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FLUORIDE-INDUCED DEVELOPMENTAL DISORDERS AND IODINE DEFICIENCY DISORDERS AS EXAMPLES OF DEVELOPMENTAL DISORDERS DUE TO DISTURBED THYROID HORMONE METABOLISM

 ABSTRACT: Both exposure to fluoride and iodine deficiency during early development can lead to disturbed thyroid hormone metabolism and produce the same spectrum of developmental disorders including short stature, bone deformities, cognitive impairment, delayed dental eruption, and dental fluorosis. The levels of creatinine-adjusted urinary fluoride experienced by pregnant women in areas with community water fluoridation are similar to those which have been found to result in cognitive impairment and increased attention deficit hyperactivity disorder (ADHD) symptoms as a result of prenatal fluoride exposure. The link between fluoride exposure during pregnancy at the fluoride levels present with community water fluoridation, disturbed thyroid hormones, and developmental disorders due to disturbed thyroid hormone metabolism is now sufficiently clear to warrant the immediate cessation of community water fluoridation schemes.

Keywords: Community water fluoridation; Fluoride-induced developmental disorders; Iodine deficiency disorders; Thyroid hormone metabolism.

In an 2016 editorial, evidence was presented that fluoride-induced developmental disorders (FIDD) in both amphibians and humans can be considered to result from disturbed thyroid hormone metabolism and sonic hedgehog signalling.[1] FIDD in amphibians involve the inhibition of metamorphosis and growth and the disturbance of hard tissue ossification. In humans, the FIDD are seen to include short stature, bone deformities, cognitive impairment, delayed dental eruption, and dental fluorosis.

In addition to the previously cited[2] studies associating prenatal fluoride exposure with impaired cognitive outcomes in children at ages 1, 2, 3, 4, and 6–12 years,[3,4] a further study by a similar investigatory team found that higher levels of F exposure during pregnancy were associated with global measures of attention deficit hyperactivity disorder (ADHD) and more symptoms of inattention as measured by the Connors' Rating Scales Revised (CRS-R) in the offspring.[5] The study was done on 213 Mexican mother-children pairs of the Early Life Exposures to Environmental Toxicants (ELEMENT) birth cohort study which had available maternal urinary samples during pregnancy and child assessments of ADHD-like behaviors at age 6–12 years. The urinary fluoride levels were measured and adjusted for creatinine (MUFcr) in spot urine samples collected during pregnancy. The CRS-R was completed by mothers, and the Connors' Continuous Performance Test (CPT-II) was administered to the children. The results showed the mean urinary fluoride adjusted for creatinine (MUFcr) was 0.85 mg/L (SD=0.33) and the Interquartile Range (IQR) was 0.46 mg/L. In multivariable adjusted models using gamma regression, a 0.5 mg/L higher MUFcr (approximately one IQR higher) corresponded with significantly higher scores on the CRS-R for DSM-IV Inattention (2.84 points, 95% CI: 0.84, 4.84) and DSM-IV ADHD Total Index (2.38 points, 95% CI: 0.42, 4.34), as well as the following symptom scales: Cognitive Problems and Inattention (2.54 points, 95% CI: 0.44, 4.63) and ADHD Index (2.47 points; 95% CI: 0.43, 4.50). The shape of the associations suggested a possible ceiling effect of the exposure. No significant

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associations were found with outcomes on the CPT-II or on symptom scales assessing hyperactivity.

Consistent with these findings that prenatal fluoride exposure can adversely affect neurodevelopment is the 2018 study by Mustafa et al. of the relationship between drinking water F levels and the schooling performance of 775 primary school pupils, 315 boys and 460 girls, aged 6–14 years, in 27 schools, in 16 rural areas remote from industrial pollution by heavy metal neurotoxicants in Khartoum state, Sudan, with a similar socioeconomic status.[6] Mustafa et al. found an inverse relationship between the F level in the drinking water, range 0.01–2.07 mg/L, and the schooling performance. Similarly, another 2018 study by Yu et al. of 2,886 children, aged 7 to 13 years, from endemic and non-endemic fluorosis areas in Tianjin, China, found that for a drinking water F range of 0.20–1.40 mg/L there was significantly decreased probability of developing excellent intelligence (IQ≥130, OR=0.60, 95% CI: 0.47 to 0.77).[7] For the drinking water F range of 1.60–2.50 mg/L, every 0.5 mg/L increment in the urinary F level was associated with a decrease of 2.67 in the IQ score (95% CI: –4.67 to –0.68).

