Fluoride causes Heart Disease, Stroke and Sudden Death

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Abstract

Fluoride uptake in coronary arteries is associated with an increased cardiovascular risk of sudden death. Fluoride causes enhanced deposition of doped Hydroxyapatite which leads to inflammation and sites for fatty deposits of atherosclerosis. Fluoride interferes with numerous enzyme systems resulting in elevation of key risk factors for cardiovascular disease. Fluoride causes oxidative stress and degeneration of heart muscle. Fluoride inhibits Thyroid function with consequential damage to heart function. Fluoride increases risk of sudden death from ruptured aorta. Diabetes, caused or exacerbated by Fluoride, further increases risk of cardiovascular death and disability.

Keywords: Fluoride, Fluoridation, Aorta, Apoptosis, Arrhythmia, Atherosclerosis, Bioaccumulation, Calcification, Calcitonin, Cardiovascular, Cerebrovascular, Diabetes, Enzyme Inhibition, Haptoglobin, Heart, Hydroxyapatite, Hyperhomocysteinemia, Hypertension, Inflammation, Interleukin, Lead, Melatonin, Monocyte chemotactic protein-1, Oxidative Stress, Periostin, Plumbosolvency, P-selectin, Review, Ryanodine receptor, Stroke, Thyroid, Vascular Cell Adhesion Molecule-1

Fluoride is a known Heart Poison

The Australian Institute of Health and Welfare states: “Coronary heart disease is the leading underlying cause of death in Australia, followed by dementia and Alzheimer disease, and cerebrovascular diseases (which includes stroke).” [AIHW 2016].

According to the Heart Research Institute “Every 12 minutes, an Australian dies from cardiovascular disease” [HRI 2016]. “Cardiovascular disease is the biggest killer in Australia and worldwide. It was responsible for a third of all Australian deaths in 2010, killing 45,500 people and affecting two out of every three families. In 2009-10, there were 482,000 hospitalisations directly caused by heart disease, and 800,000 hospitalisations where heart disease was a secondary factor.”

Fluoride continuously accumulates in the human body over a lifetime [Pain 2015b and references therein] including the heart [Stookey 1963, Panneerselvam 2015] and arteries [Greever 1971, Susheela 1990]. The accumulation of Fluoride involves microcalcification which is discussed in the next section.

The toxic impact of Fluoride on the heart and arteries has been studied by hundreds of scientists and carefully reviewed but has not attracted the interest of the media or science journalists, therefore the general public and politicians remain ignorant of the risks [Agalakova 2012, Blank 2012, Waugh 2013, FAN 2016].

The manufacturers of Fluorosilicic Acid used in fluoridation of public drinking water are aware that acute exposure to the toxin is likely to induce ventricular fibrillation and cardiac arrest [CSBP 2005].

The warning signs of a direct link to increased heart disease mortality emerged very early in human experimental Fluoride toxicology studies as discussed by Sauerheber [2013] who summarized the disaster thus:

> "Per capita cardiovascular deaths increased after Grand Rapids, MI, and Newburgh, NY, began industrial fluoridation (U.S. Public Health Service Congressional Record, Mar 24, 1952). 1,059 heart disease deaths occurred per year in 1948 in Grand Rapids, MI after 3 years of fluoridation but 585 yearly before fluoridation. The NY News, Jan 27, 1954 reported after 9 years of fluoridation in Newburgh, NY there were 882 heart deaths per 100,000 which was 74% above the National average."

In Grand Rapids there was an increase of 50%, over a period of 4 years, in the deaths from intra-cranial lesions (Stroke) following the introduction of fluoridation [Miller 1952, cited in Prystupa 2011].

A study of 69 people exposed to Fluoride in their drinking water found that 63 died suddenly, primarily due to trauma, cardiovascular disease, and cerebrovascular causes [Zipkin 1958, cited in Prystupa 2011]. Cardiac patients have been found to exhibit high serum Fluoride [Hanhijarvi 1981].

Fluoridation is known to increase systolic blood pressure [Amini 2001]. This hypertension is a primary risk factor for cardiovascular disease.

The Republic of Ireland (fluoridated) has the second highest mortality rate from ischaemic heart disease in Western Europe (non-fluoridated) and premature deaths for individuals below 65 years of age from ischaemic heart disease are above the EU15 and EU27 [Waugh 2013].

