardsen et al., 1996). In some cases the influence of residence time produces a direct relationship between fluoride concentrations and the depth at which a water sample was collected (Chae et al., 2007; Hudak and Sanmanee, 2003; Edmunds and Smedley, 2005; Kim and Jeong, 2005; Hudak and Sanmanee, 2003; Chae et al., 2007).

The influence of climate on fluoride concentrations in groundwater is largely attributed to the effect that rainfall has on recharge rates and groundwater flow (IGRAC, 2003; Edmunds and Smedley, 2005; IGRAC, 2003). Areas of high rainfall, such as humid tropical regions, are less likely to have high fluoride concentrations in groundwater because soluble ions such as fluoride are leached out and diluted. Conversely, some arid environments are noted for high fluoride because the low rates of groundwater recharge lead to prolonged water-mineral interaction and higher salinities, which enhance mineral dissolution (Handa, 1975; Fuhong and Shuquin, 1988; Smedley et al., 2002; Fuhong and Shuquin, 1988; Handa, 1975). Climate can also influence dissolved fluoride levels through the effect that temperature has on the solubility of fluorine-bearing minerals. For example, the equilibrium constant for fluoride increases from 10\(^{-10.80}\) at 10° C to 10\(^{-10.57}\) at 25° C (Edmunds and Smedley, 2005), which allows for roughly 30 percent more fluoride to dissolve in dilute solutions (see Table 3).

<table>
<thead>
<tr>
<th>Calcium Concentration</th>
<th>Fluoride Concentration at Equilibrium with Fluorite</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 mg/L (0.0001 moles/L)</td>
<td></td>
</tr>
<tr>
<td>Temperature = 10° C</td>
<td>7.56 mg/L</td>
</tr>
<tr>
<td>Temperature = 25° C</td>
<td>9.86 mg/L</td>
</tr>
</tbody>
</table>

Table 3: Effect of Temperature on Fluorite Solubility

1 Formatted: Justified
<table>
<thead>
<tr>
<th>[8 mg/L (0.0002 moles/L)]</th>
<th>5.35 mg/L</th>
<th>6.97 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>[16 mg/L (0.0004 moles/L)]</td>
<td>3.78 mg/L</td>
<td>4.93 mg/L</td>
</tr>
<tr>
<td>[32 mg/L (0.0008 moles/L)]</td>
<td>2.67 mg/L</td>
<td>3.49 mg/L</td>
</tr>
<tr>
<td>[64 mg/L (0.0016 moles/L)]</td>
<td>1.89 mg/L</td>
<td>2.46 mg/L</td>
</tr>
<tr>
<td>[128 mg/L (0.0032 moles/L)]</td>
<td>1.34 mg/L</td>
<td>1.74 mg/L</td>
</tr>
<tr>
<td>[256 mg/L (0.0128 moles/L)]</td>
<td>0.95 mg/L</td>
<td>1.23 mg/L</td>
</tr>
</tbody>
</table>

Calculations are based on a Ksp of $10^{-10.57}$ at 25°C and $10^{-10.80}$ at 10°C, ignoring the effects of ionic strength and complexes on mineral solubility.

4. Summary

The influence of fluoride on human health is well-studied, but the conclusions drawn from this body of research remain controversial. Although the presence of trace levels of fluoride in the diet is clearly associated with fewer dental caries and the formation of stronger bones, there are also a number of acute and chronic health problems associated with the intake of fluoride in high doses. The controversy centers on quantifying a threshold that separates safe from unsafe doses and whether the benefits of fluoride ingestion outweigh the potential adverse health effects. An important variable in any attempt to set threshold levels (e.g., drinking water standards) is the target population. Individuals who enjoy a variety of beverage and food choices or who move frequently have very different risks from those who live their entire lives in one place, depending on local sources of food and water.

Although anthropogenic sources of fluorine in the environment have occasionally been the cause of human health problems, the vast majority of fluoride-related health problems occur as a result of ingesting fluoride from natural sources. The fluoride content of rainfall is typically less than 0.2 mg/L, and surface waters are also rarely a source of excessive fluoride, except where affected by high evaporation or geothermal activity. Groundwater is more susceptible to fluoride accumulation through its contact with the geologic substrate. High-fluoride districts occur in areas underlain by crystalline basement rocks (especially felsic intrusive rocks and their metamorphic equivalents), alkaline volcanic rocks with associated geothermal activity, and sedimentary formations that contain fluorapatite or fluoride-enriched clay minerals. Maximum dissolved fluoride levels are usually controlled by the solubility of fluorite (CaF$_2$); thus, high concentrations are often associated with soft, alkaline, and calcium-deficient waters.

Despite the wealth of information about fluoride occurrence and its potential health effects, problems persist in Third World countries, where populations have little choice in the source of their drinking water and food. Even in developed nations, where governmental health agencies regulate the fluoride content of public drinking water, private water supplies, dietary choices, dental products, industrial emissions, and/or occupational exposure can cause an individual’s total fluoride intake to exceed safe doses. However, as epidemiological studies continue to refine our understanding of the dose-response relationship and field studies better delineate the areas of potentially high fluoride, efforts to reduce fluoride-related health problems should become more effective.

5. References


