

A Comprehensive Review of the Complex Causes of Fluorosis

Abeer K. Shams^{1*}, Khalid Zainulabdeen¹, Ali E. Kareem², Heba N. Mahgoob³

¹ Department of Chemistry, College of Science, Al-Nahrain University, Jadriya, Baghdad, Iraq

² Department of Prosthodontics, College of Dentistry, Mustansiriyah University, Baghdad, Iraq.

³ Al Amriya Specialized Dental Center, Al Karkh Health Department, Baghdad, Iraq

Article's Information

Received: 07.12.2024
Accepted: 24.05.2025
Published online 01.06.2025
Published : 01.07.2025

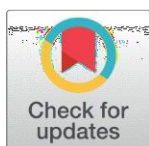
Keywords: Fluorosis, Fluorine Effect, Dental, Skeletal, Risks

Abstract

Numerous reviews and studies have shed light on the diverse causes of fluorosis, underscoring the need for comprehensive investigations to inform effective prevention and management strategies. Overconsumption of fluoride over an extended period, especially during the growth of teeth or bones, leads to fluorosis, which affects these structures. The amount, timing, and duration of fluoride exposure all influence the severity of the condition. Dental fluorosis rarely presents in more severe forms; most cases are mild to moderate. Research has also explored the effects of fluoride on the immune system, the intestinal mechanical barrier, and innate immunity. Additionally, current studies have focused on the global impacts of skeletal fluorosis and the role of oxidative stress in its progression. This review synthesizes Emerging evidence on fluoride's dual role in health, contrasting its dental benefits with risks of skeletal fluorosis and prenatal neurotoxicity. We provide novel insights into the ecological consequences of industrial fluoride pollution, supported by case studies from endemic regions, and propose evidence-based strategies for balancing public health benefits with environmental sustainability.

*Corresponding author:

E-mail: abeerkhsh@gmail.com



Pages: 117-126

DOI [https://doi.org/10.47419/](https://doi.org/10.47419/bjbabs.v6i03.350)

[bjbabs.v6i03.350](https://doi.org/10.47419/bjbabs.v6i03.350)

Distributed under the terms of
The Creative Commons
Attribution 4.0 International
License (CC BY 4.0), which
Permits unrestricted use,
distribution, and reproduction
In any medium, provided the
original author and source are
properly cited.

Copyright: © 2025 the Authors

OPEN ACCESS

1. Introduction

Fluorosis is a medical condition that results in changes in the appearance of tooth enamel due to an excessive intake of fluoride¹. Factors contributing to the development of fluorosis include age, climate, altitude, socioeconomic status, and the amount of fluoride in drinking water². Effective prevention and intervention depend on an understanding of these causal factors. For instance, it can aid in identifying populations most at risk, developing reasonable exposure limits, and implementing focused public health initiatives to decrease fluoride consumption and the likelihood of fluorosis. Developing comprehensive strategies for preventing and managing fluorosis is made possible by considering various factors that safeguard the dental health of populations³. When scientists discovered that excessive fluoride was responsible for dental and skeletal fluorosis in the 20th century, they began to investigate the development of fluorosis. Dental fluorosis is characterized by brown-stained tooth enamel, which was discovered due to past practices, such as high fluoride levels in the water supplies of some areas. Dr. Frederick McKay, a dentist, made this discovery, which eventually improved our understanding of the causes of fluorosis. In addition, in fluorosis-endemic regions like India, it has been found that drinking water containing fluoride for an extended period, beyond the daily requirement, is a significant cause of the disease^{4,5}. Insights gained from past observations regarding the causes of fluorosis have significantly contributed to our current understanding of the condition. They contributed to the discovery that skeletal and dental fluorosis can develop from prolonged exposure to fluoride. This understanding has influenced the development of safe limits for fluoride in drinking water and dental products, as well as other practices and regulations related to fluoride exposure. Additionally, historical experiences have underscored the importance of monitoring and regulating fluoride levels in water supplies to prevent fluorosis in the present day^{6,7}.

1. Fluoride

As an inorganic, monatomic fluoride anion with the chemical formula F^- , fluoride is one of its characteristics⁸. Known as a trace element, it is the most basic form of the fluorine anion. Water only contains trace levels of fluoride ions found in various minerals. Fluoride salts, which have distinctly bitter and sour tastes, include them. They are very reactive. Hydrogen fluoride is produced from fluoride, another use for fluoride, and is classified as a weak base⁹. Its smaller radius/charge ratio allows fluoride to dissolve more easily in protic solvents, setting it apart from other halides, such as chloride, in terms of reactivity. As fluoride is the

smallest single anion with the highest negative charge in polar protic solvents, it is not a nucleophilic species¹⁰.

