October 28, 2010

NEUROLOGIC RISKS OF FLUORIDATION

Considerations from Scientific Publications. See also Appendix AA

1. "Children who live in a fluorosis area have five times higher odds of developing low IQ than those who live in a nonfluorosis area or a slight fluorosis area." SOURCE: Tang QQ, DuJ, Ma HH, Jiang SJ, Zhou XJ, Fluoride and children's intelligence: a meta-analysis, Biol Trace Elem Res. 2008 Winter: 126(1-3):115-20

2. "We found that exposure to fluoride (F) in urine was associated with reduced Performance, Verbal, and Full IQ scores before and after adjusting for confounders. The same pattern was observed for models with F in water as the exposure variable.... The individual effect of F in urine indicated that for each mg increase of F in urine a decrease of 1.7 points in Full IQ might be expected."
SOURCE: Rocha-Amador D, et al. (2007). Decreased intelligence in children and exposure to fluoride and arsenic in drinking water. Cadernos de Saude Publica 23(Suppl 4):S579-87.

3. "These negative correlations between IQ and urinary As and between IQ and urinary fluoride indicate that exposure to high levels of As or fluoride, or both, could affect children's intelligence... This study indicates that exposure to fluoride in drinking water is associated with neurotoxic effects in children."
SOURCE: Wang SX, et al. (2007). Arsenic and fluoride exposure in drinking water: children's IQ and growth in Shanyin county, Shanxi province, China. Environmental Health Perspectives 115(4):643-7.

4. "In agreement with other studies elsewhere, these findings indicate that children drinking high F water are at risk for impaired development of intelligence."
SOURCE: Trivedi MH, et al. (2007). Effect of high fluoride water on intelligence of school children in India. Fluoride 40(3):178-183.

5. "Based on the findings of this study, exposure of children to high levels of fluoride may carry the risk of impaired development of intelligence."
SOURCE: Seraj B, et al. (2006). [Effect of high fluoride concentration in drinking water on children's intelligence]. Journal of Dental Medicine 19(2):80-86.

6. The 2006 NRC Report said, "A few epidemiologic studies of Chinese populations have reported IQ deficits in children exposed to fluoride at

2.5 to 4 mg/L in drinking water. Although the studies lacked sufficient detail for the committee to fully assess their quality and relevance to U.S. populations, the consistency of the results appears significant enough to warrant additional research on the effects of fluoride on intelligence." SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p. 6.

7. "Conclusion: High fluoride burden has a definite effect on the intellectual and physical development of children."
SOURCE: Wang S, et al. (2005). Effects of coal burning related endemic fluorosis on body development and intelligence levels of children. Journal of Applied Clinical Pediatrics 20(9): 897-898. (Appendix H)

8. "In our study, it was shown that the average IQ of children in a fluoride endemic area was somewhat lower than the control, but the result was not significant (P>0.05). The rate of children with “low” IQs, however, was elevated as compared to the control, and this was very statistically significant... Our study showed that, within the fluoride endemic area, the average IQ of children suffering from dental fluorosis is clearly lower than those that show no signs of the disease, and this result is very significant (P <0.01). This IQ difference of 8.12 suggests that children suffering from dental fluorosis might be particularly sensitive to excess fluoride, and that the manifestation of this is not limited to the typical symptoms of fluorosis, but, more seriously, also disrupts intellectual development."
SOURCE: Li Y, et al. (2003). The effects of endemic fluoride poisoning on the intellectual development of children in Baotou. Chinese Journal of Public Health Management 19(4):337-338. (Appendix S)

9. “Higher drinking water fluoride levels were significantly associated with higher rates of mental retardation (IQ <70) and borderline intelligence (IQ 70-79)... In endemic fluorosis areas, drinking water fluoride levels greater than 1.0 mg/L may adversely affect the development of children's intelligence.”
SOURCE: Xiang Q, et al. (2003a). Effect of fluoride in drinking water on children's intelligence. Fluoride 36: 84-94.

