THE AUSTRALIAN FLUORIDATION NEWS

ARTIFICIAL FLUORIDATION IS WATER POLLUTION

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Fluoride causes Diabetes

As the dental and medical professions promote the Fluoride "wonder drug" unquestioningly, scientific studies are continuing to reveal that Fluoride causes more harm than good, including Diabetes and Obesity. State-mandated Artificial Water Fluoridation creates the medical effects detailed here, along with unnecessary human suffering and increased business for the medical profession trying to treat the effects rather than address the actual causes.

The Western Australian Government Inquiry into Diabetes Prevention and Management refused the 2018 version of this paper without giving a reason. Perhaps the inquiry had a pre-determined conclusion and this paper would have been hard to respond to. This 2018 paper is referenced extensively and may require a medical dictionary and a knowledge of statistics to better understand its complexities. But even without medical knowledge, this paper shows clearly that there's far more to Fluoride than the dogmatic "safe and effective" mantra. How might Fluoride be affecting you?

by Geoff Pain PhD.

Abstract

Experts in endocrinology have shown that Fluoride causes Diabetes and Obesity. This review assembles the wealth of science that shows how Fluoride damages the organs that generate or use Insulin to control Glucose metabolism and the crucial involvement of other hormone systems.

Keywords: Anaemia, Anovulation, Arsenic, Autophagy, Cadmium, Cataract, Comorbity, Coronary Disease, Diabetes, Endoplasmic Reticulum Stress Fluoride, FoxO1, Ghrelin, Hypertension, Hyperinsulinemia, Hyperkalemia, Hyperlipoproteinemia, Hormone, Insipidus, Insulin, Kidney, Lead, Low-dose endocrine disruptor, Mellitus, Mercury, MHC 1, Obesity, Proinsulin, Secondary Hyperparathyroidism.

Introduction

This review updates an earlier version summarizing the peer-reviewed literature that was easily accessible to March 2015 [Pain 2015]. Since then there have been many publications that report advances in the enabling technologies, such as protein and mRNA sequencing, that add sophistication to the earlier definitive works.

The immense scale of the Diabetes problem is summarized by the World Health Organization [Bergman 2013] as follows:

> *"The number of diabetics in the world is expected to increase from 194 million in 2003 to 330 million in 2030 with three of four affected individuals living in developing countries. The global health expenditure on diabetes alone is expected to rise to US$ 490 billion in 2030 – 12% of all per capita health-care expenditures [Zhang 2010]. The burden of premature death from diabetes in developing countries is similar to that of HIV/AIDS, yet the problem is largely unrecognised in these areas."*

There has been an explosion in the incidence of diabetes in the developed countries over the last 40 years [Bergman 2013] which matches the timescale of deliberate fluoridation of public water supplies in those countries.

In simple terms Diabetes involves the disruption of key biochemical pathways involving hormone signalling, enzyme production, metabolism of food and storage of sugars and fats. The key organs involved are the Brain,

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which responds to hunger stimulus, Pancreas which produces the glucose controlling hormone Insulin, the Liver which produces Glucose, the muscles which store and use Glucose. Common to all organs damaged by Fluoride are the energy producing mitochondria [Dabrowska 2004, Maassen 2004].

Peripheral neuropathy is linked to advanced glycation products [Misur 2004, Kellow 2014]. Morbidities associated with Diabetes include pancreatic cancer, anovulation [Dunaif 1995, Franks 1996], dyslipidemia, cardiovascular disease, hypertension, infertility, endometrial hyperplasia, and endometrial cancer.

Figure 1. Factors in increased Blood Glucose levels [Khardori 2017]

[#] Increased carbohydrate intake,
Increased hepatic glucose production,
Decreased peripheral glucose uptake,
Decreased insulin secretion;
All result in increased blood glucose

Recent proteomic analysis of Fluoride damage to the jejunum could affect the neuronal functions of the gut with increased expression of numerous transporter proteins [Dionizio 2018]. This provides a possible explanation for the increased sensitivity to insulin recently reported to occur in rats with diabetes induced by streptozotocin exposed to 10 mgF/L in the drinking water [Leite 2014, Lobo 2015].

Fluoride is an Endocrine disruptor

As seen in the following Table (Figure 2), Fluoride is well known as an Endocrine disruptor [Bergman 2013].

Table 1.4. Examples of EDC with low dose effects (in animals)

Insecticides/Fungicides	**Industrial/General**
Chlordane	Arachlor 1221
Chlorothalonil	Bisphenol A /Genistein /DES
Chlorpyrifos	Dioxin
DDT	4-methylbenzylidene
Heptachlor	Methylparaben
Hexachlorobenzene	Nicotine
Maneb	Nonphenol
Parathion	Octyphenol
Methoxychlor	**Sodium Fluoride**
Tributyltin oxide	PBDEs/PCBs
Vinclozolin	Perchlorate

Figure 2. Fluoride in a Table of Low Dose Endocrine Disruptors [Bergman 2013]

Furthermore Fluoride is known to cause Diabetes by simultaneously affecting multiple hormone systems (Figure 3) [Vandenberg 2012].

[# The large table includes more than 25 endocrine disrupting chemicals (EDCs) including atrazine, BPA, Chlordane, DDT, DES, Dioxin, Parathion, PBDE, PCBs and Perchlorate. Sodium fluoride is listed as a water additive (to prevent dental caries), cleaning agent; Inhibits insulin secretion, PTH, TH (thyroid hormone); Low-dose cutoff: 4 mg/liter water ([US] EPA standard); Affected Endpoint: Bone mass and strength.]

Parts of this paper (particularly some graphical elements) have been removed as they would not reproduce well in this format, as indicated by [# ...]. In some cases they are replaced by summarising text.

Please refer to the original paper on ResearchGate at www.researchgate.net/profile/Geoff_Pain.

Figure 3. Fluoride used as a water "additive" is stated by expert endocrinologists to inhibit Insulin secretion and damage Parathyroid and Thyroid Hormone systems, also impacting on bone mass and strength [Vandenberg 2012]

The reduction in Insulin expression and the messenger RNA that controls it is clearly dose-dependent (Figure 4) [García-Montalvo 2009].