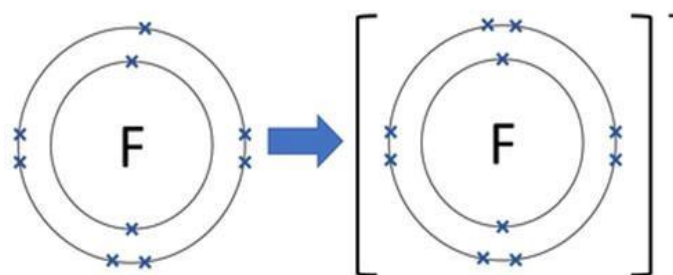


Figure (1): A diagram showing the formation of a Fluoride ion¹¹

Fluoride (F^-) is a monatomic anion derived from fluorine, the most electronegative element. Its small ionic radius (1.33 Å) and high charge density enable strong interactions with calcium and phosphate ions in biological systems, forming stable compounds like fluorapatite in tooth enamel and bone hydroxyapatite¹². This reactivity underpins its dual role in health:

Benefits:

Enamel Protection: Fluoride integrates into tooth enamel during remineralization, forming acid-resistant fluorapatite. This process reduces cavity risk by 20–40% and is the basis for water fluoridation programs¹¹.

Cost-Effectiveness: Community water fluoridation (0.7 mg/L) saves 38 dental costs per 38 dental costs per 1 invested, benefiting underserved populations disproportionately¹⁰.

Risks:

Dental Fluorosis: Excess fluoride during tooth development (ages 0–7) disrupts enamel formation, causing white streaks or brown mottling. Severe cases are rare at recommended levels but prevalent in regions with natural fluoride >1.5 mg/L¹¹.

Skeletal Fluorosis: Chronic exposure (>4 mg/L) leads to bone hardening, joint stiffness, and fracture risk. Endemic in parts of India, China, and Africa due to groundwater contamination with fluoride¹².

Neurocognitive Concerns: The National Toxicology Program (NTP) associates prolonged exposure >1.5 mg/L with lower IQ in children, though evidence at U.S. fluoridation levels (0.7 mg/L) remains inconclusive^{13,14}.

Table (1): presents the concentrations of fluoride in drinking water sourced from endemic regions.

Region	Country	Fluoride Concentration (mg/L)	Health Impact	Source
Rift Valley	Ethiopia	1.5 – 8.7	Dental fluorosis in 58% of children	[15]
Rajasthan (Groundwater)	India	1.8 – 10.0	Skeletal fluorosis in 34% of adults	[16]
Guizhou Province	China	2.4 – 8.7	Severe dental/skeletal fluorosis clusters	[17]
Nakuru County	Kenya	3.2 – 12.0	72% prevalence of dental fluorosis	[18]
Punjab (Groundwater)	Pakistan	0.7 – 24.0	65% of villages exceed WHO limits	[19]
São Francisco Basin	Brazil	0.5 – 6.8	Endemic dental fluorosis in rural communities	[20]
Volcanic Regions	Tanzania	2.0 – 15.0	High rates of skeletal fluorosis	[21]

This table synthesizes data from peer-reviewed studies to illustrate the geographic variability of fluoride concentrations in drinking water and their associated health impacts in regions where fluorosis is endemic¹⁵⁻²¹. Fluorosis, resulting from high fluoride consumption, appears as dental or skeletal abnormalities and presents a significant public health issue in regions where groundwater naturally contains elevated fluoride levels²².

Additionally, fluoride has been proposed as a treatment for osteoporosis due to its ability to enhance bone density and stimulate osteoblast activity, as well as its positive effects on dental health²³. However, the decrease in fracture risk is not well established, even though it produces denser bone. Although fluoride has many positive effects on dental health, it can be toxic if consumed in large quantities. Consequently, fluoride must be used

correctly and under adult supervision, particularly around children²⁴. A safe and effective method of preventing tooth decay, fluoridating water can cut tooth decay by 25%, according to the American Dental Association (ADA), the American Academy of Pediatrics (AAP), and the Centers for Disease Control and Prevention²⁵. Children should use fluoride toothpaste and drink fluoride-treated water. Dental or other healthcare professionals may recommend fluoride supplements if the tap water isn't fluoridated. According to the study, dental fluorosis and caries have been significantly reduced in Swiss schoolchildren, thanks to salt fluoridation schemes and low-fluoride toothpastes²⁶. Furthermore, there is some evidence that fluoride intake during pregnancy may have both positive and negative effects on maternal and fetal health. Fluoride is essential for maintaining oral health, which is linked to the health of newborn babies, so pregnant women should not decrease their fluoride intake. However, excessive fluoride intake during early pregnancy may lead to increased prevalence and severity of maternal anaemia as well as adverse fetal outcomes, as shown in Figure 2^{27,28}.