10. "As an additional part of our investigation of an association between fluoride in drinking water and children’s intelligence in two villages of Sihong County, Jiangsu Province, China, we have now determined blood lead levels of children in that study... The results show there is essentially no difference between the two villages in blood lead concentrations of the children... These results thus make it very unlikely that the differences in IQ of the children living in Wamiao and Xinhuai are the result of differences in exposure to lead rather than to fluoride."
SOURCE: Xiang Q, et al. (2003b). Blood lead of children in Wamiao-Xinhuai intelligence study. Fluoride 36: 198-199.

11. "After controlling by significant confounders, urinary fluoride correlated positively with reaction time and inversely with the scores in visuospatial organization. IQ scores were not influenced by fluoride exposure. An increase

in reaction time could affect the attention process, also the low scores in visuospatial organization could be affecting the reading and writing abilities in these children."
SOURCE: Calderon J, et al. (2000). Influence of fluoride exposure on reaction time and visuospatial organization in children. Epidemiology 11(4): S153.

12. "In terms of IQ ranking, the high fluoride groups showed significant deficits as compared to control (P<0.01)... Conclusion: When fluoride and iodine levels in excess of national standards for drinking water are present in the same area and ingested together, the harmful effects of fluoride are more pronounced, and the resulting damage compounded."
SOURCE: Hong F, et al. (2001). A study of fluorine effects on children's intelligence development under different environments. Chinese Primary Health Care 15: 56-57. (Appendix R)

13. "The IQ of the 60 children in the high-fluoride area was significantly lower than that of the 58 children in the low-fluoride area... More children in the high-fluoride area were in the retardation or borderline categories of IQ than children in the low fluoride area. An inverse relationship was also present between IQ and the urinary fluoride level. Exposure of children to high levels of fluoride may therefore carry the risk of impaired development of intelligence."
SOURCE: Lu Y, et al (2000). Effect of high-fluoride water on intelligence of children. Fluoride 33:74-78.

14. "Within the seven categories of the scores, there were significantly more borderline and low IQs in the high F area (13/60) than in the low F area (2/58) (p<0.01)." Report on the Intellectual Ability of Children Living in High-Fluoride Water Areas, Liu S, et al, Chinese Journal of Control of Endemic Diseases 2000;15(4)231-2. Fluoride 41(2)144-147 (Appendix N)

15. "A study of intelligence quotient (IQ) in China was conducted using Wickler's Intelligence Quotient Table for preschool children, in 4-7 year-old children, 147 from a district with high level of fluoride and 83 from a control area. High F intake had a significant influence on IQ of preschool children. Operation IQ was mainly affected."
SOURCE: Wang G, et al. (1996). Research on intelligence quotient of 4-7 year-old children in a district with a high level of fluoride. Endemic Diseases Bulletin 11:60-62. (Appendix G)

16. "In Shanxi Province, China, children living in the endemic fluoride village of Sima located near Xiaoyi City had average IQ significantly lower than children living to the north in the nonendemic village of Xinghua."
SOURCE: Zhao LB, et al (1996). Effect of high-fluoride water supply on children's intelligence. Fluoride 29: 190-192.

17. "The intelligence was measured of 907 children aged 8-13 years living in areas which differed in the amount of fluoride present in the environment. The Intelligence Quotient (IQ) of children living in areas with a medium or severe prevalence of fluorosis was lower than that of children living in areas with only slight fluorosis or no fluorosis. The development of intelligence appeared to be adversely affected by fluoride in

the areas with a medium or severe prevalence of fluorosis. A high fluoride intake was associated with a lower intelligence."
SOURCE: Li XS. (1995). Effect of Fluoride Exposure on Intelligence in Children. Fluoride 28:189-192.

18. "We made an investigation in 157 children, aged 12-13, born and grew up in a coal burning pattern endemic fluorosis area and an experiment on excessive fluoride intake in rat. The results showed: (1) Excessive fluoride intake since early childhood would reduce mental work capacity (MWC) and hair zinc content: (2) The effect on zinc metabolism was a mechanism of influence on MWC by excessive fluoride intake..."
SOURCE: Li Y, et al. (1994). [Effect of excessive fluoride intake on mental work capacity of children and a preliminary study of its mechanism] Hua Hsi I Ko Ta Hsueh Hsueh Pao. 25:188-91. (Appendix E)

