Significant Fluoride Studies in 2010

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http://fluoridealert.org/fan.2010.review.html

►Fluoride Compromises Brain Function

Ding Y, Gao Y, Sun H, Han H, Wang W, Ji X, Liu X, Sun D. 2010. The relationships between low levels of urine fluoride on children's intelligence, dental fluorosis in endemic fluorosis areas in Hulunbuir, Inner Mongolia, China. J*ournal of Hazardous Materials* doi:10.1016/j.jhazmat.2010.12.097. http://www.ncbi.nlm.nih.gov/pubmed/21237562

Liu YJ, Gao Q, Wu CX, Guan ZZ. 2010. Alterations of nAChRs and ERK1/2 in the brains of rats with chronic fluorosis and their connections with the decreased capacity of learning and memory. *Toxicology Letters* 192: 324-329.

More than 100 animal studies have linked fluoride to brain damage, and 24 additional studies in humans have found an association between high levels of fluoride in drinking water and reduced intelligence. Ding *et al*. (2010) studied 331 children ages 7-14 years living in Hulunbuir City, China, exposed to drinking water with fluoride levels <3 mg/L (mean: 1.31$\pm$1.05 mg/L; range: 0.24-2.84 mg/L). Urine fluoride levels, incidence of dental fluorosis (diagnosed with Dean's Index), and intelligence quotient (IQ, assessed with Combined Raven's Test for Rural China) were determined. The authors found a dose-dependent response between urine fluoride levels and incidence of dental fluorosis. Also observed was an **inverse association between urine fluoride levels and IQ: a 0.59-point decrease in IQ was observed for each 1 mg/L increase in urine fluoride.** Thus, low levels of fluoride in drinking water, even within the range of levels currently allowed, negatively impact children's intelligence and dental health.

Chronic exposure to elevated levels of fluoride results in decreased memory and learning ability, but the mechanisms underlying these effects are not known. To address this issue, Liu *et al*. (2010) exposed rats to varying concentrations of fluoride in drinking water for 6 months. As expected, **spatial learning and memory of the rats were significantly reduced in both the low- (5 mg/L) and high (50 mg/L) fluoride groups** when compared to the control group (<0.5 mg/L), as determined by increased times of Morris Water Maze tests. When compared with controls, **both the low- and high fluoride exposed groups revealed altered expression of several proteins related to cognition in both rats and humans**, including decreased protein expression for two nicotinic acetylcholine receptors (alpha- 4 and alpha-7 nAChR), increased expression for phospho- and total ERK1/2 and phospho-MEK1/2, and decreased activation rate of phospho-ERK1/2. Rats require water fluoride levels 4-5 times greater than humans to produce similar blood plasma fluoride levels. That these changes were observed in even the low fluoride group of the present study suggests similar alterations may be responsible for the decreased intelligence of children exposed to relatively low water fluoride levels, as in Ding *et al*. (above).

►CDC reports 41% of 12-15 year-olds have dental fluorosis

Beltran-Aguilar ED, Barker L, Dye BA. 2010. Prevalence and severity of dental fluorosis in the United States, 1999-2004. NCHS data brief, no 53. Hyattsville, MD: National Center for Health Statistics.

Dental fluorosis refers to hypomineralization of the teeth, producing mottled, stained, pitted surfaces. Dental fluorosis is caused by exposure to systemic (ingested) fluoride during periods of tooth development. The prevalence of dental fluorosis has been increasing in the United States with the concomitant expansion of water fluoridation and the increasing ingestion of fluoride from other sources. Data from the National Health and Nutrition Examination Survey (NHANES) between 1999-2004 were analyzed, and were compared with data from the 1986-1987 National Survey of Oral Health in U.S. School Children. Both surveys assessed all permanent teeth using Dean's Fluorosis Index. Approximately 23% of Americans aged 6-49 had some definitive form of dental fluorosis between 1999-2004, and another 17% met the criteria for "questionable" fluorosis status. Among adolescents, 33% of those aged 6-11, 41% of those aged 12-15, and 36% of those aged 16-19 had some form of dental fluorosis. **For adolescents aged 12-15, the prevalence of dental fluorosis increased from 23% in 1986-87 to 41% in 1999-2004**, indicating that a large percentage of the U.S. population is being overexposed to fluoride.

