Vascular Fluorosis

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The reason why fluoride is added to your tap water is to deliver fluoride into your bloodstream, so it is distributed throughout your entire body – including your salivary glands that secrete a small amount of fluoride into your mouth. “Saliva with fluoride incorporated into it provides a constant bathing [of] the teeth in a low concentration of fluoride all throughout the day... Incorporation of fluoride into saliva occurs systemically.” 1,2[American Fluoridation Society, Delta Dental]

The elephant in this rationale is that your vascular system (aka cardiovascular system; circulatory system) is chronically being exposed to fluoride, whose direct and indirect mechanisms of action can adversely affect vascular structure and function. This is not breaking news.

> Following the introduction in 1945 of fluoride into Newburgh, NY’s city waters, “heart-disease rate was found by researchers to be one of the highest in the United States.” Also, heart disease doubled in Grand Rapids, Michigan just five years into the nation’s other early fluoridation experiment. “Fluoride concentrates in the arteries, attracting calcium, and ‘can contribute directly to the hardening,’ according to scientists.” (1954) – *The Fluoride Deception* by Christopher Bryson 3[Bryson 2004]
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> In 1993, the U.S. Public Health Service Agency for Toxic Substances warned: “Existing data indicate that subsets of the population may be unusually susceptible to the toxic effects of fluoride and its compounds. These populations include the elderly, people with deficiencies of calcium, magnesium, and/or vitamin C, and people with cardiovascular and kidney problems... Impaired renal clearance of fluoride has also been found in people with diabetes mellitus and cardiac insufficiency.” 4[PHS 1993]

“Approximately 75%-90% of dietary fluoride is absorbed quickly by the gastrointestinal tract and enters the bloodstream, which distributes fluoride throughout the body in the form of the fluoride ion.” 5[Sun 2016]

“The fluoride ion is the toxicologically active agent.” – U.S. Public Health Service 6[PHS 2003]

> A major review (“Prevention & control of fluorosis & linked disorders: Developments in the 21st century”) by longtime fluoride expert AK Susheela notes that fluoride binds with each and every soft tissue, wherever the negatively charged fluoride ion finds a binding site. 7[Susheela 2018]

Fluorosis researchers have long focused on teeth and bones. In recent years, however, the largest body of fluorosis research has investigated fluoride’s mechanism of action on soft tissues. 8[Wei 2019]

> It is increasingly being emphasized that dental fluorosis is not an isolated symptom, but instead is accompanied by systemic disorders. The visible effect on teeth from chronic fluoride exposure is not merely a cosmetic problem. "It can lead to long latent but ultimately severe health conditions." Adults with dental fluorosis are more frequently diagnosed with osteoporosis of the long bones, degenerative changes in the spine, kidney stones, thyroid disorders, and hematological changes. 9[Strużycka 2022]

Vascular Calcification and Arterial Stiffness

Atherosclerosis is derived from the Greek word *athero* (meaning gruel or paste) and *sclerosis (*meaning hardening). 10[Adeoye 2020] Vascular calcification has an inseparable relationship with atherosclerotic vascular disease. In addition, it is known that arterial stiffness – which represents the functional disturbance of vascular calcification – is an independent predictor of cardiovascular mortality. A 2020 review ("Vascular calcification: New insights into its mechanism") found that in a clinical perspective, "reduction of arterial stiffness should be underscored as much as lowering systolic blood pressure." 11[Lee S. 2020]

> Fluoride accelerates calcification of vessels and thus reduces their elasticity. In people with fluorosis, the elastic properties of the ascending aorta are impaired. 12,13[Machoy 2004, Varol 2010]

> A retrospective review of imaging data showed a significant correlation between fluoride uptake and calcification in most arterial walls. "The coronary fluoride uptake value in patients with cardiovascular events was significantly higher than in patients without cardiovascular events." 14[Li Y 2012]

The increase of arterial stiffness at younger ages has been considered a strong predictor of cardiovascular outcomes. Results of a 2022 review are "consistent with a causality association between arterial stiffness and atrial fibrillation," the most frequent sustained arrhythmia in clinical practice. 15[Lage 2022]

Carotid intima media thickness (CIMT) testing is a safe, noninvasive, and cost effective method to detect early atherosclerotic vascular diseases. The test measures the thickness of the inner two layers of the carotid artery and alerts physicians to any thickening when patients are still asymptomatic.