The Australian Experience

Experiments on Australian humans show similar results. Townsville (subject to fluoridation) also suffers higher rates (compared to non-fluoridated Queensland) of hospital admissions for congestive heart failure and increased death rates due to circulatory system, ischaemic heart disease and cerebrovascular disease – Stroke [Queensland Hospital Data 2005-2006].

The Australian National Health and Medical Research Council (NHMRC), in its rushed review [Coleman 2007a] of the health impacts of water fluoridation, chose to deliberately ignore [Coleman 2007b] numerous examples of evidence relevant to cardiovascular damage by Fluoride that it found by literature search [Houtman 1996, Tyagi 1996, Artru 1997, Johnson 1998, Maheswaran 1999, Jehle 2000, Kousa 2004, Bogatchera 2006 and references therein].

The scope of the NHMRC survey was inadequate, failing to find other directly relevant studies such as toxic effects of fluoride on beating myocardial cells cultured *in vitro* [Wang 1998].

Perhaps the NHMRC did not want to discuss unfavourable interactions of Fluoride with metallo-enzymes [Houtman 1996, Tyagi 1996, Johnson 1998].

Perhaps the NHMRC did not want to discuss unfavourable interactions of Fluoride with Magnesium metabolism [Maheswaran 1999].

Perhaps the NHMRC did not want to discuss or draw attention to unfavourable interactions of Fluoride known to increase cardiovascular hazards interleukin-6 and interleukin-8 [Jehle 2000].

Perhaps the NHMRC did not want to discuss the results of Bogatcheva and co-workers who state "Exposure to fluorides induces inflammatory reactions, cell contractile responses, cell proliferation or cell cycle arrest, and apoptosis" and discuss Fluoride induced intracellular increase in Calcium, endothelial cytoskeletal rearrangement and changes in permeability and its toxic impact on numerous biological pathways [Bogatcheva 2006, note references therein].

The NHMRC cherry picked a single study that they thought was evidence of a "small protective effect" of Fluoride against heart attack [Kaipio 2004], but did not discuss the statistically insignificant results in Kousa [2004].

International Research

Although the toxic effects of Fluoride on the cardiovascular and cerebrovascular systems have not received adequate attention in Australia, most of the advanced world has had teams of researchers working on the details over the last 60 years.

Acute and chronic Fluoride poisoning is known to induce heart arrhythmia [Karademir 2011] and is associated with hypocalcaemia. Abnormal electrocardiograms (ECGs) are observed at higher rates among those with skeletal fluorosis [Okushi 1954, Takamori 1956, Wang 1983, Xu 1997, Ji 2004, Liao 2013].

Children with dental fluorosis have altered ECGs, including prolonged Q-T interval, a biomarker for arrhythmias and a risk factor for sudden death [Tokushima 1956, 1961, Karademir 2011]. Chronic exposure to Fluoride has been shown to increase Fluoride deposition in numerous soft tissues including the heart [Stookey 1963] and aorta [Susheela 1990] and correlates with increased prevalence of hypertension [Walland 1977, Bera 2007], increased risk of stroke, heart attack, heart failure, aortic aneurysms, and peripheral arterial disease [Susheela 1990, Tartatovskaya 1995, Amini 2011].

Fluoride derived by metabolism of common anaesthetics is a major hazard for sudden death whilst under operation or in recovery and for those in the operating room [Artru 1997, Bito 1999, Booth 1998, Conzen 2002, Haufroid 2000, McGrath 1998, Tanagami 1997].

The human observational studies are supported by deliberate experiments on animals with chronic and subacute Fluoride exposure [Dönmez 2003, Kilicalp 2004, Kant 2010, Kumar 2010].

Direct observation of damage to the heart caused by Fluoride includes vacuolar degeneration, haemorrhages, interstitial oedema, fibrous necrosis, dissolution of nuclei, thickening of the vessel walls and coronary artery ectasia [Basha 2011, Cicek 2005, Shashi 2001, Pribilla 1968, Takamori 1956, Dede 2011].

In Fluoride intoxicated rabbits regressive degeneration, cellular infiltration, hyperemia, hemorrhages and thickening of vessel wall were noted in the heart muscle [Okushi 1954].