19. "An excess of fluoride and a lack of iodine in the same environment has been shown to have a marked effect on child intellectual development, causing a more significant intellectual deficit than lack of iodine alone. The subject group of children from the high fluoride, high iodine zone have an average IQ of 76.67±7.75, which was somewhat less than the control (IQ = 81.67 ±11.9), though the different is not significant (P>0.05). However, the percentage of subject children in the low range (16.67%) is higher than the control, suggesting that a high iodine, high fluoride environment also has a definite negative influence on child intellectual ability."
SOURCE: Yang Y, et al. (1994). Effects of high iodine and high fluorine on children's intelligence and the metabolism of iodine and fluorine. Chinese Journal of Pathology 15(5):296-8. (Appendix F)

20. "The results of this study show that the children living in high fluoride areas have lower IQs than the children from the non-endemic area. Also, there were many more children from the endemic area with an IQ score ranking of below the borderline low level as compared to the control; in the endemic area, there were 18 such subject, or 30% of the total, while in the non-endemic area there were only 7, or a rate of 11.5%. The difference between the two groups is significant. The overall distribution shows marked difference, with the scores in control group on average one rank higher than the control... In summary, although diminished intellectual ability can result from a multitude of factors (both innate and acquired) that influence neural development and cell division in the cerebrum, the comparison conducted in this study of two areas where the other environment factors are basically the same shows clear differences in IQ, and it's probable that this difference is due to a high fluoride environment. It is not clear whether the underlying mechanism is fetal exposure to fluoride resulting from the poisoning of the mother or intake of fluoride after birth (in either case causing a disruption nerve cell development leading to mental deficits); this matter awaits further study."
SOURCE: Guo XC, et al. (1991). A preliminary exploration of IQ of 7-13 year old pupils in a fluorosis area with contamination from burning coal. Chinese Journal of Endemiology 10:98-100. (Appendix J)

21. "The results of this study indicate that there is significant difference between the intellectual ability of the 7 – 14 year old children from the endemic area and those of the control, and moreover that the average IQ of the children from the endemic area is clearly lower. In the endemic region, the children in the 80-89 range and below make up more

than 25% of the total, while in the control range only 18% of the children fall into that range, demonstrating that high fluoride has a direct connection with the intellectual development of children."
SOURCE: Chen YX, et al. (1991). Research on the intellectual development of children in high fluoride areas. Chinese Journal of Control of Endemic Diseases. 6(supplement):99-100. Chen, et al. **Research on the intellectual development of children in high fluoride areas**. Fluoride 41(2):120–4. 2008 (Appendix I)

22. "The significant differences in IQ among these regions suggests that fluoride can exacerbate central nervous lesions and somatic developmental disturbance caused by iodine deficiency. This may be in keeping with fluoride's known ability to cause degenerative changes in central nervous system cells and to inhibit the activities of many enzymes, including choline enzymes, causing disturbance of the nerve impulse."
SOURCE: Lin Fa-Fu; et al (1991). The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang. Iodine Deficiency Disorder Newsletter Vol. 7. No. 3.

23. "By testing of the intellectual ability of 447 elementary school students ranging in age from 9 to 10 1/2, it was discovered that both high and low fluoride had an effect on child intelligence. Fluoride levels greater than 2.0 mg/L or less than 0.2 mg/L can disrupt intellectual development."
SOURCE: Qin LS, Cui SY. (1990). The influence of drinking water fluoride on pupils IQ, as measured by Rui Wen's standards. Chinese Journal of the Control of Endemic Diseases 5:203-204.