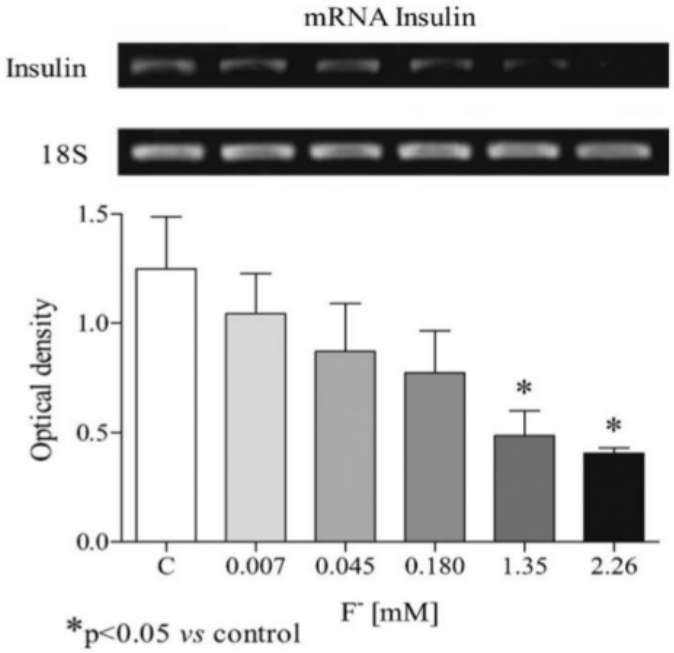


Figure 4. Clear Dose-dependent Insulin and mRNA reduction by Fluoride [García-Montalvo 2009]

I have summarized some of the hormone systems known to be damaged by Fluoride (Figure 5). Hormones and their receptors mentioned in this figure include Thyroid Stimulating Hormone, Leptin, Ghrelin, Antidiueretic Hormone, Follicle Stimulating Hormone Receptor, Luteinizing Hormone Receptor, Triiodothyronine (T#), Thyroxine (T4), Catecholamines, Insulin, Prostoglandin, Testosterone, Estradiol, Melatonin, Parathyroid Hormone, Calcitonin, CD4(+), CD8(+), Inhibin. Damage by Fluoride often proceeds by attack on key enzymes including Alkaline Phosphatase, Iodothyronine Deiodinase, Adenylate Cyclase, Vassopressin.

[# World Health Organization Low Dose Endocrine Effects] Figure 5. Hormone systems known to be damaged by Fluoride.

It has been said that there are perhaps 5 types of diabetes including Diabetes Insipidus, Type 1 Diabetes Mellitus caused by the pancreas not producing adequate amounts of Insulin, and Type 2 Diabetes Mellitus caused by the body's cells becoming less responsive to insulin that is produced. Diabetes takes a terrible toll on the quality of life and kills many Australians.

Ghrelin hormone disruption is a vital contributor to Diabetes because it enhances appetite and increases food intake in humans [Wren 2001]. **Fluoride upsets metabolism by upregulation of Ghrelin expression in the stomach upon fasting** [Toshinai 2001]. Ghrelin modulates the downstream molecules of insulin signalling in hepatoma cells [Murata 2002]. Ghrelin disruption is also implicated in salt-induced and maternal Hypertension [Hamada 2012].

[#] Over time, poorly managed diabetes can damage cells' ability to hold together, causing serious problems:
- Lost-eyesight & Blindness
- Dialysis & kidney failure
- Sores & Amputation

Figure 6. Before Premature Death, Diabetes patients suffer terrible comorbidities

Diabetes Insipidus victims of water Fluoridation suffer dreadful damage to their Teeth as shown by Australian researchers (Figure 7) [Seow 1994]. They drink very large volumes of water, up to 30 litres per day [Pivonello 1998, Prystupa 2011].

[# Fluoride damages teeth of countless people suffering Diabetes insipidus - example from Brisbane Australia. Note use of "optimal", "moderate" and "severe". Photos removed]

Figure 7. Diabetes Insipidus causes severe Fluorosis and Tooth Decay, note Mercury fillings [Seow 1994].

 # Figure 8. Far-reaching complications of Diabetes [Anon]

[# Mindmap of diabetes complications: from signs and symptoms, diagnostics, treatments, complications, non-healing wounds, and causative factors; in considerable detail.]

Epidemiology of Diabetes in relation to Fluoride

Workers in the phosphate fertilizer industry are exposed to Fluoride and experience higher incidence of diabetes as well as skeletal fluorosis [Renke 1987].

Workers in the cryolite industry also suffer Chronic Fluoride Intoxication (CFI) and have lower insulin and increased C-peptide serum levels [Tokar 1992]. It was shown that the incidence of diabetes increased with years of exposure. The observed lower serum insulin levels in Fluoride intoxication might be due to associated liver damage [Tokar 1992]. Liver damage has also been observed by Vasant and Narasimhacharya [2013a] who state *"Exposure to fluoride through drinking water not only significantly increased plasma glucose and lipid profiles, but also elevated both hepatic and renal lipid peroxidation, hepatic lipid profiles and G-6-Pase activity with a reduction in plasma HDL-C, hepatic glycogen content, hexokinase activity and antioxidant status"*.

Diabetes has been increasing in a number of countries since the 1940s in line with the roll out of Fluoridation. Insulin resistance in humans caused by chronic Fluoride exposure from drinking water is well known [Trivedi 1993, Stephen 1994, Cheoud 2008, Menoya 2008, Chiba 2010, Chiba 2012a, 2012b Bergman 2013, Vandenberg 2012].