> A study that evaluated vascular injury in Mexican children exposed to fluoride in their drinking water found significant relationships between fluoride exposure and CIMT. The results suggest that fluoride exposure is "related to early vascular alterations, which may increase the susceptibility of cardiovascular diseases in adult life." 16[Jiménez-Córdova 2019]

Significantly higher levels of arterial stiffness have been found in overweight youth. A 2021 review that summarizes the impact of obesity on vascular structure and function found that vascular stiffness is an especially common feature of obese vessels. 17,18[Univ. Georgia 2021, Martínez 2021]

A large-scale cross-sectional study of school-age children found a significant association between low-to-moderate fluoride exposure and obesity in girls. In Mexican girls, higher peripubertal fluoride exposure was significantly associated with increased levels of cardiometabolic risk factors for obesity. 19,20[Liu L. 2019, Liu Y. 2020]

Collagen and Elastin

"The largest arteries like the aorta have multiple layers of smooth muscle cells intertwined with an elaborate elastin and collagen-based matrix that is required to sustain systemic pressure under pulsatile flow." 21[Lilly 2014] The most abundant protein in the walls of the arteries is elastin, an elastic fibrous glycoprotein. "Loss of elastin is coupled with medial calcification." op. cit. 11[Lee S. 2020]

> "The vascular wall is rich in collagen fibres, and collagen fibres are one of the major sites of action of fluoride." op. cit. 8[Wei 2019]
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> A study of rabbit tissues ("Effect of sodium fluoride on collagen biosynthesis and degradation") found that the collagen produced during fluoride ingestion is degraded faster. In fluoride-treated animals, collagen contents of bone, tendon, trachea and skin were decreased. 22[Sharma 1985] In rabbits fed sodium fluoride, "the smooth muscle fibres disintegrated in the wall of the aorta." op. cit. 7[Susheela 2018]
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> Fluorine compounds modify the structure and regularity of collagen fibers and induce mineralization of collagen. The final outcome includes progressive vascular lesions. op. cit. 12 [Machoy 2004]

The Endothelium

Lining the interior of the entire vascular system is the endothelium, a single layer of endothelial cells that were long thought to be uniform. Recent research has identified clusters of endothelial cells specialized to detect specific stimuli. A high density of interlinked connections integrates multiple lines of information and coordinates endothelial responses that regulate blood flow, blood pressure, blood clotting, inflammation, and response to disease. 23,24[Univ. Strathclyde 2022], Lee M. 2022]

> Following application of the fluorinated drug 5-Fluorouracil, plasma levels of fluoride were 5 to 33 times higher. 25[Hull 1988] 5-Fluorouracil (5-FU) treatment "induced ultrastructural changes in the endothelium of various organs," including "substantial effects on the cardiovascular system." 26[Focaccetti 2015]
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> Sevoflurane, the inhaled fluorinated anesthetic used in mechanical ventilation and sedation, results in increased serum fluoride ion concentrations. 27[Goldberg 1996] A study ("Sevoflurane and isoflurane induce structural changes in brain vascular endothelial cells and increase blood-brain barrier permeability") found a "marked flattening" of endothelial cells in the brains of Sevoflurane-treated rats. 28[Acharya 2015]

> Researchers at Johns Hopkins University School of Medicine demonstrated that sodium fluoride causes "dramatic" endothelial cell barrier dysfunction, as evidenced by increases in macromolecule permeability. 29[Wang 2001]