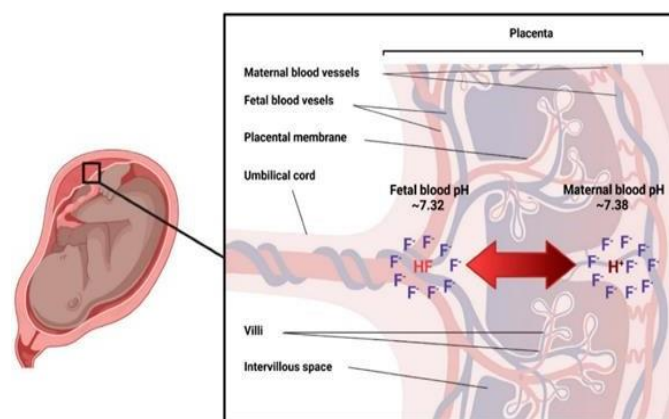


Figure (2): Fluoride, an uncharged molecule, is thought to move through lipid bilayers during pregnancy, eventually reaching the alkaline compartment. Changes in pH cause potential changes²⁸.

2. Sources of Fluoride Exposure

2.1 Natural Sources

3.1.1

People are primarily exposed to fluoride through drinking water and dental products that contain fluoride. Dental fluorosis, which results from high fluoride consumption when teeth are growing, is a typical side effect of this exposure, particularly in children eight and older. Fluoride dosage, timing, and duration all affect how severe dental fluorosis

is ²⁹. An increased incidence of dental fluorosis has been linked to higher fluoride levels in drinking water. In locations with higher fluoride concentrations, a notable proportion of children and adolescents exhibit signs of fluorosis. Regional variations in the amount of fluoride in drinking water can impact the incidence of fluorosis ³⁰. Excessive fluoride exposure, particularly from drinking water, can lead to a condition known as skeletal fluorosis, which develops when fluoride builds up in the bones and may cause joint stiffness, discomfort, and weak bones ³¹. To prevent the development of skeletal fluorosis, the U.S. Environmental Protection Agency has set a fluoride threshold for drinking water of 4.0 mg/L ²⁴. Researchers have found that higher fluoride levels in water and plasma are linked to a higher incidence of dental fluorosis. This indicates that fluoride levels in various parts of the world can impact the prevalence of fluorosis. According to these results, it may be necessary to reevaluate the current recommendations for fluoridating water to reduce excessive fluoride exposure and the associated health problems ³². Drinking water is a significant source of fluoride exposure. Variations in fluoride levels across different geographic regions can impact the prevalence of fluorosis, making it crucial to monitor and control these levels ³².

3.1.2. Soil and Air

Several factors affect the amount of fluoride in the environment, particularly soil. Fluoride exhibits low solubility, with more than 90% of its solubility detected in soil particles ³³. Fluorine soil pollution may have an impact on crop productivity and composition. Different fractions of fluorine can be found in soil, including those soluble in water, exchangeable, bound to organic matter, and coupled with iron and manganese. Elevated fluoride concentrations in the soil may impede the growth of microorganisms and the breakdown of organic materials ³³. Variations in soil fluoride levels can impact the element composition of plants due to environmental contamination containing fluorine compounds. Commercially produced fluorinated products have been more prevalent in recent years; in the case of crop protection agents, for instance, they now make up nearly 20% of all compounds on the market ²⁷.

Fluoride pollution of the soil impacts agriculture's growth and productivity, and it may also have adverse effects on the food chain, fluoride exposure in animals and humans, and the food chain itself. Increased soil fluoride concentrations can also alter the fluoride content of animal feed, which can change the fluoride content of animal-derived consumables, such as eggs ³⁴.

3. Anthropogenic Sources of Fluoride:

4.1. Dental Products:

Dental products differ in their fluoride levels based on their type. 1.4 mg of fluoride is included in one gram of toothpaste, or 1400 ppm, in most adult toothpastes available in Switzerland, according to the Helvident website ³⁵. Around 105 mg of fluoride is present in a 75 ml toothpaste tube, and roughly

0.7 mg is present in a 1 cm toothpaste (1400 ppm fluoride) used for brushing teeth. About 0.15 milligrams of fluoride are present in 75 ml of children's toothpaste (500 ppm fluoride) ³⁶. Sodium fluoride is the active element in most fluoride supplements, and it is also available in tablets, lozenges, and liquids. Sodium fluoride, usually at a concentration of 1,000 to 1,100 mg/L, is present in most toothpaste marketed in the US. A significant source of fluoride exposure, especially for youngsters, is fluoridated dental products, such as toothpaste, mouth rinses, gels, varnishes, and supplements. Studies have indicated that toothpaste with 1000–1250 ppm fluoride is superior to toothpaste without fluoride for avoiding dental cavities³⁷.

4.2 Industrial Processes:

The dumping of industrial wastewater into waterways and the release of industrial emissions into the air can both result in considerable amounts of fluoride being released into the environment due to industrial activities. Fluoride pollution can harm farm animals, wildlife, and plant growth and yield ³⁸. Fluoride contamination has led to drinking water crises worldwide, and high groundwater fluoride levels can pose a risk to human health. Too much fluoride exposure can damage bones and teeth (dental fluorosis and skeletal fluorosis). Living close to industrial regions that discharge fluoride into the environment puts nearby communities at risk of exposure and could increase the prevalence of fluorosis ³⁹.