A recent review by Susheela supports the concept of fluoride toxicity early in life leading to a number of developmental disorders which are identical to those occurring with the disturbed thyroid hormone metabolism which occurs in iodine deficiency disorders (IDD).[8] The conditions described by Susheela as occurring with both fluoride excess (>1 mg/L in drinking water) and iodine deficiency (using non-iodized salt with <5 ppm of iodine or inadequately iodized salt with 5–14 ppm of iodine) were: (i) goitre; (ii) short stature (cretin); (iii) mental retardation (low IQ); (iv) brain damage; (v) deaf-mutism (deaf and dumb); (vi) thyroid hormone abnormalities; (vii) knock-knee and bow leg; (viii) intellectual disability; (ix) psychomotor defects; and (x) abortions, still births, pre-term deliveries in pregnant women. She noted that the fluoride ion (F) was a hormone disrupter, enzyme inhibitor, and a neurotoxin that reduced the IQ of children. She commented that in diagnosing fluorosis in children, IDD could be ruled out by testing the urinary iodine. A reference was given to an Indian study by Hosur et al. which found that F-induced thyroid hormone disturbances were similar to those found with iodine deficiency despite there being an adequate iodine intake.[9]

Whether or not one of the FIDD occurs in a particular situation depends not only on the level and duration of the fluoride exposure but also on the presence of predisposing and protective factors including: (i) species differences; (ii) genetic differences; (iii) water hardness, water calcium and magnesium levels, and dietary intake of cations; (iv) dietary intake of vitamins, antioxidants, and selenium although at higher levels selenium is synergistic with fluoride and arsenic in causing toxicity; (v) dietary intake of iodine and dietary goitrogens; (vi) exposure to other toxic chemicals and drugs; and (vii) altitude.[1]

Various reports in the literature are consistent with the hypothesis that the developmental disorders due to disturbed to thyroid hormone metabolism include (i) short stature, (ii) bone deformities, (iii) cognitive impairment, (iv) delayed dental eruption, and (v) dental fluorosis and that they may occur not only with thyroid disorders, such as those due to iodine deficiency, congenital hypothyroidism, and

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thyroidectomy, but also with the thyroid dysfunction induced by systemic fluoride ingestion, both with and without iodine deficiency. A significant inverse relationship was found between urine fluoride levels and stature in children in Villa Ahumada, Mexico, with 5.3 mg F/L in their drinking water.[10.11] Short stature, retarded bone age with delayed fusion of the epiphyses and diaphyses of the long bones, cognitive impairment, delayed dental eruption, and enamel hypoplasia with increased porosity, the same as the lesions seen in dental fluorosis, can all occur in congenital hypothyroidism.[12-15] Angular limb deformities in foals have been associated with hypoplasia and incomplete ossification of the carpal and tarsal bones.[16] Foals with congenital hyperplastic goitre had retarded ossification of the cuboidal bones, especially the third and central tarsal bones.[16] Foals who were thyroidectomized when one-day-old had retarded ossification to a lesser degree.[16]

The fluoride effects on thyroid function are more severe in the presence of iodine deficiency. In the village of Ban Mae Toen, Thailand, adjacent to a polluted artificial lake water source, containing 4 mg F/L and less than 0.1 mg I/L, formed as a result of fluoride mining 40 years ago and still being used in 2007 in the dry season, 11% had goitre (20% of the women and 3% of the men) compared to 0% in two nearby control villages, 24% had lower limb deformities compared to 5% in the control villages, and 63% had discoloured teeth, consistent with dental fluorosis, which was significantly more than in the control villages, p<0.01.[17,18] Brain damage, deaf-mutism, and mental disability were reported in the children of pregnant women who drank the contaminated water.[18] A further example of impaired growth and development affecting the teeth and bones is a 20-yr-old patient with congenital hypothyroidism, short stature (114 cm), subnormal weight for her age (20 kg), and a mixed dentition with 11 retained deciduous teeth and 15 unerupted permanent teeth.[12] Radiographs showed delayed closure of the coronal, sagittal, and lamboid sutures, delayed fusion of the epiphysis and diaphysis of the phalanges, metacarpals, radius, and ulna, and non-ossification of the sesamoid bone and the hook of the hamate.[12]