Blood vessels are composed of two primary cell types, endothelial cells and smooth muscle cells, each providing a unique contribution to vessel function. A review ("We have contact: Endothelial cell-smooth muscle cell interactions") highlights the pathways that endothelial cells and smooth muscle cells utilize to communicate and how disruptions in these pathways contribute to disease. "Endothelial dysfunction" is a pathological state of the endothelium that leads to disruptions in vascular function by changing the composition of the vascular wall, most notably the smooth muscle cells. The authors note that "the literature describing endothelial dysfunction and its effects on smooth muscle cells is immense, much of which is focused on diminished NO [nitric oxide] bioavailability." op. cit. 21[Lilly 2014]

Nitric oxide is an important signaling molecule needed for cardiovascular health and circulation. "A decrease in NO bioavailability or function is associated with most of the endothelial dysfunctions observed in virtually all cardiovascular diseases." 30[Félétou 2011]

Nitric Oxide

A 2020 review ("It takes more than two to tango: Mechanosignaling of the endothelial surface") reported that a close functional interaction between endothelial cells and vascular smooth muscle cells regulates vascular tone and the ability of cells to react on different biochemical and mechanical stimuli from the streaming blood. Endothelial cells sense and encode these mechanical forces into biochemical signals transmitted to vascular smooth muscle cells, which either respond with relaxation or contraction. This well-described mechanism is mainly based on the ability of the endothelial cells to release nitric oxide which diffuses to adjacent vascular smooth muscle cells. 31[Fels 2020]

When there is a reduction in vascular nitric oxide production, the vasodilation of both macro- and micro-vessels is compromised. 32[Li YS 2024]

To produce nitric oxide, humans depend on special bacteria in the mouth that convert nitrates (found in vegetables and fruits) into nitrites, which are then swallowed and converted into nitric oxide in the stomach. 33[Cashman 2022]

> "The oral microbiome contains several species of bacteria that selectively express a nitrate reductase enzyme to perform a 2-electron reduction of nitrate to nitrite," explains leading nitric oxide researcher, Nathan S. Bryan PhD. There is "unequivocal evidence" that disruption of the oral microbiota from exposure to antimicrobials such as fluoride and mouthwashes will suppress nitric oxide production and negatively impact blood pressure. 34[Bryan 2022] "The loss of nitric oxide production is directly correlated to cardiovascular disease, the number one killer of men and women worldwide." 35[Bryan 2024]

Clinical trials have shown that antibacterial mouthwash decreases systemic nitric oxide bioavailability. “Most prescription as well as over-the-counter mouthwashes, including fluoride mouthwash for caries reduction, have bactericidal ingredients.” 36[Joshipura 2020] “Fluoride’s antibacterial effect should be common knowledge amongst dental practitioners.” 37[Nouri 2023]

A laboratory study of the mechanisms of fluoride-induced suppression of nitric oxide in human umbilical vein endothelial cells treated with sodium fluoride found that the levels of nitric oxide significantly decreased in all experimental groups. 38[Huang 2018]

Hypertension

Preeclampsia is a complex hypertensive disorder of pregnancy associated with maternal vascular dysfunction. Pregnancy is a state of maintained vasodilation, and the adaptations necessary to maintain vascular efficiency during pregnancy rely heavily on the NO pathway. Evidence from a 2020 study (“Nitric oxide signaling in pregnancy and preeclampsia”) “suggests that NO deficiency contributes to the pathophysiology of preeclampsia including the central finding of vascular dysfunction.” 39[Sutton 2020]

A 2023 study details how NO signaling is altered in the systemic vasculature, uterine artery/spiral arteries, and placenta of hypertensive disorders during pregnancy. 40[Justina 2023]

A small study compared the composition of the oral microbiota in women who do and do not develop preeclampsia. Results indicate that “the abundances of nitrate-reducing bacteria in the oral microbiota are reduced in pregnant women with future late-onset preeclampsia.” 41[Altemani 2022]

