AUTHORITY AND REASONING IN SCIENCE

SUMMARY: Studies of fluoride toxicity in both humans and animals indicate that, in addition to dental and skeletal fluorosis, a variety of organ systems may be affected with effects including colic, intermittent diarrhoea or constipation, bloating, urticaria, polyuria, polydipsia, repeated abortions, still birth, and sterility. In contrast, a recent New Zealand study did not find an adverse effect on intelligence (IQ) with community water fluoridation at 0.85 mg F/L and this was noted to be consistent with the 2011 report by the European Union Scientific Committee on Health and Environmental Risks (SCHER). However, as noted in a previous editorial, when a safe level for fluoride in drinking water was calculated by considering the levels at which definite fluoride neurotoxicity occurred and reasoning backwards, by introducing a safety factor of 10 to allow for intraspecies variation, a likely safe level for preventing the occurrence of neurotoxicity was found of 0.1 mg F/L, with the only assuredly safe level being zero. It is suggested that trust in official reports may be misplaced and that the observation of Galileo Galilei, 1564–1642, is still relevant, “In questions of science, the authority of a thousand is not worth the humble reasoning of a single individual.”

Keywords: Authority in science; Community water fluoride; Fluoride toxicity in animals; Galileo Galilei; Neurotoxicity; New Zealand; Reasoning in science.

In this issue, five abstracts by Choubisa,1-3,5 and Choubisa and Mishra,4 note that, in both humans and animals, fluoride (F) toxicity can, in addition to causing dental and skeletal fluorosis, affect many other organ systems. In humans, this may result in colic, intermittent diarrhoea or constipation, bloating, urticaria, polyuria, polydipsia, repeated abortions, still birth, and sterility. The picture is similar in animals where fluorosis may cause colic, intermittent diarrhoea, excessive urination, irregular reproductive cycles, repeated abortions, sterility, and still birth. The multiorgan nature of F toxicity is consistent with the ability of F to impair the function of mitochondrial cytochrome oxidase and alter enzyme levels, gene expression levels, and metabolite levels as well as producing ultrastructural changes in the mitochondria and granular endoplasmic reticulum.6 The ultrastructural changes have been found in humans and many animal species including mice, rats, rabbits, guinea pigs, pigs, and chickens.6 The tissues studied include liver, pancreas, testis, submandibular gland, kidney, thyroid, myocardium, skeletal muscle, sciatic nerve, spinal cord, cerebellum, hippocampus, neocortex, femur, spleen, ovary, and uterus.6

In contrast, a further abstract of a prospective study on community water fluoridation (CWF) and intelligence (IQ) in New Zealand found that CWF was not neurotoxic.7 At age 5 yr, a relatively small number of subjects (n=99) who lived in a nonfluoridated area (0.0–0.3 mg F/L) were compared to those living with CWF (n=891, 0.85 mg F/L). No information was given as to how many of the children with nonfluoridated drinking water were in the group of 139 who had taken F tablets by the age of 5 yr. The estimates from general linear models for childhood IQ by CWF and other F exposures were controlled for sex, socioeconomic status in childhood, low birth weight, and breastfeeding, while those for adult IQ were also controlled for educational achievements. Variables such as lead, iodine, and arsenic were not mentioned and dietary F was not measured. The authors found
that the assertion that F exposure in the context of CWF can affect neurologic development or IQ was not supported. They commented that study members who lived in areas with CWF before 5 yr had slightly higher IQs on average (mean 100.0 ± SD 13.5) than those who had not (mean 99.8 ± SD 13.0) although the difference (0.02) was nonsignificant (p=0.92). They did not refer to the similarly nonsignificant difference (0.05) between those who lived in areas with CWF before 5 yr and were not breast-fed who had slightly lower IQs on average (mean 97.0 ± SD 13.8) than those who were not breast-fed and lived in nonfluoridated areas before 5 yr (mean 97.5 ± SD 14.2).

Using General Linear Models, no statistically significant differences were found in IQ between the participants who had or had not resided in areas with CWF, used F toothpaste, or used F tablets, both before and after adjusting for the potential confounding variables of sex, socioeconomic status in childhood, low birth weight, breast feeding, and, for adult IQ, educational achievements. Hypothesis tests with the general linear model can be made in two ways: multivariate or as several independent univariate tests. In multivariate tests the columns of Y are tested together, whereas in univariate tests the columns of Y are tested independently, i.e., as multiple univariate tests with the same design matrix. Because the results for CWF, use of F toothpaste, and use of F tablets were reported separately, both before and after adjustment, it was not clear to me that the use of CWF and F tablets had been tested together in a multivariate test rather than separately with multiple univariate tests.