Interference with thyroid hormone metabolism during development may lead to various failures of maturation which may not be fully reversed by later treatment with thyroxine. The failure of appropriate limb ossification may lead to irreversible limb deformities.[19] Although administering thyroid hormone up to the age of 19 yr may result in exfoliation of the primary dentition and eruption of the secondary dentition, the lack of proper growth on the mandible and failure of the normal resorption of the internal aspect of the ramus may lead to impaction of the mandibular second molars.[13] The failure to properly remove amelogenic proteins and organic matrix components may lead to dental fluorosis with increased enamel porosity and impaired enamel crystal growth.[20-22] The degree of fluorosis is greatest among those teeth formed later during childhood.[23] Fluoride may replace hydroxyl ions in calcium hydroxyapatite in hard tissue to form calcium fluoroapatite and then be toxic to the respective cells of the hard tissues leading to dental fluorosis, osteomegaly and osteopenia.[24,25] Since the alveolar bone has a higher metabolic rate, than skeletal bone tissue at other sites, the recession of the alveolar bone and gingival tissue is an important sign of chronic fluoride toxicity.[25,26]

Lower limb deformities are less common and may result from the presence of particularly high fluoride levels or, possibly, fluoride toxicity being exacerbated by

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iodine deficiency. Xiang et al.[27] did not report any lower limb deformities in their study which found a significantly reduced IQ in children in Wamiao, People's Republic of China, with a drinking water fluoride level of 2.47±0.79 mg F/L while McGlashan et al.[17] found 24% of the Thai residents adjacent to lake water with 4 mg F/L, had lower limb deformities, compared to 5% in two control villages. However, the children in Wamiao had adequate urinary iodine levels, 280.70±87.16 µg/L[27] while the water sources in the study and control villages in Thailand had iodine levels below the detection limit of 100 µg/L.[17] A median urinary iodine level of 50 µg/L or less has been proposed for classifying iodine deficiency and a level of 100–199 µg/L is an adequate intake for school age children aged 6 or more years.[28] Iodine levels were not reported on in the endemic genu valgum outbreak in Mandla District of Central India but the condition only appeared there after deep bore wells began to be used as a water source and the most severe cases were in Hirapur where the only hand pump had a water fluoride level of 13.5 mg F/L.[19] Similarly, the occurrence of endemic genu valgum associated with fluorosis in Andra Pradesh, India, in 1973 followed fluoride contamination of surface water by underground water due to the construction of a dam in a nearby area.[29,30] The differential diagnosis of genu varu, genu valgum, and other bone deformities includes rickets due to vitamin D deficiency.[31]

Dental fluorosis, with increased enamel porosity and impaired enamel crystal growth, results from a failure to properly remove amelogenic proteins and organic matrix components[20,21] and is usually discussed without reference to thyroid hormone metabolism.[20,32-35] However, extracellular remodelling plays an important role during tissue remodelling in amphibian metamorphosis and extracellular matrix degrading metalloproteinases are expressed in response to thyroid hormone.[36] Sonic hedgehog (Shh) regulates the growth and morphogenesis of the tooth and when Shh is absent the polarity and organization of the ameloblast and odontoblast layers is disrupted.[37] Thyroid hormone regulates the expression of the sonic hedgehog signalling pathway in the embryonic and mammalian brain.[38] This suggests that thyroid hormone metabolism may be relevant in the development of dental fluorosis in agreement with Schuld who found in 2005 that understanding thyroid hormone metabolism was essential in understanding fluoride toxicity including dental and skeletal fluorosis and the effects on IQ.[39] Although dental fluorosis is usually considered mainly with respect to tooth appearance and function, it is also important as a marker for fluoride-induced cognitive impairment.[40]

Two recent studies have found the fluoride negatively affects thyroid hormones. In the first study Kheradpisheh et al. reported that elevated fluoride from drinking water impacts on the T_3, T_4, and TSH hormones.[41] The aim was to study the impacts of drinking water fluoride on the T_3, T_4, and TSH hormones in the YGA (Yazd Greater Area) in Iran. In the case-control study, 198 cases and 213 controls were selected. Fluoride was determined by the SPADNS Colorimetric Method. T_3, T_4, and TSH hormones were tested in the Yazd Central Laboratory by the RIA (Radio Immuno Assay) method. The average amount of TSH and T_3 hormones, were compared in cases with hypothyroidism (n=198) and in healthy controls (n=213) based on the drinking water fluoride level at two concentration ranges, 0–0.29 and 0.3–0.5 mg F/L. The TSH was significantly higher for the higher fluoride range (0.3–0.5 mg/L) in