Cardiovascular Calcification caused by Fluoride

Fluoride doping stabilizes and enhances precipitation of Hydroxyapatite [Pain 2015a]. Hydroxyapatite is the major constituent of the calcified deposits seen in atherosclerotic vessels [Morgan 2005, Tomazic 2001, Stary 2000] and its presence is a cause of coronary events including death [Fitzgerald 1992, Arad 2000].

Coronary calcification dramatically increases the adjusted risk of a coronary event and sudden death, by a factor of 7.73 among participants with coronary calcium scores between 101 and 300 and by a factor of 9.67 among participants with scores above 300 ($P<0.001$ for both comparisons) [Detrano 2008].

As expected, arterial calcifications are associated with skeletal fluorosis [Tuncel 1984]. The aorta has been found to accumulate Fluoride up to 8,400 ppm [Greever 1971]. The elastic properties of the ascending aorta are impaired in patients with mild levels of fluoride toxicity [Varol 2010].

The use of positron emission tomograghy with the radioisotope ^{18}F has enabled detailed studies of calcification sites in arterial walls, the aorta and the heart [Opie 1997, Derlin, Wykrzykowska 2009, Li 2011, Dweck 2014].

Calcification also requires phosphate. Phosphate-induced aortic calcification is accelerated following exposure of uremic rats to fluoride in water at around 1.5 mg/L [Martin-Pardillos].

Fluoride-induced oxidative stress and Inflammation

Fluoride-induced oxidative stress with reduced activity of antioxidant enzymes in the heart has been demonstrated in humans and experimental animals [Barbier 2010, Cheng 2013].

More recent research [Panneerselvam 2015] shows that Fluoride accumulates in the heart and causes measurable myocardial necrosis with increased levels of myocardial troponin I, creatine kinase, lactate dehydrogenase and aspartate transaminase. In this detailed study Fluoride increased reactive oxygen species, lipid peroxidation, protein carbonyl content and nitrate levels and decreased the antioxidant enzymes superoxide dismutase 2, catalase, glutathione peroxidase and glutathione s transferase. Fluoride also reduced glutathione. Increased cardiac expression of Nox4 and p38α MAPK was also observed [Panneerselvam 2015].

Fluoride is a pro-inflammatory factor increasing the formation of reactive oxygen species (ROS) and apoptotic cells in a dose-dependent pattern [Gutowska 2010, Flora 2011].

Cell apoptosis in the heart, caused by Fluoride, follows a similar pattern to its devastating effects on the liver [Cao 2013], hippocampus [Zhang 2013] and kidney [Xu 2006] where altered expression of B-cell lymphoma/leukemia 2 (Bcl-2), Bcl-2-associated protein X (Bax) is observed. Fluoride also triggers apoptosis through increased cytochrome c, caspase 3p20 and terminal deoxynucleotidyl transferase dUTP nick end labeled positive cells [Agalakova 2012, Panneerselvam 2015].

Inflammatory response with increased gene expression of inflammatory-related molecules involved in cell adhesion, chemokines, and pro-inflammatory cytokines has been induced by Fluoride in rabbit aorta [Ma 2012]. Fluoride increased expression of genes involved in leukocyte adhesion [P-selectin

(P-sel) and vascular cell adhesion molecule-1(VCAM-1)], recruitment and transendothelial migration of leukocyte [interleukin-8 (IL-8) and monocyte chemotactic protein-1 (MCP-1)] and those involved in pro-inflammatory cytokines [interleukin-6 (IL-6)].

VCAM-1 plays a critical in atherosclerosis [O'Brien 1993, Ramos 1999, Ley 2001].

P-selectin on activated endothelium and platelets binds monocytes, neutrophils, stimulated T cells, and platelets. This process of adhesion is an important factor in the development of early atherosclerotic lesions [Johnson 1997, Ramos 1999]. Fluoride therefore increases fatty streak formation of the aorta and other sites.

Fluoride increases pro-inflammatory Interleukin-6 (IL-6) levels which are elevated in patients with acute coronary syndromes contributing to the exacerbation of atherosclerosis [Schieffer 2004].