In chronic exposures, effects on glucose metabolism occurred when plasma fluoride concentrations exceeded 0.1 mg/L (5 µmol/L) [Rigalli 1992, 1995], or just one 15th the concentration allowed in Australian drinking water. The US National Research Council [2006] stated *"In general, impaired glucose metabolism appears to be associated with serum or plasma fluoride concentrations of about 0.1 mg/L or greater in both animals and humans."*

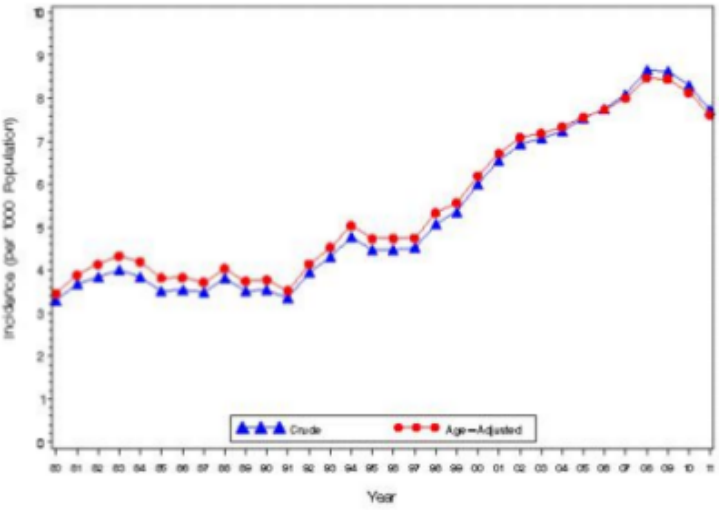


Figure 9. USA increase in Diabetes incidence 1980-2011 [CDC]

More detailed analysis of Diabetes incidence in USA was provided (Figure 10) [Waugh]:

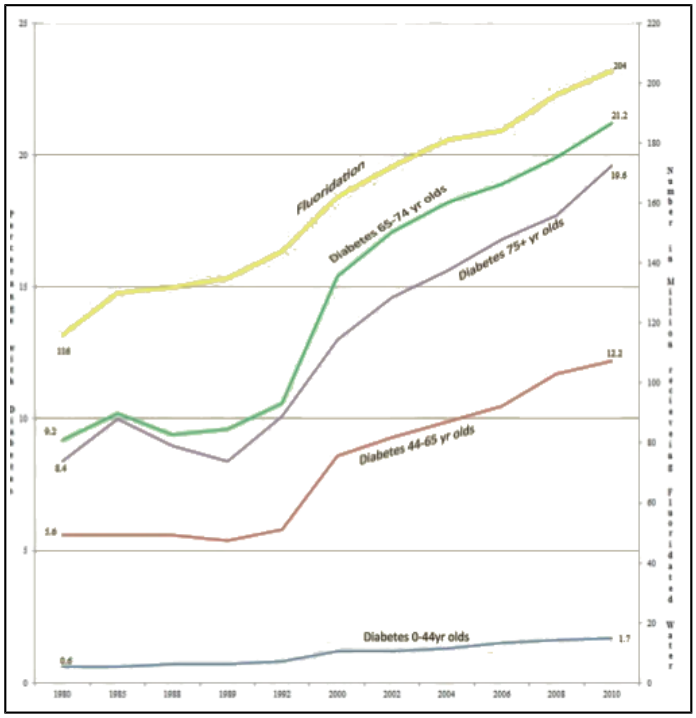


Figure 10. More detailed analysis of Diabetes incidence in USA [Waugh 2014] [# The uppermost line shows the increase in fluoridation between 1980 and 2010. The remaining four lines show the increase in diabetes for different age groups, as shown in the table below.]

Group / Diabetes Prevalence	% Increase
(USA Fluoridation, from 116m – 204 million)	**176%**
75+ yr olds	125%
65 – 74 yr olds	140%
45 – 64 yr olds	118%
0 – 44 yr olds	**167%**

Canada displays regional variations in Type 1 Diabetes that correlate with Fluoridation status [Chafe 2018].

Diabetes Mortality has increased in the Republic of Ireland (Fluoridated) much more than in Northern Ireland [Waugh].

Fig 11. **[removed]** Higher Diabetes Death rate in Fluoridated Republic of Ireland [Waugh 2014]. **[#** "Versus Northern Ireland (non-fluoridated)... 1989-1998. The Directly Standardised Mortality Rate for persons in the Republic of Ireland was significantly higher than it was in Northern Ireland (372%)"**]**

Diabetes in Australia

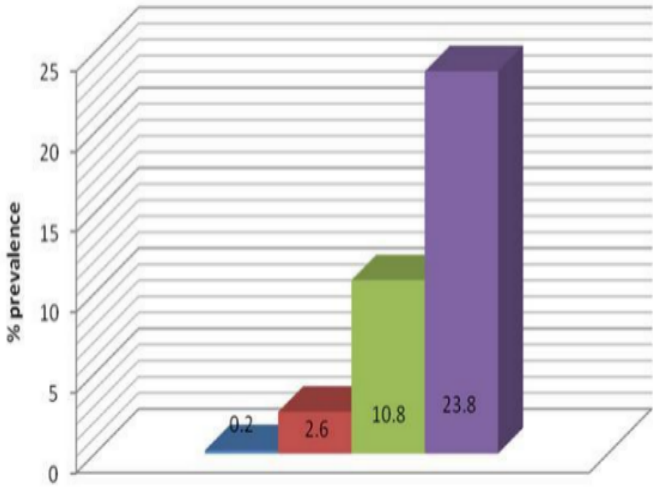
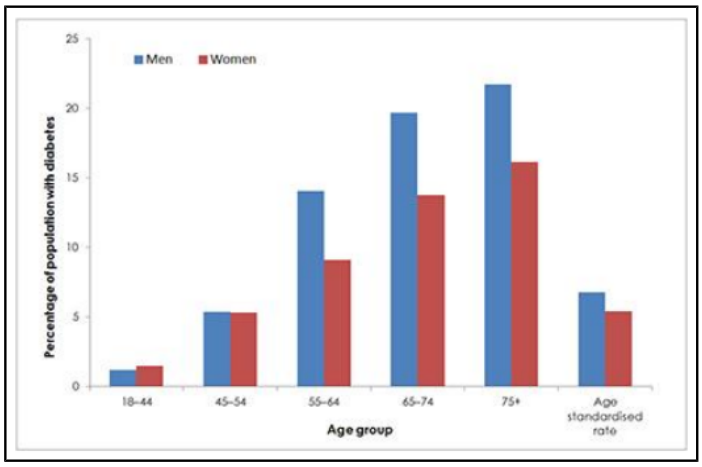


Figure 12. Prevalence of Diabetes in Australia versus Age

[# Columns from left to right are *Age Ranges*: < 20 (0.2%); 20-39 (2.6%); 40-59 (10.8%); 60+ (23.8%)]

Figure 13. Diabetes Gender difference with Age in Australia

There is strong gender dependence with men [at left] more affected than women [at right] with increasing age.