The author’s 2015 report presents diverse evidence implicating fluoride and fluorosis in the pathogenesis of preeclampsia. It concluded that measuring blood fluoride levels during pregnancy should be routine. 42[MacArthur 2015] A 2020 case-control study did so and found that serum fluoride levels were significantly higher in the preeclampsia cases. A maternal serum fluoride level of 1.8 mg/L can be considered as a diagnostic biomarker for predicting preeclampsia and the related pregnancy outcomes. 43[Changalvala 2020]

Arterial stiffness measurements may also be useful in predicting preeclampsia. A systemic review found “significant increases in arterial stiffness measurements” in women with preeclampsia compared to those with gestational hypertension. 44[Hausvater 2012]

Patients with essential hypertension have abnormal endothelium-dependent vasodilation because of a defect in the endothelium-derived nitric oxide system. 45[Panza 1993] Hypertension is a major cause of vascular cognitive impairment and is the “single most important modifiable risk factor for adult stroke.” 46[Kupferman 2017] “A stroke doubles the chance of developing dementia.” 47 [Hachinski 2019]

A comprehensive 2024 study published in *Ecotoxicology and Environmental Safety* enhances our understanding of the consequences of fluoride exposures on “blood pressure regulation and cardiovascular well-being.” For example, it showed that fluoride leads to “pathological changes in

the aorta of rats." By elucidating underlying molecular mechanisms, it "provides compelling evidence of the deleterious effects of fluoride exposure through drinking water on hypertension." 48 [Yang 2024]

Metalloproteinases (MMPs)
Metalloproteinases are enzymes that can break down proteins. A 2021 review provides "strong evidence that hypertension is associated with increased vascular MMP activity, resulting in impaired vascular function... Activation of MMPs, especially MMP-2 and MMP-9, are responsible for the degradation of extracellular matrix proteins, including elastin and collagen... These modifications result in the accumulation of collagen degradation products and increase vascular wall stiffness.**"** 49[Prado 2021]

"The biological aging process is always associated with arterial stiffness, which is accelerated by arterial hypertension." Worldwide, it's estimated that 9.4 million deaths per year are related to arterial hypertension, a highly relevant risk factor for stroke, coronary artery disease, and heart failure. 50[Mikael 2017]

"Arterial stiffness correlates with the pathogenesis of a large spectrum of vascular disorders: hypertension, stroke, kidney dysfunction, cerebrovascular disease, dementia, and Alzheimer's disease." Arterial stiffness is an important risk marker for poor brain aging and dementia through its associations with β-amyloid deposition, brain atrophy, cognitive impairment, and cerebral small vessel disease. 51[Hughes 2015]

Mild cognitive impairment is linked to blood vessel dysfunction in the brain's temporal lobes – the seat of memory – according to a new USC-led study. During MRI, volunteers held their breath for 15-second intervals, an exercise designed to dilate the brain's blood vessels, a natural process called "cerebrovascular reactivity" which regulates oxygen levels in the brain. Researchers paid special attention blood to vessels supplying the temporal lobes, located on the sides of the head. Participants whose blood vessels didn't dilate properly showed signs of cognitive impairment. These findings "underscore the need to focus on vascular health as a critical factor in memory decline." 52[USC Jan 2025]

Cerebral small vessel disease (SVD) is a leading cause of age-related cognitive decline and contributes to 45% of dementia cases worldwide. A 2023 experimental study explains: Blood vessels are built around a type of scaffolding known as an "extracellular matrix" that supports the small blood vessels in the brain. In their disease model, the researchers found that the extracellular matrix is disrupted, particularly at its so-called "tight junctions" which "zip" cells together. "This leads to the small blood vessels becoming leaky – a key characteristic seen in SVD, where blood leaks out of the vessels and into the brain." Matrix metalloproteinases play a key role in this damage. 53[Univ. Cambridge 2023]

