FLUORIDE, IQ, AND ADVICE ON TYPE I AND II ERRORS

SUMMARY: A 38-year prospective study of 992 New Zealand children on fluoride (F) and IQ, of whom an uncertain number (0–101) had not received, at age 5 years, additional F with F tablets (taken: 139, not taken: 763, unknown: 90), community water fluoridation (CWF) (lived in CWF area: 891, never lived in CWF area: 99, unknown: 2) or F toothpaste (always used: 634, sometimes used: 240, never used: 22, unknown: 96), has led to differing advice on avoiding Type I and Type II errors. Consideration of eight studies on F and IQ, and introducing a safety factor of 10 to allow for individual differences in water intake and sensitivity (between- and within-subject variations), suggests a maximum contaminant level goal (MCLG) for F in drinking water of 0.1 mg F/L. Whilst achieving this may be difficult in many areas, at the least no active steps should be taken to raise water F levels above 0.1 mg F/L. Some evidence suggests that the only assuredly safe level of F in drinking water is zero.

Keywords: Fluoride in drinking water; IQ; Maximum contaminant level goal; New Zealand study.

After studying community water fluoridation (CWF) and IQ in a 38-yr prospective study in a cohort from Dunedin, New Zealand, Broadbent et al. concluded with the implication that, "Scientists and policy makers should be reminded of the necessity of caution in attributing causality when evidence for it does not exist."[1,2] This is advice to avoid Type I errors, where evidence is found to reject the null hypothesis when the null hypothesis is, in fact, true.[3] Using racing parlance, British statistician and psychiatrist Professor Max Hamilton (1912–1988) described a Type I error as "backing a loser." A similar caution is noted in a letter to the editor in this issue (pp.266-71), where Broadbent is quoted, by Perrott, as commenting that the towns studied in an Iranian IQ study were not comparable.[4] A critic of the Iranian study, Perrott, suggested that the IQ differences found (IQ 104.25±20.73 with 0.25 mg F/L in the drinking water vs IQ 81.21±16.17 with 3.94 mg F/L in the drinking water, p=0.0004) were likely to be due to cultural and educational differences rather than the differences in the drinking water fluoride (F) levels.[5] This claim is refuted by the authors.[4] Similarly, Broadbent et al. suggested that the IQ differences observed in a meta-analysis of 27 studies of F neurotoxicity, by Choi, Sun, Zhang, and Grandjean,[6] "may be attributable to urban-rural or socioeconomic differences, or removal of lead from drinking water."[1] Broadbent et al. noted that water improvement plans were likely to remove lead from drinking water, and such facilities were more likely to be in urban or affluent areas.[1] However this explanation does not explain the IQ differences found by Xiang et al. (IQ 100.41±13.21, range 60–128, with 0.36±0.15 mg F/L, range 0.18–0.76 mg F/L, in the drinking water vs IQ 92.02±13.00, range 54–126, with 2.47±0.79 mg F/L, range 0.57–4.50 mg F/L, in the drinking water, $p<0.01$) in a study in two rural villages on children, who did not differ significantly in their blood lead levels, and whose parents did not differ significantly in socioeconomic status (family income and parental educational level).[7-9] Similarly, the differences could not be attributed to differences in iodine or arsenic levels.[7,9] In contrast, a significant inverse relationship was found between serum F and IQ with the mean IQ being significantly higher, with fewer children with an IQ less than 80, in the two quartiles with a serum F level of less than 0.05 mg F/L.[10,11]

The advice on avoiding Type I errors was acknowledged by Grandjean, but after reviewing the Broadbent et al. study, he noted that "we should also be reminded that an adverse effect may well be present, even when it could not be demonstrated in a

particular study, especially one that can be characterized as weak or non-informative."[12] This is advice to avoid Type II errors, where there is a failure to find evidence to reject the null hypothesis when the alternative hypothesis is, in fact, true.[3] Using racing parlance, Hamilton described a Type II error as "missing a winner." Grandjean found that although IQ data from almost 1000 subjects (992) were available in the Broadbent et al. study, the range of F exposures was narrow and the classification of F exposure was imprecise.[12] At age 5 yr, an uncertain number (0–101) had not received additional F with F tablets (taken: 139, not taken: 763, unknown: 90), CWF (lived in CWF area: 891, never lived in CWF area: 99, unknown: 2) or F toothpaste (always used: 634, sometimes used: 240, never used: 22, unknown: 96).[1] No analysis appeared to be present comparing IQ in those that never received additional F, as F tablets, CWF, or F toothpaste, with IQ in those that received one or more of these forms of additional F.[1]

In three papers, abstracted in this issue (pp. 273-5), Susheela et al. note that fluoridated toothpaste and dental products are among the F sources that lead to fluorosis, a multisystem disease with symptoms including gastro-intestinal discomfort, polyuria, polydipsia, muscle weakness, fatigue, and joint pain.[8-10] They noted that while early reports on fluorosis focussed on F-contaminated water as the F source, attention was also given now to other sources including food and beverages containing black rock salt (CaF_2, fluorspar, fluorite), fluoridated dental products, and industrial emissions of F-containing dust and fumes.[13-15]

Thus, with only 0–101 subjects in the study by Broadbent et al. not having received additional F, the power of the study to avoid a Type II error was uncertain and limited. Grandjean commented that the statistical confidence limits suggested that a loss of 2–3 IQ points could not be excluded by their findings.[12]

Rather than the Broadbent et al. study being taken as a reassurance that no concerns should be felt about the effect on brain development of the F burden, from food, beverages, F toothpaste, and industrial F sources, being increased by the addition of F or silicofluorides to community water supplies, the weakness of the study for avoiding a Type II error should be kept in mind. That F can cause neurotoxicity, at a sufficient dose, is not under dispute.[16] The urine and blood F levels at which toxicity occurs have been documented.[16] Although the concentration of F in CWF can be controlled, the dose taken by an individual cannot be controlled and some persons, such as those with iodine deficiency, are more sensitive to F-induced neurotoxicity.[17] When measures were taken to reduce F-intake in an endemic coal-burning fluorosis area, the rate of mental retardation in 8–10-yr-old children was significantly reduced.[18]

Heeding the advice on avoiding Type I and II errors, accepting the evidence that at a measurable, relatively low dose, F is a neurotoxin (e.g., corresponding to using drinking water containing 1.85 mg F/L[7] or having a serum F level of 0.064 mg F/L[10,11]), and seeking to reduce brain drain by reducing environmental exposure to all identified neurotoxins, including F, is the optimal course for all countries to take.[19-22] Consideration of eight studies on F and IQ, and introducing a safety factor of 10 to allow for individual differences in water intake and sensitivity (between- and within-subject variations), suggests a maximum contaminant level goal (MCLG) for F in drinking water of 0.1 mg F/L.[16] Whilst achieving this may be difficult in many areas,

at the least no active steps should be taken to raise water F levels above 0.1 mg F/L. An analysis of the study by Ding et al. suggests that the only assuredly safe level of F in drinking water is zero.[11,16,23]

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