Looking at data from New South Wales, which is almost completely Fluoridated, we see an alarming increase if Diabetes in children from 1990 to 2002 **(Figure 14).**

[# Trend line increasing from 14 to 21 per 100,000]

Figure 14. Alarming increase if Diabetes [Type I] in NSW children from 1990 to 2002 **[# Graph Removed]**

If Fluoridation is a factor in increased Diabetes, we would expect to see lower incidence in communities that have not received the poison in their drinking water. Byron in New South Wales has resisted relentless pressure from the Fluoride waste disposal industry and indeed shows lower Diabetes incidence.

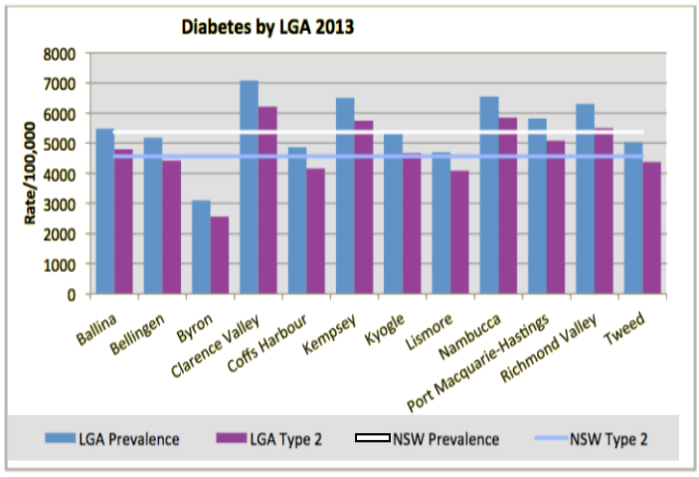


Figure 44 Diabetes Registrations/100,000 by LGA 2013 [28]

Figure 15. Byron is not Fluoridated and shows lower Diabetes incidence [* Byron is the third set of columns from left]

Townsville in the state of Queensland, Australia, fluoridated since 1964, suffers 10% higher rate of diabetes than the rest of non-fluoridated Queensland (not poisoned with Fluoride until 2008) [PHIDU 2005].

Townsville also suffers higher rates of hospital admissions for unspecified dental conditions, as well as asthma, congestive heart failure, convulsions and epilepsy, congestive obstructive pulmonary disease, ear nose and throat conditions and pyelonephritis. Townsville also suffers increased death rates due to circulatory system, ischaemic heart disease, cerebrovascular disease – Stroke, chronic lower respiratory disease and cancer of the trachea [Queensland Hospital Data 2005-2006]. **Townsville can therefore be considered a randomised control trial centre for Fluoride toxicology.**

Fluoride alteration of Insulin levels

A recent study [Rogalska 2017] found, unsurprisingly, that Plasma fluoride levels in Wistar rats after 30 days of drinking fluoridated water were significantly ($p < 0.05$) higher in the group exposed to NaF 50 ppm (0.0823 ± 0.0199 µg/ml) in comparison to control (0.0541 ± 0.0135 µg/ml) and NaF 10 ppm (0.0596 ± 0.0202 µg/ml).

Plasma glucose concentration trend was up but did not significantly differ among the experimental groups.

However, plasma insulin levels (Figure 16) were significantly higher as fluoride concentration increased in drinking water, attaining significance between control (0.48 ± 0.24 µg/ml) and fluoride (50 ppm) groups (0.72 ± 0.13 µg/ml). Hyperinsulinemia enhances myocardial calcification [Ng 1998].

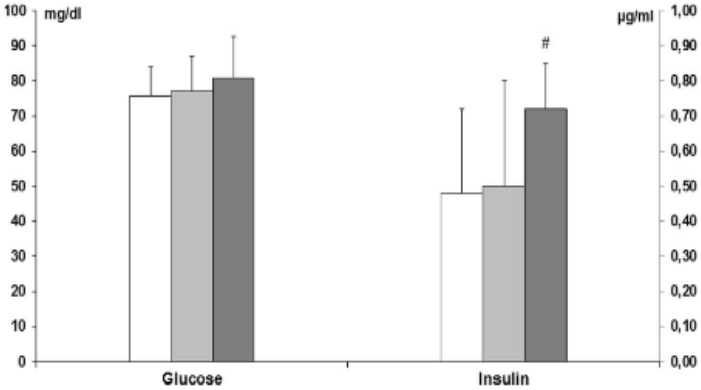


Figure 16. Increased Plasma Insulin in Fluoride treated Wistar rats [Rogalska 2017]

Simultaneously, glucose uptake by the rat Brain increased with Fluoride dose, initiating an elevation in carcinogenic malondialdehyde (the end product of lipid peroxidation) and an increase in damage to hippocampal neurons [Rogalska 2017]. Various regions of the brain are affected by Insulin, including the hypothalamus, ventral tegmental area, substantia nigra, and amygdala. Positive feedback of damage has been demonstrated by the finding that diet-induced obesity induces endoplasmic reticulum stress (also induced directly by Fluoride [Sharma 2008, Ito 2009]) and insulin resistance in the amygdala of rats [Castro 2013].

Fluoride interference with Insulin will also translate to the disruption of the adipocyte hormone Leptin, which is involved in the regulation of food intake, energy expenditure, and body fat stores [Mueller 1998].