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both the cases with hypothyroidism (p=0.003) (11.85±7 mIU/L for the F level of 0–0.29mg/L; 20.5±12.8 mIU/L for the F level of 0.3–0.5 mg/L; normal range 0.17–4.5 mIU/L) and the healthy controls (p=0.001) (2.2±0.95 mIU/L for the F level of 0–0.29 mg/L; 2.8±0.9 mIU/L with the F level of 0.3–0.5 mg/L). The T_3 was not significantly higher for the higher fluoride range (0.3–0.5 mg/L) in the cases with hypothyroidism (p=0.19) (115.3±22 ng/dL for the F level of 0–0.29mg/L; 117.8±36.6 ng/dL for the F level of 0.3–0.5 mg/L; normal range 78–180 ng/dL) but was significantly increased in the controls (p=0.026) (135±18.4 ng/dL for the F level of 0–0.29 mg/L; 138.5±21.6 ng/dL with the F level of 0.3–0.5 mg/L). In the multivariate regression logistic analysis, the independent variables associated with hypothyroidism were: gender (odds ratio: 2.5, CI 95%: 1.6–3.9), family history of thyroid disease (odds ratio: 2.7, CI 95%: 1.6–4.6), exercise (odds ratio: 5.34, CI 95%: 3.2–9), diabetes (odds ratio: 3.7, CI 95%: 1.7–8), hypertension (odds ratio: 3.2, CI 95%: 1.3–8.2), water consumption (odds ratio: 4, CI 95%: 1.2–14). It was found that fluoride impacts human thyroid hormones, especially TSH and T_3, even in the standard concentration of less than 0.5 mg/L. Application of standard household water purification devices (such as reversed osmosis, electrodialysis, activated carbon filter, and other adsorption/ion-exchange methods) was recommended for patients with hypothyroidism since they have a higher consumption of drinking water. The purification systems can help remove fluoride which interferes with thyroid function.

In the second study Malin et al. reported that fluoride exposure has the potential to disrupt thyroid functioning, though adequate iodine intake may mitigate this effect.[42] Their study was the first population-based study to examine the impact of chronic low-level fluoride exposure on thyroid function, while considering iodine status. The objective of the study was to determine whether urinary iodine status modifies the effect of fluoride exposure on thyroid stimulating hormone (TSH) levels. The cross-sectional study utilized weighted population-based data from Cycle 3 (2012–2013) of the Canadian Health Measures Survey (CHMS). Information was collected via a home interview and a visit to a mobile examination centre. The weighted sample represented 6,914,124 adults in Canada aged 18–79 years who were not taking any thyroid-related medication. Urinary fluoride concentrations were measured in spot samples using an ion selective electrode and adjusted for specific gravity (UF_{SG}). Serum TSH levels provided a measure of thyroid function. Multivariable regression analyses examined the relationship between UF_{SG} and TSH, controlling for covariates. The results were that approximately 17.8% of participants fell in the moderately-to-severely iodine deficient range. The mean±SD age of the sample was 46.5±15.6 years and the median UF_{SG} concentration was 0.74 mg/L. Among iodine deficient adults, a 1 mg/L increase in UF_{SG} was associated with a 0.35 mIU/L increase in TSH [95% CI: 0.06, 0.64; p=0.01, one-tailed]. The authors concluded that adults living in Canada who have moderate-to-severe iodine deficiencies and higher levels of urinary fluoride may be at an increased risk for underactive thyroid gland activity.