4.3 Nutritional Habits:

Diet plays a crucial role in determining the amount of fluoride to which humans are exposed. Individual factors, nutrition Figure (3), and staying hydrated affect how our bodies deal with fluoride. Research from Ethiopia suggests that health, altitude, and duration of fluoride exposure can influence the development of fluorosis⁴⁰. Reduced fluoride absorption can be achieved by eating a diet rich in calcium, magnesium, and antioxidants. Good oral hygiene and limiting free sugar can also prevent tooth decay. Fluorosis may be less common if you drink rainwater and eat foods high in calcium, according to research from places like Guizhou, China, and Ethiopia's Rift Valley ^{41,42}. The American Dental Association (ADA) recommends

consuming fluoridated food and water to prevent tooth decay, suggesting a diet low in sugar, healthy snacks, and good oral hygiene ⁴⁰. A study from the UK stresses the importance of labelling fluoride content, especially on baby products. This helps manage fluoride intake, reducing the risk of fluorosis. Naturally, high-fluoride foods include grapes, raisins, melons, apples, strawberries, bananas, peaches, potatoes, spinach, shrimp, crab, coffee, and black tea⁴³.

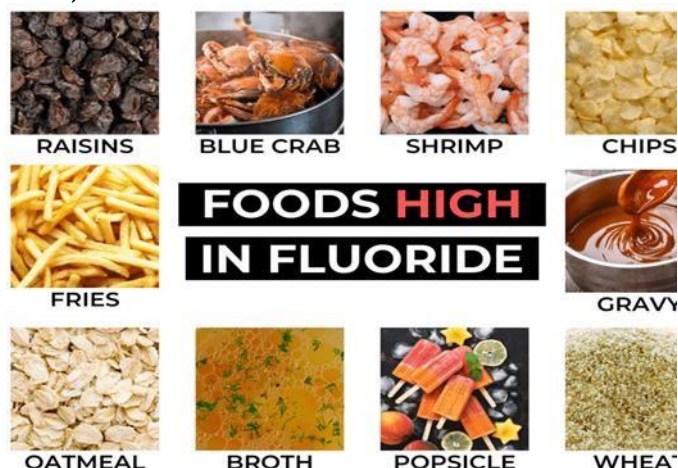


Figure (3): Foods highest in fluoride ³⁶

4.4 Dental Effects

Fluoride, especially in small children, can have both beneficial and detrimental effects on oral health. It can help prevent early decay and tooth decay by strengthening the enamel's resistance to acid attacks. Fluorosis, a disorder linked to aberrant enamel growth, can result from excessive fluoride, particularly in young children (under seven years old) ⁴⁴. Fluorosis, usually brought on by consuming large amounts of naturally occurring fluoride, such as that present in healthy water, can produce tooth discoloration that varies from light white to dark brown patches (Figure 4). It's critical to provide children with the appropriate dosage of fluoride to prevent tooth decay without contributing to fluorosis. Dentists can offer guidance on using fluoride correctly to promote children's dental health³⁷.



Figure (4): The effects of fluorosis on teeth are long-lasting, although cosmetic procedures can address or conceal the discoloration and flaws³⁸.

Fluoridation initiatives, aiming to achieve a concentration of one part per million (mg/l), are currently in progress in the Basel-Stadt canton of Switzerland ³⁹. Official recommendations include the use of fluoride salts found in dental hygiene products and table salt. According to the Swiss Society of Nutrition (SSN), adults should aim for a daily fluoride intake between 3.1 and 3.8 mg. Fluoride concentrations in drinking water exhibit variations across Switzerland. Supplementation is necessary to meet acceptable levels where natural fluoride is insufficient ²⁹. Switzerland has begun fluoridating its water, following broader European practices that involve adding fluoride to table salt. The City of Basel started this. The fact that less fluoride-related dental plaque forms in Switzerland's younger people is due mainly to the widespread use of low-fluoride toothpaste, which became popular in 1986 and stayed popular until 1992 ⁴⁰.

4. Environmental Implications of Fluoride:

Ecosystems and Soil Health

Fluoride contamination poses significant risks to ecosystems and soil health, with cascading effects on biodiversity and agricultural sustainability. Natural sources like volcanic emissions and geogenic weathering release fluoride into soil and water, while anthropogenic activities, such as industrial emissions, phosphate fertilizer use, and water fluoridation exacerbate contamination ⁴⁵.

4.1 Soil Health Degradation

Excessive fluoride in soil disrupts the microbial communities that are critical for organic matter decomposition and nutrient cycling. For instance, soils near phosphorus chemical plants in China's karst regions showed fluoride levels up to 1,496 mg/kg, 172% above national baselines, impairing crop yields and altering plant nutrient uptake ⁴⁶. Fluoride binds to soil particles, reducing solubility but persisting in the environment, which inhibits root growth and lowers agricultural productivity. Leafy vegetables, such as spinach and pakchoi, exhibit higher fluoride bioaccumulation, threatening food safety ⁴⁷.