24. "The effect of a harmful environment containing both high fluoride and low iodine on the development of child mental ability has yet to be reported on. To investigate this question, the authors used the Wechsler Intelligence Test to determine the IQs of a total of 329 eight- to fourteen-year-old children living in nine high fluoride, low iodine villages and seven villages that had only low levels of iodine. We discovered that the IQs of children from high fluoride, low iodine villages were clearly lower than those from the villages with low iodine alone."
SOURCE: Ren Da-Li. (1989). An investigation of intelligence development of children aged 8-14 years in high-fluoride and low-iodine areas. Chinese Journal of Control of Endemic Diseases 4:251. (Appendix B)

HUMAN STUDIES- Fluoride's Impact on the Developing Brain (Fetuses/Infants):

25. "The effects of excessive fluoride intake during pregnancy on neonatal neurobehavioural development and the neurodevelopment toxicity of fluoride were evaluated. Ninety-one normal neonates delivered at the department of obstetrics and gynecology in five hospitals of Zhaozhou County, Heilongjiang province, China were randomly selected from December 2002 to January 2003. The subjects were divided into two groups (high fluoride and control) based on the fluoride content in the drinking water of pregnant women. The results showed that the urinary fluoride levels of mothers from the high fluoride group were higher than those of the control group. There were significant differences in the

neonatal behavioral neurological assessment score and neonatal behavioral score between the subjects in endemic areas and the control group. There were also significant differences in the non-biological visual orientation reaction and biological visual and auditory orientation reaction between the two groups. It is concluded that fluoride is toxic to neurodevelopment. Excessive fluoride intake during pregnancy can cause adverse effects on neonatal neurobehavioural development."
SOURCE: Li J, Yao L, Shao Q-L. (2004). Effects of high-fluoride on neonatal neurobehavioural development. Chinese Journal of Endemiology 23:464-465. (Appendix T)

26. "The levels of neurotransmitters and receptors in brain tissue of aborted fetuses from areas of endemic fluorosis were tested. The results showed that in 10 subjects from a high fluoride area ranging in age from 5 to 7 months, the levels of norepinephrine, 5-hydroxyltryptamine, and α1-receptor were lower and the level of epinephrine higher as compared with levels seen in the control fetuses from a non-fluorosis endemic area; each of these results was statistically significant ($P<0.05$). Other monoamine neurotransmitters and metabolic products, such as dopamine, 5-hydroxy-indole acetic acid, and 3,4-dihydroxybenzoic acid showed no significant differences ($P>0.05$). The results suggest that the accumulation of fluoride in the brain tissue can disrupt the synthesis of certain neurotransmitters and receptors in nerve cells, leading to neural dysplasia or other damage."
SOURCE: Yu Y, et al. (1996). Changes in neurotransmitters and their receptors in human foetal brain from an endemic fluorosis area. Chinese Journal of Endemiology 15:257-259. (Appendix L)

27. "Fifteen therapeutically aborted fetuses at the 5th-8th gestation month from the endemic fluorosis area were compared with those from the non-endemic area. Stereological study of the brains showed that the numerical density of volume of the neurons and the undifferentiated neuroblasts as well as the nucleus-cytoplasm ratio of the neurons were increased. The mean volume of the neurons was reduced. The numerical density of volume, the volume density and the surface density of the mitochondria were significantly reduced. The results showed that chronic fluorosis in the course of intrauterine fetal life may produce certain harmful effects on the developing brain of the fetus."
SOURCE: Du L. (1992). [The effect of fluorine on the developing human brain]. Chung-hua Ping Li Hsueh Tsa Chih. 21:218-20. (Appendix D)

28. "Fluoride can pass through the blood-brain barrier and accumulate in brain tissue, thus in our study the brain tissue of the fetuses from the fluoride endemic area showed higher fluoride levels than the control. The mechanisms involved are not yet clear. Besides increased amounts of fluoride, the brain tissue of the endemic subjects also showed nerve cells with swollen mitochondria, expanded granular endoplasmic reticula, grouping of the chromatin, damage to the nuclear envelope, a lower number of synapses, fewer mitochondria, microtubules, and vesicles within the synapses, and damage to the synaptic membrane. These changes indicate that fluoride can retard the growth

and division of cells in the cerebral cortex. Fewer mitochondria, microtubules, and vesicles within the synapses could lead to fewer connections between neurons and abnormal synaptic function, influencing the intellectual development after birth. These questions await further research."
SOURCE: Han H, et al. (1989). The effects of fluorine on human fetus. Chinese Journal of Control of Endemic Diseases 4:136-138. (Appendix C)

HUMAN STUDIES- Fluoride's Impact on the Adult Brain:

29. "The results of the NCTB (neurobehavioral core test battery) testing show the exposed groups with significant differences for various indices as compared to the reference standards and the control, with particular deficits in attention, auditory retention, and physical dexterity and acuity as well as abnormal emotional states. This is consistent with the symptoms of endemic fluoride poisoning, suggesting occupational exposure to fluoride has a harmful effect on the higher functions of the central nervous system, negatively influencing both cognitive and autonomic functioning. There is a definite relationship between the damage caused by fluoride and the level of exposure. The correlation analysis shows that, with the exception of visual retention and digit symbol testing, serum fluoride is negatively correlated with all relevant indices, further demonstrating the cause and effect relationship between occupational fluoride exposure and neurobehavioral function; these tests can be used as early indicators to help protect the health of workers exposed to fluoride as part of their jobs."
SOURCE: Guo Z, et al. (2001). Study on neurobehavioral function of workers occupationally exposed to fluoride. Industrial Health and Occupational Disease 27:346-348. (Appendix Q)

30. “Sulfuryl fluoride exposure over the year preceding examination was associated with significantly reduced performance on the Pattern Memory Test and on olfactory testing... CONCLUSIONS: Occupational sulfuryl fluoride exposures may be associated with subclinical effects on the central nervous system, including effects on olfactory and some cognitive functions.”
SOURCE: Calvert GM, et al. (1998). Health effects associated with sulfuryl fluoride and methyl bromide exposure among structural fumigation workers. American Journal of Public Health 88:1774-80.

31. "Although the blood-brain barrier is relatively impermeable to fluoride, it does not pose an absolute barrier and fluoride has the ability to enter the brain. The literature was examined to assess the quality of the evidence for cerebral impairment occurring due to exposure to fluoride from therapeutic or environmental sources. Several surveys of persons chronically exposed to industrial fluoride pollution reported symptoms related to impaired central nervous system functioning with impaired cognition and memory. Examination of individual case reports showed the evidence for aetiological relationships between symptoms and fluoride exposure to be of variable quality. The evidence was seen as being suggestive of a relationship rather than being definitive. The difficulties with concentration and memory described in relation to exposure to fluoride did

not occur in isolation but were accompanied by other symptoms of which general malaise and fatigue were central. Possible mechanisms whereby fluoride could affect brain function include influencing calcium currents, altering enzyme configuration by forming strong hydrogen bonds with amide groups, inhibiting cortical adenylyl cyclase activity and increasing phosphoinositide hydrolysis."
SOURCE: Spittle B. (1994). Psychopharmacology of fluoride: a review. International clinical psychopharmacology 9:79-82.

ANIMAL STUDIES - Fluoride's Impact on Brain (Behavior/ Learning/ Memory):

32. "Epidemiological investigations reveal that high fluoride and low iodine have strong adverse effects on the intelligence quotient (IQ) of children. . . we first report on the proteomic changes in brain proteins in offspring rats . . . The identified proteins are mainly related with cellular signaling, energy metabolism, and protein metabolism and provide a valuable clue to explore the mechanism underlining the neurotoxicity of high fluoride and low iodine."
SOURCE: Ge Y et al, Proteomic analysis of brain proteins of rats exposed to high fluoride and low Iodine, Arch Toxicol. 2010 Apr 3 www.ncbi.nlm.nih.gov/pubmed/20364248

33. "Overall, these results suggest that moderate intoxication with sodium fluoride has potentially deleterious effects on learning and memory."
SOURCE: Chioca LR, et al. (2007). Subchronic fluoride intake induces impairment in habituation and active avoidance tasks in rats. European Journal of Pharmacology Oct 25; [Epub ahead of print]

34. "The results of the present study indicate that perinatal exposure to sodium fluoride (NaF), at dose levels below those associated with gross malformations and/or overt neurotoxic effects, produces both short and long term sex and dose specific neurobehavioural alterations in rat offspring."
SOURCE: Bera I, et al. (2007). Neurofunctional effects of developmental sodium fluoride exposure in rats. European Review for Medical and Pharmacological Sciences 11(4):211-24.

35. "Additional animal studies designed to evaluate reasoning are needed. These studies must be carefully designed to measure cognitive skills beyond rote learning or the acquisition of simple associations, and test environmentally relevant doses of fluoride."
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p. 187.