Diabetes from Fluorinated Drugs and Drugs used in Fluoridated areas

Many Fluorine containing drugs are metabolized to liberate free Fluoride ions. A recent study showed that exposure to statins increased risk of Diabetes with increasing dose of statin from the hazard ratio of 1.17 (95% CI 0.84-1.65) for the lowest dose to 1.51 (95% CI 1.14-1.99) for the highest dose [Jones 2017].

Autoimmune Destruction of Pancreas Cells caused by Fluoride produces Type 1 Diabetes

A very important study that the NHMRC ignored in its 2017 Review was submitted by me as vital evidence [Irmak 2014]. **One can easily see why the NHMRC wants to bury this key paper by reading the authors' own words (with minor edits for clarity):**

"The incidence of Type 1 diabetes has increased substantially in Finland. We know that use of amoxicillin and anti-cariogenic fluoride tablets is a common practice for children in Finland. It seems that beta-cell destruction is initiated by modification of the proinsulin by combined effects of fluoride and amoxicillin.

"Amoxicillin especially when used together with clavulanic acid results in an acid environment around the beta-cells that promotes the conversion of Fluoride ion to hydrogen fluoride (HF).

"Unlike Fluoride ion, HF can diffuse easily into the beta-cell cytosol. Because the cytosol has a neutral pH, virtually all HF reverts to Fluoride ion in the cytosol and Fluoride ion cannot easily diffuse out of the cell.

"Exposure to excess promotes proinsulin covalent dimerization and simultaneously hyperexpression of MHC Class I molecules.

"Proinsulin dimers then migrate to the cell membrane with MHC class I molecules, accumulate at the beta-cell membrane and produces a powerful immunogenic stimulus for the cytotoxic T-cells.

"Production of cytotoxic cytokines from the infiltrating Tcells initiates the destruction of beta-cells. In Finnish children, this might be helped along by a higher beta-cell activity and by a reactive thymus-dependent immune system induced by higher levels of thyroid hormones and calcitonin respectively. After repeated similar attacks, more and more effector T-cells are raised and more and more beta-cells are destroyed, and **clinical diabetes occurs.**" [Irmak 2014].

However the idea that Fluoride defeats the diffusion barrier by entering the cell as Hydrogen Fluoride and is converted to Fluoride ions, allowing it to concentrate above the extracellular concentration is not new.

Experiments were performed to show that Fluoride is more toxic at lower pH [Sharma 2010].

As shown in Figure 17 there is absolutely no doubt that the above mechanism for Fluoride bioaccumulation is occurring daily in people exposed to the toxin.

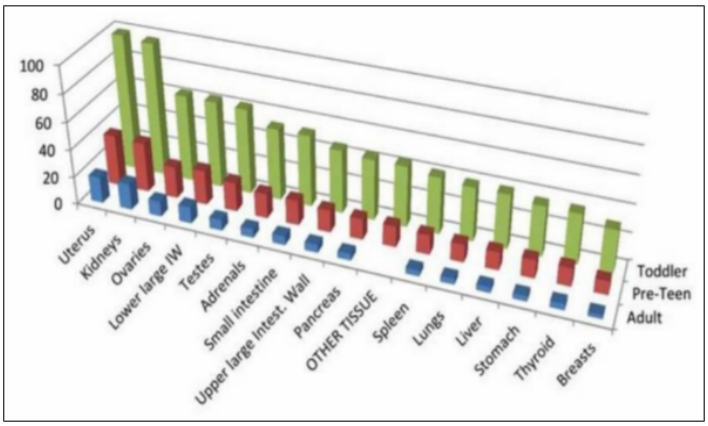


Figure 17. Bioaccumulation of Fluoride is demonstrated at all ages in Humans through use of Radioactive 18F [By Organ, for Toddler, Pre-teen and Adult; by percentage]

Autoimmune diseases represent a spectrum of disorders caused by inflammation of organs due to production of antibodies against self-structures and cytotoxic action of T cells and such antibodies can affect multiple organs. Type 1 Diabetes Mellitus is associated with anti- thyroid-stimulating hormone receptor, anti- thyroid peroxidise, and anti-thyroglobulinantibodies [Fröhlich 2017].

Thyroid hormone disruption can be measured when the Fluoride concentration is just 0.5 ppm. Hypothyroidism in people exposed to Fluoride in drinking water is closely associated with other diseases including Diabetes (odds ratio: 3.7, 95% Confidence Interval (CI): 1.7–8), Hypertension (odds ratio: 3.2, CI 95%: 1.3–8.2), and volume of water consumption (odds ratio: 4, CI 95%: 1.2–14) [Kheradpisheh 2018].

Epidemiology of Pancreatic Cancer

Fluoridated areas suffer higher Pancreatic Cancer Death and incidence rates than non-Fluoridated areas in the USA [Takahashi 2001] and we know Australia's NHMRC was still discussing this fact in 2013. Ghrelin, up-regulated by Fluoride, promotes pancreatic adenocarcinoma cellular proliferation and invasiveness [Volante 2002, Duxbury 2003].

[# Pancreas Cancer rate is 34% higher in Fluoridated communities – only 7% survival rate after 5 years]

Figure 18. Higher Death Rates for Pancreas and Liver Cancer in Fluoridated areas

One of the key reasons that there is such a low survival rate for Pancreatic Cancer is that general practitioners might easily ignore warning signs (Figure 19).

[# Ten Warning Signs of Pancreatic Cancer: Jaundice, Diabetes, Abdominal & Lower Back Pain, Weight Loss, Nausea & Vomiting, Greasy or Light coloured stool, Lack of Appetite, Changes in Urine Colour, Fatigue & Weakness, Bloating**]**

Figure 19. Common warning signs ignored leading to high Pancreatic Cancer Mortality

Pancreatic Cancer Deaths for men are higher than those for women in Australia (Figure 20). This is in line with the incidence of Diabetes shown above in Figure 13.