A further recent study by Till et al.[43] has found that the levels of creatinine-adjusted urinary fluoride present in pregnant women in Canada receiving community water fluoridation are comparable to those previously described by Brough et al.[44] in pregnant women receiving community water fluoridation in New Zealand and those

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in the studies of Bashash et al.,[3] Thomas et al.,[4] and Bashash et al.[5] where prenatal fluoride exposure was associated with impaired cognitive outcomes or increased attention deficit hyperactivity (ADHD) symptoms. The background to the Till et al.[43] paper noted that fluoride exposures have not been established for pregnant women who live in regions with and without community water fluoridation. Their aim was to measure urinary fluoride levels during pregnancy, to assess the contribution of drinking-water and tea consumption habits to maternal urinary fluoride (MUF) concentrations, and to evaluate the impact of various dilution correction standards, including adjustment for urinary creatinine and specific gravity (SG). They measured the MUF concentrations in spot samples collected in each trimester of pregnancy from 1,566 pregnant women in the Maternal-Infant Research on Environmental Chemicals cohort. They calculated the intraclass correlation coefficients (ICCs) to assess the variability in the MUF concentrations across pregnancy. They used regression analyses to estimate associations between MUF levels, tea consumption, and water fluoride concentrations as measured by water treatment plants. The results showed that the creatinine-adjusted MUF values (MUF_{CRE}) (mean±SD) were almost two times higher for pregnant women living in fluoridated regions (0.87±0.50 mg/L) compared with nonfluoridated regions (0.46±0.34 mg/L; p<0.001). The MUF values tended to increase over the course of pregnancy using both unadjusted values and adjusted values. Reproducibility of the unadjusted and adjusted MUF values was modest (ICC range=0.37–0.40). The municipal water fluoride level was positively associated with creatinine-adjusted MUF (B=0.52, 95% CI: 0.46, 0.57), accounting for 24% of the variance after controlling for covariates. Higher MUF concentrations correlated with the numbers of cups of black (r=0.31–0.32) but not green tea (r=0.04–0.06). The estimated amount of fluoride intake from tea consumption (factoring in fluoride from an average cup as well as from a 200 mL cup of tap water) was also correlated with both MUF_{SG} and MUF_{CRE} concentrations (r=0.16–0.18). Urinary creatinine and SG correction methods were highly correlated (r=0.91) and were interchangeable in models examining predictors of MUF. They concluded that community water fluoridation is a major source of fluoride exposure for pregnant women living in Canada. Urinary dilution correction with creatinine and SG were shown to be interchangeable for their sample of pregnant women.

The mean maternal urinary F level, adjusted for urinary creatinine, in the Bashash et al. study on cognitive outcomes[3] for all of the mothers with complete data (n=299) was 0.90±0.35 mg/L (mean±SD) and for all 512 of the mothers studied, including those with incomplete data, the urinary F was 0.88±0.34 mg/L, range 0.02–2.36 mg/L, and 0.64, 0.82, and 1.02 mg/L for the 25th, 50th, and 75th percentiles, respectively. In the Thomas et al. study on cognitive outcomes,[4] the median maternal urinary F adjusted for urinary creatinine was 0.835 mg/L (range 0.195–3.673 mg/L).[10] In the Bashash et al. study on ADHD symptoms,[5] the mean MUF_{CRE} was 0.85 mg/L (SD=0.33) and the Interquartile Range (IQR) was 0.46 mg/L. These levels of maternal urinary F of 0.90 (mean), 0.88 (mean), 0.835 (median), and 0.85 (mean) mg/L, which were associated with adverse neurodevelopmental outcomes, are comparable to mean MUF_{CRE} found by Till et al.[43] for pregnant women living in fluoridated regions of Canada of 0.87±0.50 mg/L, (mean±SD) and the median urinary F concentration of 0.82 (0.62, 1.03) mg/L (µg/mL) reported by Brough et al.[44] in 59 pregnant women in Palmerston North, New Zealand, in 2009–2011, where

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the community water supply was fluoridated, in accordance with the New Zealand Ministry of Health recommendation, to give a concentration of 0.7–1.0 mg/L. The levels of exposure to F experienced during pregnancy by the mothers in the studies by Bashash et al.[3-5] and Thomas et al.[4] were thus comparable to those in pregnant women in Palmerston North, New Zealand,[44] with water fluoridation at the level of 0.7–1.0 mg/L, and in pregnant women in seven cities in Canada with community water fluoridation (Toronto, Hamilton, Ottawa, Sudbury, Halifax, Edmonton, and Winnipeg)[43] where the mean water treatment plant fluoride level was 0.61±0.11 mg/L (mean±SD), median 0.56 mg/L, and range 0.41–0.87 mg/L and where, after F from tea drinking was also considered, the mean urinary fluoride level was 0.87±0.50 mg/L.