4.2 Ecosystem Disruption

Fluoride's bioaccumulation in terrestrial and aquatic food chains amplifies ecological risks. Insects near aluminum smelters in Montana accumulated up to 585 ppm fluoride, passing toxicity to predators like birds and mammals ⁴⁸. Chronic exposure causes skeletal fluorosis in wildlife, as seen in chipmunks with bone fluoride levels exceeding 13,000 ppm [48]. Aquatic

ecosystems are equally vulnerable: freshwater invertebrates like *Hyalella azteca* suffer growth inhibition at 4 mg/L, while marine algae experience reproductive disruptions⁴⁹. Figure 5 displays a Flowchart of fluoride's environmental pathways and health impacts.

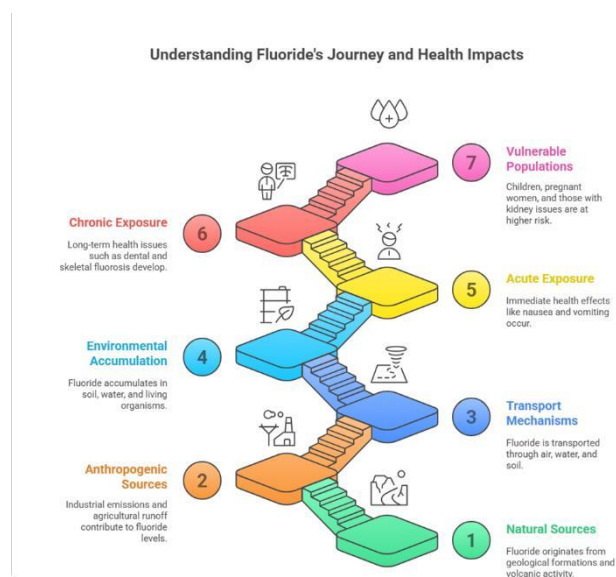


Figure (5). Flowchart of fluoride's environmental pathways and health impacts

5. Prevention and Management Strategies for Fluorosis

Effective prevention and management of fluorosis require a multi-faceted approach targeting fluoride exposure reduction, public health education, and environmental stewardship.

5.1 Water Source Management

5.1.1 Defluorination: These Technologies employ diverse methods to address excessive fluoride in water. Activated Alumina, utilized in India's National Programme for Prevention and Control of Fluorosis (NPPCF), efficiently removes 90% of fluoride at a low cost (\$0.02–0.05 per liter), making it scalable for rural communities. Reverse Osmosis (RO), deployed in Rajasthan, India, effectively reduces fluoride levels to safe levels (<1.5 mg/L), but faces challenges such as high energy demands and maintenance costs, which limit accessibility in resource-poor areas²¹. Rainwater Harvesting, promoted in Ethiopia's Rift Valley, offers a sustainable, low-fluoride alternative by capturing rainfall, though its success depends on seasonal availability and infrastructure. Together, these strategies strike a balance between efficacy, cost, and local feasibility to combat fluorosis in endemic regions⁴⁴.

5.2 Policy Interventions: Policy Interventions involve regulatory and adaptive measures to manage fluoride levels in drinking water. The U.S. Environmental Protection Agency (EPA) enforces

a maximum contaminant level of 4.0 mg/L to safeguard against skeletal fluorosis and other health risks, ensuring water systems comply through routine monitoring and corrective actions

⁵⁰. Meanwhile, regions like Basel-Stadt, Switzerland, implement tailored adjustments to community water fluoridation, balancing naturally occurring fluoride (0.1–0.4 mg/L) with minimal supplementation to maintain optimal dental benefits while avoiding excess exposure⁵⁰. These strategies collectively prioritize public health by harmonizing regulatory standards with localized, data-driven practices to mitigate fluoride-related risks.

6. Conclusion:

The primary health advantages of fluoride are its ability to prevent tooth decay and promote dental health. Pregnant women should not reduce their fluoride intake because fluoride is necessary for maintaining oral health, which is linked to the health of newborn babies. However, fluorosis, whether dental or skeletal, results from prolonged excessive fluoride consumption, particularly during tooth or bone growth. Water is a significant source of fluoride exposure, and variations in fluoride levels across geographic regions can influence the prevalence of fluorosis, highlighting the importance of monitoring and regulating fluoride concentrations in drinking water to prevent adverse health consequences. Additionally, polluting the soil with fluoride can harm the growth and productivity of crops, impacting the food chain and the amount of fluoride to which people and animals are exposed. To limit the amount of fluoride that enters their systems and reduce the risk of dental fluorosis, food and drink products should have fluoride labels, which is especially important for infants and young children.

Acknowledgments: We would like to acknowledge the support of all institutions and individuals who contributed to the completion of this research.

DECLARATIONS

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Authors' contributions.