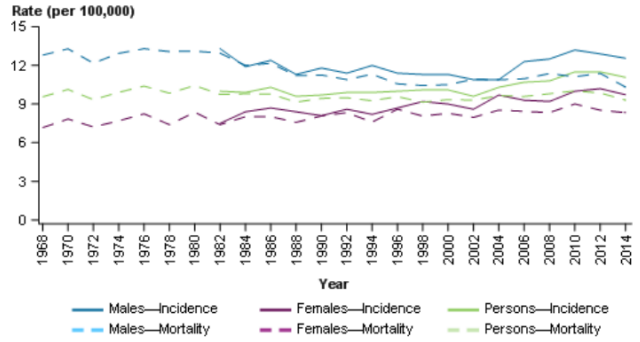


Figure 20. Gender difference for Death and Incidence rates of Pancreatic Cancer in Australia [AIHW]. [# Males at top; persons: middle; females: lower]

Kidney and Diabetes patients need extra protection from Fluoride

Previous studies have emphasized the adverse impact of Fluoride on diabetic patients because they typically consume much larger quantities of water than average humans and have impaired kidney function leading to higher risk from the diverse toxic effects of Fluoride [see for example Prystupa 2011, Doull 2006, Marier 1977]. It has also been shown that Fluoride toxicity is greater in diabetics [Banu Priya 1997].

Diabetics suffer impaired glucose tolerance (IGT), hypertension, hyperlipoproteinemia and coronary disease. They have a higher risk of death from breast cancer [Youlden 2009], pancreatic cancer [Michaud 2004], uterine cancer [Purdie 2001] and colorectal cancer [Youlden 2008]. Diabetics also suffer reduced bone mass and strength through Fluoride exposure [Dunipace 1996]. The Pancreas has been shown to produce a bone/calcium metabolism-regulating factor which is disrupted by Fluoride [Izbicka 1996].

Diabetics have a higher incidence of chronic kidney disease which leads to impaired renal clearance of fluoride [Hanhijarvi 1974], the "vicious cycle" that too often results in Death or the need for transplant.

The role of Diabetes in **End Stage Renal Failure (ESRF)** is highlighted in Figure 21 [Atkins 2005].

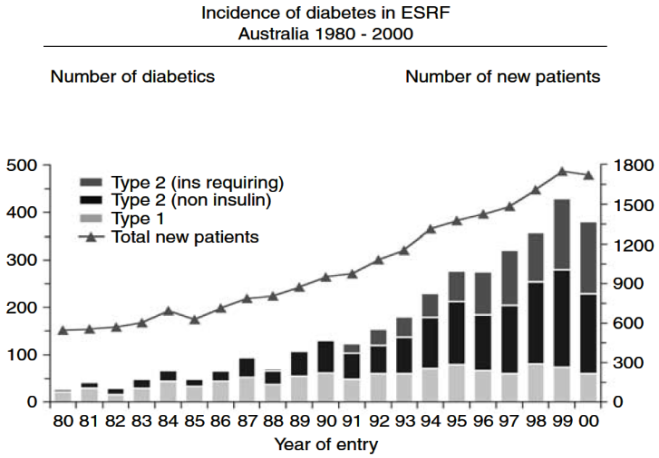


Figure 21. Incidence of Diabetes in ESRF Australia from 1980 to 2000 [Atkins 2005]

In 2005, 18% of adult Australians had at least one indicator of chronic kidney disease, including hematuria (5.6%), proteinuria (2.4%), albuminuria (5.3% in males and 7.1% in females), and renal impairment, defined by a calculated GFR of less than 60 mL/m, was 12.1% [Atkins 2005].

The Australian Institute of Health and Welfare has forecast the proportion of diabetics undergoing transplants or dialysis would rise to 64 per cent in 2020 from 45 per cent in 2009 [Henderson 2012].

The total number of Australians being treated for end-stage kidney disease is forecast to rise by up to 80 per cent to about 4300 in the coming decade.

Comparison of people with diagnosed Kidney disease residing in Catalonia, Spain [have] serum fluoride concentration ranging from 28 to 185 micrograms per litre compared to the control group who ranged from 1 to 47 micrograms per litre [Torra 1998].

Hyperkalemia in dialysed patients is caused by Fluoride [Nicolay 1999]. Patients who drank Vichy St-Yorre water had plasma Fluoride levels of 100 to 380 µg/ l, or 5.26 to 20 µmol/l.

Anomalies in Birth Weight due to Fluoride and Diabetes

Diabetic women generally have a higher risk of premature birth and low birth weight children [Patel 1975].

Preventing gastrointestinal damage by lowering the F intake can lead to improved absorption of nutrients and increased fetal growth [Susheela 2010].

However it has been found that in the infants of well nourished diabetic mothers, there is increased glucose transfer to the fetus resulting in β-cell hyperplasia, increased insulin secretion, and greater fetal adiposity [Dunger 2007]. A continuous relationship has been observed between maternal glucose levels and the birth weight of the offspring [Sacks 2010].

These apparently anomalous results have been explained [Aghaei 2015], whereby mechanisms could be present in which raised Fluoride intake could lead to fetal growth being either increased, via increased maternal hyperglycaemia, or decreased, via increased damage to the microvilli with reduced nutrient absorption and anaemia. The net effect depends on the relative strengths of the two effects.

Fluoride directly reduces insulin synthesis in rats [Lin 1976]. Microcirculatory defects, increased capillary permeability and altered protein biosynthesis in the pancreas is associated with Fluoride exposure.

Because human hormones interact with each other, the known adverse effect of Fluoride on melatonin production and the knock-on effect on insulin should also be considered [Rasmussen 1999]. The fact that Fluoride causes hypothyroidism and also exacerbates the damage to diabetics through reduction of peripheral glucose metabolism [Cettour-Rose 2005]. Hypothyroidism induces Secondary Hyperparathyroidism which can contribute to Diabetes.

A genetically inherited condition demonstrates an association between pineal gland hyperplasia and insulin resistance [West 1980].

Blood fluoride level of just 234 ppb after a single acute exposure caused significant impairment in glucose metabolism, as evident by sharp rises in blood glucose and decreases in insulin [Whitford 1987]. Similar results have been measured in rats and human volunteers [Rigalli 1990, Suketa 1985].

