

Statement by Professor C V Howard. MB. ChB. PhD. FRCPath., addressing the developmental toxicity of fluoride, for consideration by the US NTP in their forthcoming review of the topic.

1. Background

1.1: I am a medically qualified toxico-pathologist and have expertise on the effects of toxic substances on the fetus and infant during the developmental period of life. I am a Past President of the International Society of Doctors for the Environment, which is a World Health Organisation and United Nations recognised NGO representing some 30,000 medical doctors around the world. I have served on UK Government regulatory committees, including 6 years as a toxicologist on the Advisory Committee on Pesticides. Currently I am Emeritus Professor of Bioimaging in the Centre for Molecular Biosciences at the University of Ulster. I am also a Fellow of the Collegium Ramazzini.

1.2: The level of fluoride in the sea averages about 1.4 ppm, however the evolutionary process appears to have taken little advantage of this availability. While fluoride readily accumulates in hard tissues there appears to be no known use of fluoride in any biochemical process. There is no evidence that fluoride is an essential nutrient as far as mammalian systems are concerned.

1.3 There are now many different sources of both therapeutic and pollutant-derived fluoride. The former can be taken, under informed consent, for dental health purposes. It is generally accepted that the predominant action of fluoride on dental enamel is a topical one and that there is little additional benefit to be derived from systemic administration (CDC, 1999).

1.4: The 'one dose fits all' method of administration of fluoride to whole populations via the public drinking water supply is known to be unreliable. This particularly applies to the neonatal infant being fed formula milk, when it is reconstituted using fluoridated tap water. In the latter case it is acknowledged overdosing is occurring. A baby drinking formula made up with fluoridated tap water at 1 ppm will get up to 250 times more fluoride than a breast-fed baby.

1.5: Breast milk contains very low levels of fluoride (0.004 ppm, NRC, 2006, p.40), even when the lactating mother has been administered fluoride. Though the serum level of fluoride increased, the breast milk level remained very low (Ekstrand, 1981, 1984)). This is certainly not the case with all mono-valent ions, sodium and chloride ions for example. It is my surmise that this could be the result of a specific exclusion mechanism that has evolved to protect the neonate from exposure to anything other than very low levels of fluoride, during critical windows of development of a number of organs and in particular the brain.

1.6: The scientific evidence used to justify the introduction of drinking water fluoridation is not strong. This statement is supported by the York Review (McDonaugh et al: 2000) and, more recently the Cochrane Review (2015) that reviewed the benefits of water fluoridation.

2. The reduced IQ debate

2.1: There is extensive evidence that fluoride is neurotoxic. Over 300 studies - both animal and human - support this conclusion (For a complete listing, see <http://tinyurl.com/zsyrbmq>). These studies include evidence of developmental neurotoxicity from exposure to fluoride, expressed as reduced IQ distributions in populations, when compared epidemiologically with populations with lower exposures.

There now have been 49 studies in four countries: China, India, Iran and Mexico (complete listing at www.FluorideAlert.org/studies/brain01/). These have found a lowered IQ associated with even modest exposure to fluoride. For example Xiang et al. (2003) found a threshold for IQ lowering at 1.9 ppm. Ding et al. (2010), in what they describe as a preliminary study, have found a lowering of IQ in the range of 0.3 to 3 ppm. Moreover, they and other researchers, have reported a correlation between the extent of the IQ lowered and the level of fluoride exposure as measured in the urine.

2.2: Recently a team from Harvard University (Choi et al, 2012) reviewed 27 of these IQ studies using a meta-analysis. They found a remarkable consistency in the results even though they were derived from widely different geographical areas in China and Iran. Of the 27 studies comparing villages with low levels of fluoride and with villages with modest to high levels of fluoride (0.88- 11.5 ppm), 26 revealed a lower IQ in the children from the “high” fluoride village. The mean difference was 7 IQ points, which from a population perspective is highly significant. Such a shift would reduce the number of geniuses in a large population by at least 50%, and approximately double the number of mentally handicapped.