A safe daily intake of F for pregnant women to give protection from F-induced neurotoxicity can been estimated to be approximately 0.04 mg F/day (0.0006 mg F/kg bw/day for a 70 kg woman).[45] The quantity of water, fluoridated with 0.7 mg F/L (0.7 ppm) which contain 0.04 is 72 mL, approximately a third of a cupful (1 cup = 8 oz = 237 mL). With this being less than 10% of the mean daily water intake for an adult, in order to prevent F-induced IQ loss in children, pregnant women should avoid the use of fluoridated community water supplies and other dietary sources high in F including tea and fluoridated dental products that may be swallowed such as fluoridated toothpaste and professionally applied fluoride gels and varnishes. Using the safe dose of F for preventing *in utero* foetal neurotoxicity, derived with the LOAEL/NOAEL method, of 0.04 mg F/day, and taking the body weight of a pregnant adult woman as 70 kg, the oral reference value for longer-term (up to 10% of an average life span) exposure (RfV_{LO}) can be calculated to be approximately 0.0006 mg/kg bw/day (0.04÷70=0.00057). This level is 100 times less than the current reference dose (RfD) of 0.06 mg/kg bw/day for preventing objectionable dental fluorosis of moderate or severe severity.[45]

There is thus evidence that the fluoride level recommended for community water fluoridation, 0.7 mg/L,[42,46] and indeed the lower fluoride range of 0.3–0.5 mg/L,[41] can disturb thyroid hormone metabolism, especially when moderate-to-severe iodine deficiency is present, and that pregnant women who use fluoridated water with 0.7 mg F/L will have children with a significantly increased rate of cognitive impairment and ADHD symptoms. These neurological impairments can be seen to be part of a broader disease spectrum of developmental disorders due to disturbed thyroid hormone metabolism which may arise for various reasons such iodine deficiency and congenital hypothyroidism and well as exposure to high levels of fluoride, especially in association with iodine deficiency. In humans, the developmental disorders due to disturbed thyroid hormone metabolism can be seen to include short stature, bone deformities, cognitive impairment, delayed dental eruption, and dental fluorosis. If the reduced dental decay rates of deciduous teeth in 5-year-olds in fluoridated areas compared to nonfluoridated areas[47] are seen to be part of a wider picture of developmental disorders due to disturbed thyroid hormone metabolism, including neurological impairment, it is unlikely that community water fluoridation could be rationally recommended as a public health policy. The 1998 Wingspread statement of the Precautionary Principle stated that when an activity raises threats of harm to human health... precautionary measures should be taken even if some cause and

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effect relationships are not fully established scientifically.[48] The link between fluoride exposure during pregnancy at the fluoride levels present with community water fluoridation, disturbed thyroid hormones, and development disorders due to disturbed thyroid hormone metabolism is now sufficiently clear to warrant the immediate cessation of community water fluoridation schemes.

Community water fluoridation for the prevention of dental decay first started in the United States of America and Canada in 1945 in response to concerns about the damaging effects of fluoride pollution caused by aluminium production and the development of the atomic bomb in the Manhattan project.[49-51] Some other countries followed the lead of the USA but then discontinued the practice.[52] For example Wei and Wei reported that water fluoridation in China began in 1964 in Guangzhou and was discontinued in 1983 after a 6.5 fold increase in dental fluorosis was observed with only a marginal decrease in dental caries.[53] In 2000 Wei published *A special report on fluoridation and prevention of dental caries*[54] and Wei and Wei[53] hoped that the information in that report would be carefully weighed before any further attempt was made to re-introduce fluoridation in China. In countries which do not currently practice community water fluoridation with first hand experience or expert knowledge of fluorosis and active centres of fluoride research, such as the People's Republic of China, India, Iran, Japan, and Poland, the current findings of water fluoridation affecting thyroid hormone metabolism and leading to impaired neurological development will be seen as affirmation of the correctness of the present policies. The lead has been given by India with the requirement (acceptable limit) for drinking water of 1.0 mg/L (ppm) having a rider that the "lesser the fluoride the better, as fluoride is injurious to health."[55]