►Increased risk of fluorosis from infant formula reconstituted with fluoridated water

Levy SM, Broffitt B, Marshall TA, Eichenberger-Gilmore JM, Warren JJ. 2010. Associations between fluorosis of permanent incisors and fluoride intake from infant formula, other dietary sources and dentifrice during early childhood. *Journal of the American Dental Association* 141(10): 1190-1201.

In the United States, the primary source of ingested fluoride is fluoridated water, including that used in the preparation of foods and other beverages. For many infants, formula is a major source of nutrition, and this formula is often reconstituted with fluoridated tap water. The concentration of fluoride in infant formulas reconstituted with "optimally" fluoridated water is up to 200 times greater than that found in breast milk. The Iowa Fluoride Study (IFS), as reported in Levy *et al*. (2010) determined fluoride intake of children starting at age 1.5 months via questionnaires completed by parents, and determined incidence and severity of dental fluorosis via dental exams administered when children were about 9 years of age. An increased incidence of dental fluorosis of permanent incisors was associated with increased fluoride intakes from reconstituted infant formulas between ages 3-9 months. According to the authors, **fluorosis was associated with "higher consumption of powdered concentrate formula and higher fluoride levels in the water used to reconstitute the formula."** The majority of participants in this study lived in areas with "optimally" fluoridated water. The authors state that **formula prepared with "low-fluoride-content water would result in much less fluoride ingestion and, presumably, substantially less or milder dental fluorosis."** Also reported was an **increased risk of fluorosis due to higher intake of fluoridated toothpastes between 16-36 months.**

►At least one-quarter of UK population over-exposed to fluoride

Mansfield P. 2010. Fluoride consumption: the effect of water fluoridation. *Fluoride* 43(4): 223-231.

Over-consumption of fluoride is an issue of concern worldwide, as fluoride has been linked to adverse health effects such as dental fluorosis, reduced thyroid function, weakened bones, skeletal fluorosis, and reduced intelligence. Mansfield (2010) re-analyzed data from the 2000-2003 UK National Diet and Nutrition Survey (NDNS). Using a revised calculation to estimate fluoride intake (i.e. 45% fluoride excretion rate based on current literature, instead of 100% excretion rate as was originally proposed), the author found that the original estimate of those exceeding the Safe Intake (SI) level for fluoride (0.05 mg/kg body weight/day, as established by the Committee on the Medical Aspects of Food Policy) was an order of magnitude too low**--25% of the UK population is now estimated to exceed the SI for fluoride, and nearly two-thirds of those living in fully fluoridated areas exceed the SI for fluoride.** The author concludes that "fluoridating water pushes the majority of consumers into excessive fluoride intake," and that small children are more susceptible to the long-term adverse health effects related to over-consumption, as they retain more fluoride than adults.

►Fluoride decreases bone strength

Chachra D, Limeback H, Willett TL, Grynpas MD. 2010. The long-term effects of water fluoridation on the human skeleton. *Journal of Dental Research* 89(11): 1219-1223.

Community water fluoridation has long been touted as a safe and effective means to reduce dental caries in a population, yet data on the long-term safety of low levels of systemic fluoride exposure on the myriad of body systems are either inconclusive or completely lacking. Ingested fluoride is incorporated into the bones, suggesting that exposure over a lifetime, even to the relatively low levels experienced via fluoridated water, may affect the structural or mechanical properties of bone. Chachra *et al.* (2010) compared bone specimens from residents of fluoridated Toronto to those of non-fluoridated Montreal, with the hypothesis that these populations would reveal patterns consistent with differences in long-term fluoride exposure. The fluoride content of bones from the fluoridated area was significantly higher than those from the non-fluoridated area. Bone from Toronto residents showed greater mean strain at ultimate compressive stress (UCS, an indicator of fracture risk) and greater energy absorbed to failure than bone from Montreal residents. However, the authors failed to control for age, which was greater for those residents in non-fluoridated Montreal. Bones typically weaken with age, and thus the effects of a more elderly population in Montreal may have obscured the full effect of fluoride on the Toronto population. A more relevant finding is that **UCS and yield stress declined with increasing fluoride content of bone, indicating that bone strength decreases with increasing bone fluoride level.** While similar animal studies have been performed, this is the first human epidemiological study to utilize such an analysis to study fluoride levels and risk of bone fracture, and thus should be seriously considered by public health officials when performing evidence-based risk assessments for fluoride exposures for the whole of the population.