36. "In comparison with control rats, the learning and memory ability of the offspring rats was depressed by high fluoride, low iodine, or the combination of high fluoride and low iodine."
SOURCE: Wang J, et al. (2004). Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats. Fluoride 37: 201-208.

37. "Fluoride intoxicated animals also performed poorly in motor co-ordination tests and maze tests. Inability to perform well increased with higher

fluoride concentration in drinking water."
SOURCE: Bhatnagar M, et al. (2002). Neurotoxicity of fluoride: neurodegeneration in hippocampus of female mice. Indian Journal of Experimental Biology 40: 546-54.

38. "Administration of sodium fluoride with drinking water produced both behavioural and dental toxicities and not lethality in the present study. A suppression of spontaneous motor activity, a shortening of rota-rod endurance time, a decreased body weight gain and food intake, a suppression of total cholinesterase and acetylcholinesterase activities and dental lesion were observed in test animals."
SOURCE: Ekambaram P, Paul V. (2001). Calcium preventing locomotor behavioral and dental toxicities of fluoride by decreasing serum fluoride level in rats. Environmental Toxicology and Pharmacology 9(4):141-146.

39. "The main results showed that the learning capability of mice drinking higher concentration of fluoride presented remarkable deterioration."
SOURCE: Zhang Z, et al. (2001). [Effects of selenium on the damage of learning-memory ability of mice induced by fluoride]. Wei Sheng Yan Jiu. 30(3):144-6. (Appendix P)

40. "Learning and memory abilities of high-fluoride exposed groups were significantly lower than that of the control group, while the brain ChE activities of high-fluoride exposed groups were significantly higher. Conclusions: High fluoride concentration in drinking water can decrease the cerebral functions of mice. Fluoride is a neurotoxicant."
SOURCE: Sun ZR, et al. (2000). Effects of high fluoride drinking water on the cerebral functions of mice. Chinese Journal of Epidemiology 19: 262-263. (Appendix O)

41. "The main results are as follows: the learning ability of mice drinking high concentration of fluoride presented remarkable deterioration... The results suggested that the impairment on the learning capability induced by fluorosis may be closely related with the pathological changes of synaptic structure in the brain of mice."
SOURCE: Zhang Z, et al. (1999). [Effect of fluoride exposure on synaptic structure of brain areas related to learning-memory in mice] [Article in Chinese]. Wei Sheng Yan Jiu 28(4):210-2. (Appendix M)

42. "Sodium fluoride treatment suppressed spontaneous motor activity but no change was observed in the motor coordination of these animals. A suppression of spontaneous motor activity suggests that fluoride has, by a central action, inhibited motivation of these animals to exhibit locomotor behavior."
SOURCE: Paul V, et al. (1998). Effects of sodium fluoride on locomotor behavior and a few biochemical parameters in rats. Environmental Toxicology and Pharmacology 6: 187–191.

43. "In this experiment, the freeze response to auditory stimuli in the pups showed significant delay, indicating that relatively high doses of fluoride can negatively influence the development of auditory nerves. Guan Zhizhong et al[8] report that the offspring of rats exposed to fluoride have retarded cerebral development and exhibit changes in neural cell ultrastructure. The results of the

present experiment suggest that the effects of high doses of fluoride on the behavior development of the offspring are visible primarily as slight delays in response times, particularly with regard to motor and coordination function and well as muscle strength. The measurement of the thickness of the cerebral cortex of offspring on day 21 revealed that the 25 mg/L group had a significantly thinner cerebral cortex as compared to the control; this histological analysis indicates that fluoride slows the growth of brain cells."
SOURCE: Wu N, et al. (1995). Research on the abnormal behavior of rats exposed to fluoride. Chinese Journal of Control of Endemic Diseases 14(5):271. (Appendix K)

44. “This study demonstrates a link between certain fluoride exposures and behavioral disruption in the rat. The effect on behavior varied with the timing of exposure during CNS development. Behavioral changes common to weanling and adult exposures were different from those after prenatal exposures... Experience with other developmental neurotoxicants prompts expectations that changes in behavioral function will be comparable across species, especially humans and rats... [A] generic behavioral pattern disruption as found in this rat study can be indicative of a potential for motor dysfunction, IQ deficits and/or learning disabilities in humans.”
SOURCE: Mullenix P, et al. (1995). Neurotoxicity of Sodium Fluoride in Rats. Neurotoxicology and Teratology 17:169-177.