2.3: A consideration of the mechanism by which IQ could be affected by fluoride exposure will form a key part of the NTP Review. Currently such a potential mechanism is not fully understood, though there appear to be two main areas to consider.

-Firstly, a direct toxicological action by fluoride on the developing nervous system is biologically feasible. There have now been well over one hundred animal studies indicating that fluoride can cross the blood brain barrier and cause changes in the brain (see Appendix 1 in the book “The Case Against Fluoride” by Connett, Beck and Micklem).

-Secondly, an indirect mechanism, via disturbance of thyroid hormone metabolism (See chapter 8 of the National Research Council report *Fluoride in Drinking Water: A Review of EPA’s standards*, NRC, 2006, for a comprehensive review of fluoride’s interactions with the endocrine system).

The prior therapeutic use of high dose fluoride to reduce thyroid hormone levels in cases of thyrotoxicosis is well documented (Goldemberg, (1926, 1930, 1932); May (1935, 1937); Orłowski (1932) and Galletti and G. Joyet, (1958)). A recent study by Peckham et al (2014) reported that hypothyroidism was significantly raised in the ~10% of the UK that is fluoridated, as compared to the unfluoridated regions. The incidence of hypothyroidism was found to be almost twice as high in the West Midlands (fluoridated) as compared to the Greater Manchester (unfluoridated) area. Thus there are grounds for anticipating thyroid disruption as a likely sequel to the fluoridation of drinking water.

Therefore a consideration of the sensitivity of the developing human nervous system to even marginal reductions in thyroid hormone is germane. At one end of the spectrum of deficiency, Benham-Rassoli et al (1991) were the first to demonstrate in rats that profound hypothyroidism in the pregnant dam didn’t have any effect on total neuronal number in the offspring. It did have a devastating effect on subsequent neuronal differentiation and neurite outgrowth, leading to the equivalent of cretinism in humans. However what happens when the reduction in maternal thyroid levels are more subtle? Clearly the development of the neuropil has to be the primary focus. The finding that even variations in thyroxin levels within the human maternal euthyroid

(normal) range can subtly adversely affect the IQ of offspring (Pop et al 1995, 1999) highlights the very critical role of the hormone in controlling normal neural development and additionally what a delicate balance is required. This raises some further critical points for the NTP review to address. Are humans more susceptible to neuro-behavioural damage from small changes in maternal thyroid levels than experimental rodent models? Are animal neuro-behavioural models adequate to predict subtle changes in human IQ?

3. Conclusions

There is scientific evidence to support nervous system damage by fluoride both via a direct neurotoxicological mechanism or by an indirect endocrine disruption mechanism. The observed epidemiological deficits in human IQ could be as the result of both mechanisms. The fact that the majority of animal studies have been made on post weaned animals would lend weight to a direct action. However in humans, in my opinion, an indirect mechanism for fluoride developmental neurotoxicity through maternal thyroid hormone disruption is more likely to predominate and therefore be demonstrated at the population level. This is primarily because of the exquisite sensitivity of the human brain to minimal hypothyroidism, apparently even within the euthyroid range. In addition there appear to be biological mechanisms in action to deny direct access of fluoride to the suckling neonate. In humans breast feeding rates can be low and it has been shown that neonates being fed formula feed made up with fluoridated tap water are receiving more than the recommended dose (FSAI, 2006). This would indicate a further possible human vulnerability to damage from fluoride.

4. Statement on conflicts of interest. I have no commercial interests or research grants, current or past, concerning the fluoridation of drinking water. I hold no shares in any companies involved in water fluoridation.

Professor Charles Vyvyan Howard MB. ChB. PhD. FRCPath.

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Centre for Molecular Biosciences,
University of Ulster,
Cromore Road,
Coleraine BT52 1SA,
County Londonderry,
Northern Ireland

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