Short-term acute exposures to high levels of fluoride generated by metabolism of the fluorinated anesthetic

methoxylflurane impairs the kidney's ability to concentrate urine and produces a diabetes insipidus-like condition marked by excessive urination [Mazze 1977].

Directly observed toxic effects in the pancreas of albino rats caused by Fluoride includes hematological, biochemical, DNA damage, histilogical & immunohistochemical alteration [Agha 2012].

Pancreas pathological morphometry analysis via β cells [Hu 2012] of rats exposed to Fluoride showed increased islet size. The same rats exhibited increased alkaline phosphatise and osteocalcin, increase of serum insulin level and a general decrease of glucagon level. **The complex hormonal interplay between insulin, osteocalcin and other hormones in relation to bone metabolism and glucose metabolism allows Fluoride to intervene at many points in the system and involves FoxO1** [Rached 2010, Kode 2012, Guntur 2012].

Rats with Fluoride induced diabetes that were encouraged to exercise demonstrated accelerated skeletal fluorosis [Lombarte 2013]. Diabetic rats also show enhanced contractile responses of arteries to sodium fluoride which directly stimulates GTP-binding proteins (G-proteins) [Weber 1996].

Fluoride induced hyperglycemia has been stated to be mainly due to increased hepatic glycogenolysis [Varadacharyulu 1997]. **Rabbits fed 16 mg of Fluoride per day exhibited hyperglycemia as well as reduction of bone strength through fluorosis [Turner 1997].**

People exposed to high Fluoride levels in their drinking water suffer a high incidence of skeletal fluorosis.

As demonstrated by Xie et al. [2000] they exhibit a higher and longer lasting blood glucose level after an oral glucose tolerance test (OGTT). Impaired glucose tolerance in humans has been reported in separate studies at F intakes of 0.07–0.4 mg/kg/day, corresponding to serum F concentrations above about 0.1 mg/L [Doull 2006 cited in Ahhaei 2015]. Those with diagnosed skeletal fluorosis demonstrate high levels of serum insulin.

Diabetics are exposed to an acceleration of their disease due to water fluoridation. They typically drink much larger volumes of water [Prystupa 2011] and accumulate, or retain, more Fluoride.

According to Australia's NHMRC, *"People with kidney impairment have a lower margin of safety for fluoride intake. Limited data indicate that their fluoride retention may be up to three times normal"* [NHMRC Australian Drinking Water Guidelines 2004 and 2011].

The mechanisms by which Fluoride induces diabetes most likely include antagonism to calcium and magnesium centred biochemistry [De Valk 1999, Simmons 2010]. Insulin secretion (both basal and glucose-stimulated) by isolated islets of Langerhans in vitro is inhibited as a function of fluoride concentrations [Rigalli 1990, 1995].

Diabetics are more susceptible to Fluoride induced arterial contraction [Hattori 2000] increasing risk of cardiovascular disease. 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].

Fluoride induced diabetes will also cause damage to the periodontum and tooth loss [AHMAC 2001].

Diabetics are a "Sensitive Subpopulation" or "Vulnerable Group" and no attempt has been made by Australian health authorities to warn diabetics about Fluoride toxicity or protect them from harmful exposure.

Breast feeding is known to have a protective role against insulin dependent diabetes [Mayer 1988]. **Breast fed children have much less exposure to Fluoride because human mothers' milk contains very low Fluoride, despite Australian Federal and State government attempts to increase it by Fluoridation.**

Fluoride the Universal Toxin

Fluoride is a bio-accumulative toxin with no nutritional value.

One of the primary mechanisms of Fluoride toxicity, in virtually all studied cell types, is disruption of Guanine nucleotide-binding proteins (G proteins) transmit extracellular chemical signals from transmembrane G-protein-coupled receptors to intracellular targets by activating the cascades of second messengers. This toxic mechanism often involves Aluminium which forms FluoroAluminate ions that mimic Phosphate ions (Figure 22) [Agalakova 2012].

The summary reads: *"**Fluoride is able to stimulate G-proteins** with subsequent activation of downstream signal transduction pathways such as PKA-, PKC-, PI3-kinase-, Ca2+-, and MAPK-dependent systems. G-protein-independent routes include tyrosine phosphorylation and protein phosphatase inhibition. **Along with other toxic effects, fluoride was shown to induce oxidative stress leading to excessive generation of ROS**, lipid peroxidation, decrease in the GSH/GSSH ratio, and alterations in activities of antioxidant enzymes, **as well as to inhibit glycolysis thus causing the depletion of cellular ATP and disturbances in cellular metabolism. Fluoride triggers the disruption of mitochondria outer membrane** and release of cytochrome c into cytosol, what activates caspases-9 and -3 (intrinsic) apoptotic pathway. Extrinsic (death receptor) Fas/FasL-caspase-8 and -3 pathway was also described to be implicated in fluoride-induced apoptosis. Fluoride decreases the ratio of antiapoptotic/proapoptotic Bcl-2 family proteins and upregulates the expression of p53 protein. Finally, fluoride changes the expression profile of apoptosis-related genes and causes endoplasmic reticulum stress leading to inhibition of protein synthesis."*

[#Removed] Figure 22. Mechanisms of Fluoride Toxicity with or without Aluminium [Agalakova 2012]

A similar scheme was published by another group of leading Fluoride toxicologists in 2010 (Figure 23)

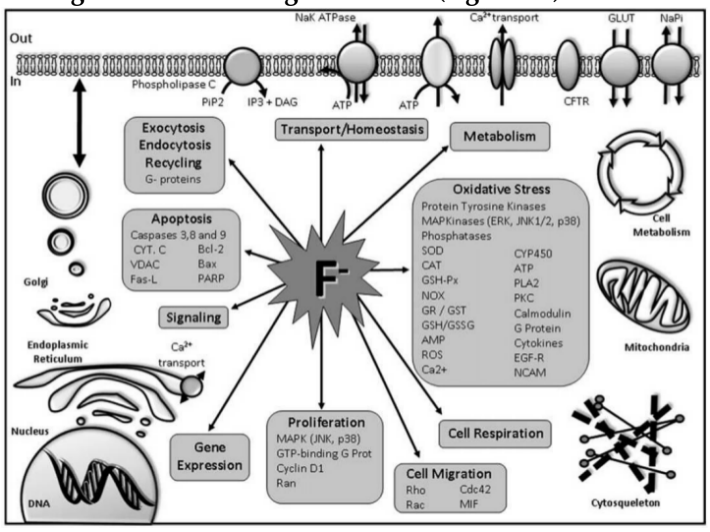


Figure 23. Devastation caused to mammalian cells by Fluoride [Barbier 2010]

Of specific relevance to Diabetes is the destruction of normal Pancreas function.