Contributor Role	Degree of Contribution		
	Lead	Equal	Supporting
Conceptualization	AKS	AEK	HNM
Data curation	AKS	AEK	HNM
Formal analysis	AEK	AEK	HNM
Funding acquisition	AKS	AEK	HNM
Investigation	AKS	AEK	HNM
Methodology	AKS	AEK	HNM
Project administration	AKS	AEK	HNM
Resources	AKS	AEK	HNM
Software	AKS	AEK	HNM
Supervision	AKS	AEK	HNM
Validation	AKS	AEK	HNM
Visualization	AKS	KZ	AEK
Writing-original draft	AKS	AEK	HNM
Writing-review & editing	AKS	KZ	AEK

Ethical approval: The study was approved by the relevant ethics committee. Informed consent was obtained from all participants.

Funding resources: No funding resources.

Conflict of interest: The authors declare no conflict of interest with other previous studies.

References

- [1] Boobalan S, Sidhu L. Dental fluorosis – A review. *International Journal of Community Dentistry* (2023);11(1):1–6. <https://doi.org/10.56501/intjcommunitydent.v11i1.695>.
- [2] Thilakarathne BKG, Ekanayake L, Schensul JJ, Reisine S. Impact of dental fluorosis on the oral health related quality of life of adolescents in an endemic area. *Journal of Oral Biology and Craniofacial Research* (2023);13(3):448–452. <https://doi.org/10.1016/j.jobcr.2023.03.015>
- [3] Guan ZZ. Coal-burning Type of Endemic Fluorosis. Springer, Singapore (2021):3–11. https://doi.org/10.1007/978-981-16-1498-9_1
- [4] Chandrajith R, Dissanayake CB, Barth JAC. Geochemistry of fluoride in the environment and human health. In: Bickle MJ, ed. *Medical Geology*. Wiley (2023):143–153. <https://doi.org/10.1002/9781119867371.ch9>
- [5] Zhang K, Lu Z, Guo X. Advances in epidemiological status and pathogenesis of dental fluorosis. *Frontiers in Cell and Developmental Biology* (2023);11:Article 1168215. <https://doi.org/10.3389/fcell.2023.1168215>
- [6] Mihalas E, Gavrilă L, Sirghe A, Toma V, Decolli Y, Savin C. Evaluation of fluoride concentration in commercially available bottled water in Romania—A potential risk factor for dental fluorosis. *Applied Sciences* (2023);13(13):7563. <https://doi.org/10.3390/app13137563>.
- [7] National Institute of Dental and Craniofacial Research. The story of fluoridation. NIDCR Website. Retrieved October 12, 2023, <https://www.nidcr.nih.gov/health-info/fluoride/the-story-of-fluoridation>.
- [8] National Center for Biotechnology Information. Fluoride ion. PubChem Database. Retrieved October 12, 2023, from <https://pubchem.ncbi.nlm.nih.gov/compound/Fluoride-ion>.
- [9] Tressaud A. Fluorine. Academic Press, London (2018):1–456.
- [10] Alshangiti O, Galatolo G, Rees GJ, Guo H, Quirk JA, Dawson JA, Pasta M. Solvent-in-salt electrolytes for fluoride ion batteries. *ACS Energy Letters* (2023);8(6):2668–2673. https://doi.org/10.1021/acsenergylett.3c004_93.
- [11] Key Stage Wiki. Fluorine. Retrieved October 12, 2023, from <https://keystagewiki.com/index.php/Fluorine>.
- [12] American Dental Association. How fluoride fights cavities. Mouth Healthy. Retrieved October 12, 2023, from <https://www.mouthhealthy.org/how-fluoride-fights-cavities>. Horst JA, Tanzer JM, Milgrom PM. Fluorides and other preventive strategies for tooth decay. *Dental Clinics of North America* (2018);62(2):207–234. <https://doi.org/10.1016/j.cden.2017.11.003>.
- [13] Aoun A, Darwiche F, Hayek SA, Doumit J. The fluoride debate: The pros and cons of fluoridation. *Preventive Nutrition and Food Science* (2018);23(3):171–180. <https://doi.org/10.3746/pnf.2018.23.3.171>.
- [14] Kebede A, Retta N, Abuye C, Whiting S, Kassaw M, Zeru T, Tessema M, Kjelleevold M. Dietary fluoride intake and associated skeletal and dental fluorosis in school age