►Fluoride increases serum lead concentrations

Sawan RMM, Leite GAS, Saraiva MCP, Barbosa Jr. F, Tanus-Santos JE, Gerlach RF. 2010. Fluoride increases lead concentrations in whole blood and in calcified tissues from lead-exposed rats. *Toxicology* 271(1-2): 21-26.

Silicofluorides are used in more than 90% of artificially fluoridated water in the United States. However, an association between silicofluoride-treated community water and increased blood lead concentrations among children has been previously reported. Early exposure to lead results in cognitive impairment and lower IQ scores in children. Sawan *et al*. (2010) examined the effects of fluoride (as fluosilicic acid, H2SiF6, containing 100 mg/L F), co-administered with lead (as lead acetate, containing 30 mg/L Pb) on Wistar rats exposed from the beginning of gestation. As this was a proof-of-concept study, high levels of fluoride were administered to maximize the influence of fluoride on lead concentrations. After 81 days there were **significantly higher blood lead concentrations, and two- to threefold higher lead concentrations in calcified tissues, in the F+Pb Group compared to the Pb Group.** Thus, a biological effect not yet recognized may underlie the association between water fluoridation and increased blood lead levels observed in children.

►Fluoride disrupts cardiac function

Varol E, Akcay S, Ersoy IH, Koroglu BK, Varol S. 2010a. Impact of chronic fluorosis on left ventricular diastolic and global functions. *Science of the Total Environment* 408(11): 2295-2298.

Varol E, Akcay S, Ersoy H, Ozaydin M, Korogly BK, Varol S. 2010b. Aortic elasticity is impaired in patients with endemic fluorosis. *Biol Trace Elem Res* 133: 121-127.

Elevated levels of fluoride in the blood lower the availability of calcium to the body, which can impair cardiac function. In cases of acute fluoride poisoning, for example, the levels of available calcium can be so low as to cause cardiac arrest. Exposure to sub-acute levels of fluoride may have more subtle effects on the heart. Research by Varol *et al*. (2010a) found that fluorosis patients had significantly higher urine fluoride levels than controls, as expected. In addition, left ventricular myocardial performance index (MPI), calculated as (isovolumic contraction time+isovolumic relaxation time)/aortic ejection time, was also significantly higher in fluorosis patients than in matched controls, suggesting that **patients with endemic fluorosis have left ventricular diastolic and global dysfunctions.**

A related study by Varol *et al*. (2010b) found significantly lower aortic strain (AS) and aortic distensibility (AD), but significantly higher aortic strain index (ASI) in endemic fluorosis patients than in controls, indicating that **the elastic properties of the ascending aorta are impaired in patients with endemic fluorosis.** Thus sub-acute exposures to fluoride may manifest as cardiac dysfunction, potentially increasing future risks of cardiac-related problems.

►Fluoride as a pro-inflammatory factor

Gutowska I, Baranowska-Bosiacha I, Baskiewicz M, Milo B, Siennicka A, Marchiewicz M, Wiszniewska B, Machalinski B, Stachowska E. 2010. Fluoride as a pro-inflammatory factor and inhibitor of ATP bioavailability in differentiated human THP1 monocytic cells. *Toxicology Letters* 196: 74-79.

Inflammatory reactions underlie the pathogenesis of the atherosclerotic process, and oxygen free radicals formed during these reactions contribute to aggravation of atherosclerotic lesions. Gutowska *et al*. (2010) incubated differentiated human THP1 monocytic cells (macrophages) in NaF solution for 48 h at concentrations similar to fluoride concentrations found in human serum (1, 3, 6 and 10 μM). Incubation of macrophages in fluoride solutions significantly decreased the amount of synthesized cellular ATP, and increased the formation of reactive oxygen species (ROS) and apoptotic cells in a dose-dependent pattern. Thus **fluoride may be considered pro-atherogenic and pro-apoptotic**, and long-term exposure to low concentrations of fluoride may lead to harmful changes in cellular metabolism.