However, in countries currently practising community water fluoridation the new knowledge is likely to be received differently. Experience, as with removing lead from petrol,[56] shows that rather than new knowledge quickly resulting in policy changes the new knowledge is actively resisted by those with an investment in the *status quo*. As the Russian novelist Leo Tolstoy commented in 1885 in the opening sentence of Chapter 14 of *What is art?*, as translated by Richard Pevear and Larissa Volokhonsky,[57] "I know that the majority of people who are not only regarded as intelligent but are indeed intelligent, capable of understanding the most difficult scientific, mathematical and philosophical reasonings, are very rarely capable of understanding a most simple and obvious truth, if it is such as requires that they admit that a judgement they have formed about something, sometimes with great effort, a judgement they are proud of, which they have taught to others, on the basis of which they have arranged their entire life—that this judgement may be wrong."

The German theoretical physicist Max Planck, sadly remarked, "A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it."[58] Similarly he noted, "An important scientific innovation rarely makes it way by gradually winning over and converting it opponents: it rarely happens that Saul becomes Paul. What does happen is that its opponents gradually die out, and that the growing generation is familiarized with the ideas from the beginning: another instance of the fact that the future lies with the youth."[58] The slowness to see the light has been termed tardive photopsia.[59]

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The Italian physicist, mathematician, engineer, astronomer, and philosopher, Galileo Galilei (15 February 1564–8 January 1642) noted, "In the sciences, the authority of thousands of opinions is not worth as much as one tiny spark of reason in an individual man."[60]

An example of deference to authority rather than the use of reason[61] was shown in the response of the Hon Dr David Clark, Minister of Health, New Zealand, to a letter, dated 16 February 2018 informing him of the 2017 Bashash et al. study,[3] enclosing a copy of the paper, and giving a calculation of the safe dose of fluoride that might be consumed by pregnant women that avoids the risk of foetal neurotoxicity.[62] Dr Clark's response[63] included the comments, "Fluoride is naturally present in water. The Ministry of Health supports community water fluoridation (CWF) as an effective, safe and affordable public health measure to improve oral health. The Ministry's recommended drink-water fluoridation levels are based on World Health Organization guidelines.

"You may be aware that in August 2014, the report *Health Effects of Water Fluoridation: A Review of the Scientific Evidence* was published on behalf of the Royal Society of New Zealand and the Office of the Prime Minister's Chief Science Advisor. This report comprehensively reviewed the scientific evidence for and against the efficacy and safety of CWF. The report found that there are no significant adverse effects of CWF within the range of concentrations currently recommended by the Ministry and used in New Zealand, and provides compelling evidence of dental health benefits for New Zealanders. The report can be found on the Office of the Prime Minister's Chief Science Advisor's website (www.pmcsa.org.nz) by searching the title.

"The report also recommended that a review of the scientific evidence be repeated or updated every ten years, or earlier if a large, well-designed study were [sic] published that appeared to have shifted the balance between health benefit and risk."

The logic of countering the findings of a 2017 paper by referring to an 2014 review was not clear. Hopefully the writers of the authoritative 2014 report[64] will follow the example of John Colquhoun, one time Principal Dental Officer for Auckland, New Zealand, who persuaded the Auckland City Council to fluoridate its water (apart from that supplied to Onehunga) and who subsequently changed his mind on the safety and efficacy of the practice,[65] so that the public of New Zealand will not have to wait until 2024 for the scientific evidence to be again reviewed.

DISCLAIMER

The views expressed in this editorial are the personal views of the Editor-in-Chief and do not represent the opinion of the International Society for Fluoride Research. As noted by Gene Miller in 1992[66] "The ISFR is not a political society nor does it endorse or oppose public views on fluoride. It can, however, provide the forum for scientific exchange and publication of sound research. It will hopefully for many years to come motivate scientists to research fluoride effects and report findings that may gain application to benefit mankind." Similarly, in 1992, Colquhoun[67] remarked that "The fact remains that the International Society for Fluoride Research is the only organization which brings together fluoride researchers and provides a forum for interchange of ideas and findings. As such, it is willing to publish the varying views

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and interpretations of data of its members. But, unlike some other professional organizations, ISFR does not endorse or oppose any political matters concerning fluoride nor try to influence or persuade its members on such matters.

Bruce Spittle, Editor-in-Chief, *Fluoride*, Dunedin, New Zealand

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