- children in rural Ethiopian Rift Valley. *International Journal of Environmental Research and Public Health* (2016); 13(8): 756.
<https://doi.org/10.3390/ijerph13080756>.
- [15] Craig L, Lutz A, Berry KA, Yang W. Recommendations for fluoride limits in drinking water based on estimated daily fluoride intake in the Upper East Region, Ghana. *Science of the Total Environment* (2015);532:127–137.
<https://doi.org/10.1016/j.scitotenv.2015.05.126>.
- [16] Liu J, Yang S, Luo M, Chen T, Ma X, Tao N, Zhao X, Wang D. Association between dietary patterns and fluorosis in Guizhou, China. *Frontiers in Nutrition* (2020);6:Article189.
<https://doi.org/10.3389/fnut.2019.00189>.
- [17] Hanse A, Chabukdhara M, Gohain Baruah S, Boruah H, Gupta SK. Fluoride contamination in groundwater and associated health risks in Karbi Anglong District, Assam, Northeast India. *Environmental Monitoring and Assessment* (2019);191(12):741.
<https://doi.org/10.1007/s10661-019-7970-6>.
- [18] Shaji E, Sarath KV, Santosh M, Krishnaprasad PK, Arya BK, Babu MS. Fluoride contamination in groundwater: A global review of the status, processes, challenges, and remedial measures. *Geoscience Frontiers* (2024);15(2):101734.
<https://doi.org/10.1016/j.gsf.2023.101734>.
- [19] Hung M, Hon ES, Mohajeri A, Moparthi H, Vu T, Jeon J, Lipsky MS. A national study exploring the association between fluoride levels and dental fluorosis. *JAMA Network Open*(2023);6(6):e2318406.
<https://doi.org/10.1001/jamanetworkopen.2023.18406>.
- [20] Jha SK, Mishra VK, Sharma DK, Damodaran T. Fluoride in the environment and its metabolism in humans. In: Whitacre DM, editor. *Reviews of Environmental Contamination and Toxicology*. Vol. 211. Springer;(2011):121–142.
https://doi.org/10.1007/978-1-4419-8011-3_4.
- [21] Srivastava S, Flora SJ. Fluoride in drinking water and skeletal fluorosis: a review of the global impact. *Current Environmental Health Reports*(2020);7(2):140–146.
<https://doi.org/10.1007/s40572-020-00278-4>.
- [22] Pak CYC, Sakhaee K, Zerwekh JE, Parcel C, Peterson R, Johnson K. Safe and effective treatment of osteoporosis with intermittent slow-release sodium fluoride: Augmentation of vertebral bone mass and inhibition of fractures. *Journal of Clinical Endocrinology and Metabolism* (1989);68(1):150–159.
<https://doi.org/10.1210/jcem-68-1-150>.
- [23] Levy SM, Warren JJ, Phipps K, Letuchy E, Broffitt B, Eichenberger-Gilmore J, Burns TL, Kavand G, Janz KF, Torner JC, Pauley CA. Effects of life-long fluoride intake on bone measures of adolescents. *Journal of Dental Research*(2014);93(4):353–359.
<https://doi.org/10.1177/0022034514520708>.
- [24] American Dental Association. Fluoridation in water [Internet]. [cited 2023 Oct 12]. Available from:
<https://www.ada.org/resources/community-initiatives/fluoride-in-water>.
- [25] Walsh T, Worthington HV, Glenny AM, Marinho VC, Jeroncio A. Fluoride toothpastes of different concentrations for preventing dental caries. *Cochrane Database of Systematic Reviews* (2019);3:CD007868.
<https://doi.org/10.1002/14651858.CD007868.pub3>.
- [26] Singh P, Goyal L, Bakshi D, Arora J, Manchanda A. Assessment of fluoride levels during pregnancy and its association with early adverse pregnancy outcomes. *Journal of Family Medicine and Primary Care* (2020);9(6):2693–2698.
<https://doi.org/10.4103/jfmpc.jfmpc.213.20>.
- [27] Green R, Lanphear B, Hornung R, Flora D, Martinez-Mier EA, Neufeld R, Ayotte P, Muckle G, Till C. Association between maternal fluoride exposure during pregnancy and IQ scores in offspring in Canada. *JAMA Pediatrics* (2019);173(10):940–948.
<https://doi.org/10.1001/jamapediatrics.2019.1729>.
- [28] Castiblanco-Rubio GA, Martinez-Mier EA. Fluoride metabolism in pregnant women: a narrative review of the literature. *Metabolites* (2022);12(4):324.
<https://doi.org/10.3390/metabo12040324>.
- [29] DenBesten P, Li W. Chronic fluoride toxicity: Dental fluorosis. In: Fejerskov O, Kidd E, editors. *Fluoride and the Oral*