In the discussion on causation, a 2011 report by the Scientific Committee on Health and Environmental Risks (SCHER) of the European Commission was referred to and it was noted that a plausible biological link for an association between fluoridated water and IQ had not been established. Broadbent et al. found no plausible biological mechanism exists for such a link and suggested that any observed link may be attributed to covariance by urban-rural status and, in some past studies, exposure to lead. They noted that SCHER reported on the F-IQ studies and found them to be of simplistic methodological design with no, or at best little, control for confounders such as nutrition, exposure to iodine or lead, or socioeconomic status.

The SCHER report has been criticized for not referring to the IQ studies by Xiang et al. which did control for lead, iodine, and arsenic as well as rural status, parental income, and parental education. The SCHER report had relatively few references in its section on neurotoxicity. In the section on animal studies it had references to three papers, from 2003, 2005, and 2009, while in the section on human studies it referred to four papers, from 2003, 2007, 2007, and 2008. From the human studies considered, they found that F is not considered to be an endocrine disrupter. They concluded that the F intake from drinking water at the level occurring in the European Union (EU) did not appear to hamper children’s neurodevelopment and IQ levels. The EU permits a water F level, both natural and as a result of fluoridation, of up to 1.5 mg/L.
This compares to the threshold found by Xiang et al. for when IQ effects began to appear of 1.85 mg F/L.\textsuperscript{11} A further Chinese study by Ding et al. found that IQ fell below the mean with a drinking water F level of 0.81 mg F/L or more.\textsuperscript{12} However, their graph did not illustrate a true threshold effect below which IQ was not adversely affected.\textsuperscript{13} The IQ difference from the mean was 0.42 higher with a water F of 0.10 mg F/L compared to the IQ at a water F of 0.81 mg /L.\textsuperscript{13} Their study suggested that there was no safe threshold in drinking water below which F had no neurotoxicity.\textsuperscript{13}

Even if both Broadbent et al. and SCHER are correct and no effects on IQ can be demonstrated in relatively small populations with CWF, this only means that the lowest-observed-adverse-effect-level (LOAEL) is greater than 0.85–1.5 mg F/L. Controlling the drinking water F concentration is different from controlling the dose consumed by individuals, some of whom have higher intakes. Drinking water with 0.85 mg F/L is also unsafe for infants and those who are iodine deficient.\textsuperscript{14} If a safety factor of 10 is introduced to allow for intraspecies variations in water intake and sensitivity to adverse effects from F, the data from Xiang et al. give a level for F in drinking water likely to protect against neurotoxicity of 0.185 mg F/L.\textsuperscript{13} Similar reasoning and the lack of a true threshold in the Ding et al. study suggests that the safest level of F in drinking water is zero.\textsuperscript{13} When a pool of eight studies were examined, it was found that neurotoxicity from F was likely to occur when the total F intake from water, dietary, airborne, and other sources resulted in a urinary F of approximately 2.5 mg F/L or more.\textsuperscript{13} Using a safety factor of 10, it was argued the level of urinary F unlikely to be associated with neurotoxicity was 0.25 mg F/L. Using the empirical data from the pool of eight studies, this was found to correspond to a drinking water F level of 0.1 mg F/L. Thus reasoning, based on data where F neurotoxicity has been demonstrated, suggests that drinking water F should not exceed 0.1 mg F/L, although the lack of a true threshold for F neurotoxicity means that the only assuredly safe level is zero.\textsuperscript{13}

The reference by Broadbent et al. to the 2011 SCHER report for the lack of an association between fluoridated water and IQ and the absence of a plausible biological mechanism suggests that misplaced trust in official reports still occurs.\textsuperscript{15} The SCHER report omitted consideration of the studies of Xiang et al. and Ding et al. and also of work that has identified plausible biological mechanisms for F toxicity such as the G-protein false messenger effects of aluminofluoride complexes described by Strunecká and Patočka.\textsuperscript{16} In contrast, another official report in 2006 from the National Research Council (NRC) on Fluoride in drinking water: a scientific review of EPA’s standards found F to be an endocrine disruptor in the broad sense of altering normal endocrine functions or response, although probably not in the sense of mimicking a normal hormone.\textsuperscript{17} The NRC report found that the consistency of the collective results of the effect of F on human cognitive abilities warranted additional research on the effects of F on intelligence.

Broadbent et al. appear to give reassurance on the safety of CWF by placing undue trust in an official report which has incompletely considered the available
evidence, rather than finding a level likely to be safe by reasoning backwards from the level of F known to cause definite neurotoxicity and introducing an appropriate safety factor for intraspecies differences. This brings to mind an observation of the Italian physicist, mathematician, engineer, astronomer, and philosopher, Galileo Galilei (15 February 1564–8 January 1642). He noted, “In questions of science, the authority of a thousand is not worth the humble reasoning of a single individual.”

Bruce Spittle, Editor-in-Chief

REFERENCES