Fluoride increases Interleukin-8 (IL-8). As has been stated "there is sufficient evidence to support beyond any doubt the involvement of IL-8 in the establishment and preservation of the inflammatory micro-environment of the insulted vascular wall" [Apostolakis 2009].

Fluoride increases Monocyte chemotactic protein-1 (MCP-1) which induces infiltration of macrophages at vessel walls and formation of atherosclerotic lesions [Namiki 202, Kusano 2004].

Similar results are obtained with rats [Afolabi 2014]. Fluoride induces contractions in rabbit aorta [Adeagbo 1991]. Fluoride induces vascular contraction through activation of the RhoA/Rho kinase pathway [Yang 2012].

Heart damage resulting from Thyroid damage by Fluoride

Fluoride is well known as a destructive influence on the Thyroid [Durrant-Peatfield 2004] and this has been linked to heart damage caused by insufficient release of T3 and T4, and decrease in the protein-dependent iodine levels of blood [Dönmez 2003]. Reduction of T4 has been linked to hypertension [Streeton 1988] and heart disease [Rodondi 2010]. A study of breakdown and death of racehorses exposed to Fluoride found 12 deaths from sudden heart failure from aortic rupture or myocarditis [UC Davis, cited in Sauerheber 2013]. Many of the horses dying of heart failure were being treated with thyroxine.

Mechanisms leading to cardiovascular damage by Fluoride

As discussed, Fluoride damages the heart in many ways through inhibition of endocrine systems, ion transport, enzymes and calcification leading to inflammation and oxidative stress.

Very useful overviews of the molecular mechanisms of Fluoride toxicity have been provided [Barbier 2010, Agalakova 2012]. Fluoride modulates genes related to the stress response, metabolic enzymes, the cell cycle, cell–cell communications and signal transduction.

Fluoride can also be released by metabolism of Fluorine containing molecules. For example (Z)-4',5'-Didehydro-5'-deoxy-5'-fluoroadenosine and , 5'-deoxy-5'-difluoroadenosine inhibit liver S-adenosyl-L-homocysteine hydrolase [Mehdi 1990] causing Hyperhomocysteinemia. This condition is a risk factor for atherothrombotic vascular disease in the coronary, cerebrovascular, and peripheral arterial circulation [Weiss 2002]. Fluoride thus induces impaired endothelium-dependent regulation

of vascular tone and blood flow, increases recruitment and adhesion of circulating inflammatory cells to the endothelium, and prevents endothelial cell antithrombotic function. Fluoride induced hyperhomocysteinemia increases oxidative stress by decreasing bioavailability of the endothelium-derived signaling molecule nitric oxide [Weiss 2002].

Fluoride attacks the Ryanodine receptor (RyR), a tetrameric, high molecular weight protein that functions as a calcium release channel [Butanda-Ochoa 2006]. RyR is involved in signal transduction, excitation-contraction and excitation-secretion coupling. Fluoride causes Hyperthermia maligna (a common cause of death from fluorinated anaesthetics), central core disease and myocardial infarction by its action on RyR.

Energy production in heart mitochondria is reduced by Fluoride [Pacauskiene 2009]. Further details of mitochondrial damage have emerged from detailed study of damage done to teeth by Fluoride [Suzuki 2015].

Fluoride can act in combination with Aluminium by forming complex ions that mimic phosphate and interfere with normal G protein functions. However Fluoride can also act alone in causing unnatural contractions of arteries and Diabetics are at higher risk of the effect [Hattori 2000].

Fluoride interferes with magnesium availability and this deficiency is associated with arrhythmia and inflammation [Elwood 1994].

Fluoride increases the production of calcitonin. Increased calcitonin levels are associated with coronary artery disease [Waugh 2016].

Fluoride inhibits Periostin, a protein that plays an active role in tissue repair in the heart [Waugh 2016]. Periostin deficiency is associated with cardiac aortic valve abnormalities [Snider 2008].

Fluoride causes coronary vasospasms by stimulating release of endothelium-derived relaxing factor, known to be a major risk factor in ischemia and stroke [Waugh 2016, Cushing 1990].

Fluoride induces catecholamine release from the adrenal glands [Niloufer 1996]. Elevated catecholamine contributes to hypertension, atherosclerosis and myocardial ischemia.