> Chronic fluoride exposure leads to high expression of MMP-9 and increasing permeability of the blood-brain barrier. 54[Qing-Feng 2019] Research suggests that "changes in the expression of metalloproteinases and their inhibitors in the brain, caused by fluorine, could be an important factor of neurotoxicity of fluorine." 55[Gutowska 2018]

> In a study that evaluated fluoride's mechanism of action in the cardiac muscle, male Wistar rats were administered a human-equivalent chronic dose of fluoride for 75 days. MMP-9 was significantly higher in the cardiac muscle after chronic fluoride exposure, and there was significant damage to cardiac muscle fibres. 56[Quadri 2018]

Increased expression of matrix metalloproteinase has been identified in aged human aortic wall and atherosclerotic lesions. 57[Chen Y. 2020] Increased levels of MMPs in the aorta and plasma are a consistent finding in abdominal aortic aneurysm (AAA), a slow and progressive disease. "The late stages of AAA are characterized by degenerative changes in the extracellular matrix and smooth muscle components of the aortic wall." 58[Chew 2004]

Bone-Like Cells

Although a similar mineralization process is shared by bone cells and vascular cells, they have completely opposite outcomes: "Soft tissues become hard while hard tissue become soft," says Yabing Chen, PhD. Over the past two decades, numerous important signaling pathways and integrated regulatory mechanisms have been identified that define the transition of vascular smooth muscle cells into "bone-like" cells. op. cit. 57[Chen Y. 2020]

Yabing Chen was awarded two National Institutes of Health grants to further her research into vascular diseases. One is a five-year, $2.2 million grant from the National Institute on Aging to study novel regulation in vascular dementia. Chen said, "Vascular pathology has been linked to dementias, notably Alzheimer's disease." The other is a four-year, $2.86 million grant from the National Heart, Lung, and Blood Institute to examine mechanisms in the calcification of vascular smooth muscle cells. Chen notes that there is no current treatment for vascular calcification. 59[Univ. of Alabama at Birmington 2023]

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A new study by University of Calgary researchers shows that blood vessels in the brain might hold an important clue to Alzheimer's disease. Dr. Minh Dang Nguyen, PhD, compares the brain's vascular system to a tree. The complex branches – arteries, capillaries and veins – are critical to delivering nutrients throughout the brain. The cerebrovascular system in Alzheimer's patients, he says, doesn't deliver those nutrients properly. Nguyen says the discovery, published in the journal *Neuron*, reveals important factors to consider about how the brain interacts with the vascular system and, particularly, the cells that form the brain blood vessels, called brain endothelial cells. 60[Univ. of Calgary 2025]

Conclusion

Fluoride accumulates not only in bone tissues but also in soft tissues, especially the cardiovascular system. A comprehensive 2022 report ("Necessity to pay attention to the effects of low fluoride on human health") found that *in vivo* and *in vitro* studies based on low fluoride have confirmed that fluoride causes damage in the "cardiovascular system, nervous system, hepatic and renal function, reproductive system, thyroid function, blood glucose homeostasis, and the immune system." Based on extensive literature, the authors "define a low fluoride concentration as ≤ 1.5 mg/L for humans." 61[Zhou 2022]

According to the American Heart Association's 2025 Heart Disease and Stroke Statistics Update, heart disease remains the leading cause of death:

- "Nearly 2,500 people in the U.S. die from cardiovascular disease every day."
- "Cardiovascular diseases, including heart disease and stroke, claim more lives than all forms of cancer and accidental deaths – the #2 and #3 causes of death – combined." 62[American Heart Association 2025]

It's high time we acknowledge the elephant in our vascular system: fluoride's direct and indirect mechanisms of action involved in vascular dysfunction and disease. Time to end chronic exposure to low fluoride in tap water and beverages manufactured with it. Time to reduce fluoride in our bloodstream. Time to prevent and diminish vascular fluorosis.

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