- Environment. Karger; (2011):81–96.
<https://doi.org/10.1159/000327028>.
- [30] Kurdi M. Chronic fluorosis: The disease and its anaesthetic implications. *Indian Journal of Anaesthesia* (2016);60(3):157–158.
<https://doi.org/10.4103/0019-5049.177867>.
- [31] Simon MJK, Beil FT, R  ther W, Busse B, Koehne T, Steiner M, Pogoda P, Ignatius A, Amling M, Oheim R. High fluoride and low calcium levels in drinking water is associated with low bone mass, reduced bone quality and fragility fractures in sheep. *Osteoporosis International* (2014);25(7):1891–1903.
<https://doi.org/10.1007/s00198-014-2707-4>.
- [32] Han J, Kiss L, Mei H, Remete AM, Ponikvar-Svet M, Sedgwick DM, Roman R, Fustero S, Moriwaki H, Soloshonok VA. Chemical aspects of human and environmental overload with fluorine. *Chemical Reviews* (2021);121(8):4678–4742.
<https://doi.org/10.1021/acs.chemrev.0c01263>.
- [33] Hanse A, Chabukdhara M, Gohain Baruah S, Boruah H, Gupta SK. Fluoride contamination in groundwater and associated health risks in Karbi Anglong District, Assam, Northeast India. *Environmental Monitoring and Assessment* (2019);191(12):741.
<https://doi.org/10.1007/s10661-019-7970-6>.
- [35] Helvident. Fluoride in Switzerland: how much to consume? [Internet]. [cited 2023 Oct 12]. Available from: <https://helvident.ch/en/fluoride-in-switzerland/>.
- [36] Wong MCM, Clarkson J, Glenny AM, Lo ECM, Marinho VCC, Tsang BWK, Walsh T, Worthington HV. Cochrane reviews on the benefits/risks of fluoride toothpastes. *Journal of Dental Research* (2011);90(5):573–579.
<https://doi.org/10.1177/0022034510393346>.
- [37] Shaji E, Sarath KV, Santosh M, Krishnaprasad PK, Arya BK, Babu MS. Fluoride contamination in groundwater: A global review of the status, processes, challenges, and remedial measures. *Geoscience Frontiers* (2024);15(2):101734.
<https://doi.org/10.1016/j.gsf.2023.101734>.
- [38] Dar FA, Kurella S. Fluoride in drinking water: An in-depth analysis of its prevalence, health effects, advances in detection and treatment. *Materials Today: Proceedings* (2023).
<https://doi.org/10.1016/j.matpr.2023.05.645> Dai, S., Ren, D., & Chou, C.-L. (2016). Fluoride exposure from coal combustion and its relationship to dental fluorosis in Guizhou, China. *Environmental Geochemistry and Health*, 38(2), 679–688.
<https://doi.org/10.1007/s10653-015-9755-3>.
- [39] Tekle-Haimanot R, Melaku Z, Kloos H, Reimann C, Fantaye W, Zerihun L, Bjorvatn K. The geographic distribution of fluoride in surface and groundwater in Ethiopia and its linkage to bone health. *Science of the Total Environment* (2016);557–558:347–355.
<https://doi.org/10.1016/j.scitotenv.2016.03.108>.
- [40] Clark MB, Keels MA, Slayton RL, Braun PA, Fisher-Owens SA, Huff QA, Karp JM, Tate AR, Unkel JH, Krol D. Fluoride use in caries prevention in the primary care setting. *Pediatrics* (2020);146(6):e2020034637.
<https://doi.org/10.1542/peds.2020-034637>.
- [41] Centers for Disease Control and Prevention. Dental fluorosis. CDC Website (2022).
<https://www.cdc.gov/fluoridation/faqs/dental-fluorosis/index.html>.
- [42] Kamruzzaman M, Khan MS, Ritu SA, Khanom S, Hossain M, Islam MR, Uddin S. Diving deep: Exploring fluoride in groundwater causes, implications, and mitigation. In: *Fluorides in Drinking Water: Source, Issue, and Mitigation Strategies*. Springer Nature, Cham; (2025):189–221.
- [43] Kidodent. Dental fluorosis: what is it? [Internet]. [cited 2023 Oct 12]. Available from: <https://kidodent.org/oral-and-dental-conditions/dental-fluorosis-what-is-it/>.
- [44] Cheng KK, Chalmers I, Sheldon TA. Adding fluoride to water supplies. *BMJ* (2007);335(7622):699–702.
<https://doi.org/10.1136/bmj.39318.562951.b.e>.
- [45] Wu S, Wang Y, Iqbal M, Mehmood K, Li Y, Tang Z, Zhang H. Challenges of fluoride pollution in environment: mechanisms and pathological significance of toxicity—a review. *Environmental Pollution* (2022);304:119241.
<https://doi.org/10.1016/j.envpol.2022.119241>.

- [46] Vasconcelos V, Azevedo J, Silva M, Ramos V. Effects of marine toxins on the reproduction and early stages development of aquatic organisms. *Marine Drugs* (2010);8(1):59–79. <https://doi.org/10.3390/md8010059>.
- [47] US Environmental Protection Agency. National primary drinking water regulations. US EPA Website [Internet]. [cited year month day]. Available from: <https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations>.
- [48] Van Loveren C. Pharmacokinetics in the oral cavity: fluoride and other active ingredients. In: Duckworth LCM, editor. *Toothpastes*. Karger Medical and Scientific Publishers; (2013):125–139.
- [49] Whelton HP, Spencer AJ, Do LG, Rugg-Gunn AJ. Fluoride revolution and dental caries: evolution of policies for global use. *Journal of Dental Research*. 2019 Jul;98(8):837-46.
- [50] Jamakala O, Chintada V, Veeraiah K. Fluoride in Groundwater: Toxicological Exposure and Remedies. In: *Fluorides in Drinking Water: Source, Issue, and Mitigation Strategies 2025* Jan 1 (pp. 305- 332). Cham: Springer Nature Switzerland.
- [51] Gerber E. How is the hazard landscape changing in Swiss cities and how do they adapt: The case of Basel (Master's thesis, University of Zurich).