Optical microscopy revealed increased width of connective tissue and increased mitotic activity in pancreases rats [Ogilvie 1953]. Fluoride-induced ultrastructural changes in exocrine pancreas cells of rats involve disruption the export of zymogens from the rough endoplasmic reticulum [Matsuo 2000].

Dose-dependent toxic Fluoride effects involving Gαi protein have been demonstrated in the clonal RINm5F pancreatic β-cells and rat Langerhans islets [Loweth 1996, Elliott 2001, Elliott 2002].

Fluoride inhibits tyrosine kinase activity of insulin receptors purified from rat skeletal muscles and human placenta by direct binding to the receptors [Vinals 1993].

Reactive oxidation species induced by Fluoride are extremely effective killers of cells. Mouse pancreatic β-cells exposed to 1.35–2.26 mM Fluoride were shown to have elevated superoxide anion resulting in impaired glucose tolerance [García-Montalvo 2009].

Diabetes, metabolic disorders and Cataract

Metabolic cataracts include those associated with Diabetes Mellitus, Galactosaemia, Hypercholesteraemia, Lipidemia, Endocrinological cataract associated with Hypothyroidism and Hypercalcaemia and cataracts associated with certain skin diseases such as Atopic Dermatitis [Dawson 1981, Kador 2008].

Elevated Plasma albumin, bilirubin, calcium, cortisol, glucose, sodium and γ- glutamyl transpeptidase levels in cataract patients were linked to liver disease [Donnelly 1995]. **Fluoride is a known hepatotoxin.**

Diabetes is associated with severe mitochondrial disorders such as Kearns-Sayre syndrome and Mitochondrial Encephalomyopathy, Lactic Acidosis, and Strokelike episodes (MELAS). Mitochondrial forms of diabetes mellitus occur in conjunction with hearing loss, myopathy, seizure disorder, strokelike episodes, retinitis pigmentosa, external ophthalmoplegia and cataracts.

Fluoride is very effective in damaging the retina through inhibition of glycolysis [Sorsby 1960].

There is evidence of maternal inheritance [van den Ouweland 1992, Khardori 2017]. Increased glycated haemoglobin level was associated with increased risk of nuclear and cortical cataracts in those with diabetes [Klein 1998]. Fluoride is known to cause Diabetes [Pain 2015c].

Diabetes is associated with low birth weight and while there is a genetic component to low birth weight [Wang 2016], Fluoride is known to cause low birth weight in exposed populations [Hart, MacArthur 2013].

Prevalence studies on diabetes complications reported up to the early 1990s gave widely variable figures.

These have been reviewed in two studies and include figures ranging from 9 to 16 percent for cataract, 7 to 52 percent for retinopathy, 6 to 47 percent for neuropathy, 6 to 30 percent for nephropathy, and 1 to 5 percent for macroangiopathy [Mbanya 2003; Rolfe 1997].

Women diabetics suffer higher rates of cataract and earlier surgery than men. Risk factors from the Framingham heart study that were significantly associated with cataract formation included: elevated blood sugar, elevated blood pressure, increased serum phospholipids, decreased pulmonary vital capacity, small stature, and less than seven years of schooling [Kahn 1977].

A patient suffering diabetes, ischemic heart disease, hypertension and renal dysfunction and taking insulin developed hydroxyapatite cataracts 4 months after implantation of an intraocular lens. Another patient, diabetic and taking insulin developed hydroxyapatite cataracts 9 months after implantation. Another patient in good overall health developed hydroxyapatite cataracts 15 months after implantation. All patients received dexamethasone sodium phosphate eye drops [Yu 2001].

Prescribed Insulin increases risk of Cataracts, Odds Ratio = 3.38 (95% CI 1.61, 7.08) [Klein 2001].

In cases of suspected suicide by Insulin injection, the vitreous humour of the eye is analysed for the presence of Insulin.

Diabetes and anaemia are comorbidities [Antwi-Bafour 2016]. Anaemia is a direct toxic effect of Fluoride [Susheela 2010].

Laboratory animals with induced diabetes mellitus (NIDD-non insulin-dependent diabetes) demonstrated more vulnerability to fluoride toxicity than non-diabetic animals [Singer 1976].

Vitamin D, Fluoride and Diabetes

Vitamin D deficiency is a risk factor for Diabetes [Holick 2005]. A survey of Canadians living in Toronto, Canada (Fluoridated) found that more than 93% of the total sample had concentrations of serum 25-hydroxyvitamin D [25(OH)D], the main indicator of vitamin D status, below 75 nmol/L [Gozdzik 2008]. Fluoride interference with Vitamin D metabolism and consequent health damage will be reviewed elsewhere.

Other Toxins impacting Diabetes incidence

Diabetes is associated with Arsenic exposure [Del Razo 2011, Gonzalez-Horta 2012, Maull 2012, Currier 2014, Chafe 2018].

Korean researchers found an association between Diabetes and exposure to Lead, Mercury and Cadmium [Moon 2013].

References

Note: Those marked * were deliberately excluded from the NMRC 2007 Review.

Those marked ** were deliberately excluded from the NMRC 2017 Review.

The full (ten page) list of References can be found at: **www.researchgate.net/profile/Geoff_Pain**

Note: *The Australian Fluoridation News* is also available at: **www.fluoride.website/ausfnews/**