Fluoride stimulates Haptoglobin, a recognized risk factor for coronary artery disease and hypertension [Jethanandani 1995].

Low dose fluoride exposure of human cells ranging from 0.1-0.45ppm induced a 40% increase in lipid peroxidation. Lipid peroxidation is associated with atherosclerosis and ischemic heart disease through increased production of free radicals, known as oxidative stress.

Depletion of thioretinaco ozonide from cellular membranes has been suggested to underlie the carcinogenic and atherogenic effects of fluoride and other electrophilic carcinogens [McCully 2009, cited in Osmunson 2015].

Fluoride interferes with Melatonin production. Melatonin is known to suppress LDL receptor activity and synthesis of cholesterol, it decreases blood pressure [Scheer 2004], heart rate, serum lipids and atherogenic index [Kearney 2015]. Melatonin has the capacity to scavenge free radicals resulting from oxidative stress. Decreased nocturnal synthesis of Melatonin is observed in patients with

coronary artery disease [review by Pandi-Perumal 2006, cites Arangino 1999, Girotti 2003, Scheer 2003, Yaprak 2003].

Sophisticated proteomics techniques have been applied to the study of the toxic mechanism of Fluoride on heart muscle. [Lu 2009]. Twenty-one differentially expressed proteins were found, of which 15 were identified, including Telomerase reverse transcriptase, 4SNc-Tudor domain protein, protein disulfide isomerase ER-60, Tuba1 protein, mitogen-activated protein kinase 10, and SMC4 protein.

Vulnerable Groups

The U. S. Center for Disease Control Agency for Toxic Substances and Disease Registry states that, "These populations (those who are at higher risk of the adverse effects of Fluoride) include the elderly, people with deficiencies of calcium, magnesium, and/or vitamin C, and people with cardiovascular and kidney problems." [US Department of Health and Human Services 1993].

Fluoridation of drinking water at 1.5mg/L "dramatically increased the incipient aortic calcification observed in rats with experimental chronic kidney disease" [Martín-Pardillos 2014, cited in MacArthur 2015].

There is clear evidence that Fluoride causes Diabetes [Pain 2015d]. Diabetics are at increased risk of Fluoride toxicity and cardiovascular disease [Hattori 2000]. This is confirmed by animal studies. Streptozotocin induced diabetic rats experience enhanced contractile responses of arteries to sodium fluoride [Weber 1996]. Hyperinsulinemia enhances myocardial calcification [Ng 1998].

In 2003–2006, after adjusting for population age differences, cardiovascular disease death rates were about 1.7 times higher among adults aged 18 years or older with diagnosed diabetes than among adults without diagnosed diabetes. Rates for heart attack were 1.8 times higher among adults aged 20 years or older with diagnosed diabetes. Rates for stroke were 1.5 times higher [CDC 2014].

Sudden cardiac death in young children has been investigated in fluoridated Republic of Ireland [Morris 2009].

Fluoridation delivers Lead to the Cardiovascular system

Fluoridation of public drinking water directly raises the amount of Lead intoxication of the unwitting population through the process of Plumbosolvency [Pain 2015c]. Fluoride enhances sudden death by Lead intoxication.

Lead exposure significantly increases all-cause, circulatory and cardiovascular mortality [Lustberg 2002]. Lead increases mortality from myocardial infarction and stroke with increasing blood lead concentration after a 12 year follow-up of 13,946 adults [Menke 2006]. The association of Lead with hypertension has been investigated [Navas-Acien 2008].

The recent water crisis in Flint Michigan which saw over 100,000 residents delivered contaminated drinking water with toxic doses of Lead and Fluoride will unfortunately claim victims of cardiovascular disease as well as neurological damage in future years.

Conclusion

This brief survey shows that hundreds of scientists have studied the toxic impact of Fluoride on the cardiovascular system for over 70 years and the detailed evidence of harm is overwhelming. The general public needs to be warned to minimize their total Fluoride intake. Especially vulnerable groups such as the unborn, diabetics and those with compromised kidneys or thyroid must be protected. Promotion of Fluoride and Fluoridation must cease. Politicians must purge the bureaucracy of Fluoride promoters. Not a single excess death caused by water fluoridation can be tolerated.

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