45. " When rats were treated 6 hr a day for 5 mo. with HF concentrations of 3, 1, 0.5, and 0.1 mg/m-3, it caused functional changes in the CNS, as shown by the condition reflex method and the measurement of chronaxy. There was inhibition of the blood alkaline phosphatase activity and pathomorphological changes in the CNS, bone and tooth tissues and internal organs. The extent of the changes depended on the concentration of HF. The maximum allowable concentration of HF for the air at working places presently accepted, 0.5 mg/m-3, is too high."
SOURCE: Vishnevskii VL, El Nichnykh LN. (1969). (A toxicological and morphological characterization of the action of different concentrations of inhaled hydrogen fluoride on the body.). Tr Tsentr Nauchno-Issled Proektn-Konstr In. 2: 143-147.

46. "General malaise, asthenia, and apathy developed to a marked degree in the monkeys exposed to the BeF2 (beryllium fluoride) aerosol, and in those under the heaviest BeHPO4 exposure. The monkeys retreated to the furthest corner of their cages and paid no attention to light flashed at them. They remained in this withdrawn and listless condition until death. Monkeys which inhaled the BeSO4 aerosol faired best of all."
SOURCE: Schepers GWH. (1964). Biological action of beryllium: Reaction of the monkey to inhaled aerosols. Industrial Medicine and Surgery 33: 1-16.

ANIMAL STUDIES - Fluoride's Impact on Brain:

47. "Lipids and phospholipids, phosphohydrolases and phospholipase D, and protein content have been shown to be reduced in the

brains of laboratory animals subsequent to fluoride exposure. The greatest changes were found in phosphatidylethanolamine, phosphotidylcholine, and phosphotidylserine. Fluorides also inhibit the activity of cholinesterases, including acetylcholinesterase. Recently, the number of receptors for acetylcholine has been found to be reduced in regions of the brain thought to be most important for mental stability and for adequate retrieval of memories.

It appears that many of fluoride's effects, and those of the aluminofluoride complexes are mediated by activation of Gp, a protein of the G family. G proteins mediate the release of many of the best known transmitters of the central nervous system. Not only do fluorides affect transmitter concentrations and functions but also are involved in the regulation of glucagons, prostaglandins, and a number of central nervous system peptides, including vasopressin, endogenous opioids, and other hypothalamic peptides. The AlFx binds to GDP and ADP altering their ability to form the triphosphate molecule essential for providing energies to cells in the brain. Thus, AlFx not only provides false messages throughout the nervous system but, at the same time, diminishes the energy essential to brain function.

Fluorides also increase the production of free radicals in the brain through several different biological pathways. These changes have a bearing on the possibility that fluorides act to increase the risk of developing Alzheimer's disease. Today, the disruption of aerobic metabolism in the brain, a reduction of effectiveness of acetylcholine as a transmitter, and an increase in free radicals are thought to be causative factors for this disease. More research is needed to clarify fluoride's biochemical effects on the brain."
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p. 186.

48. "Studies of rats exposed to NaF or AlF3 have reported distortion in cells in the outer and inner layers of the neocortex. Neuronal deformations were also found in the hippocampus and to a smaller extent in the amygdala and the cerebellum. Aluminum was detected in neurons and glia, as well as in the lining and in the lumen of blood vessels in the brain and kidney. The substantial enhancement of reactive microglia, the presence of stained intracellular neurofilaments, and the presence of IgM observed in rodents are related to signs of dementia in humans. The magnitude of the changes was large and consistent among the studies."
SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p. 187.

49. "In the present study, levels of glutathione and activities of catalase, GSH-PX, and SOD were significantly decreased, whereas lipid peroxide levels were enhanced in the brain of adult rats by treatment with NaF, As2O, or NaF + As2O3, in agreement with earlier reports."
SOURCE: Chinoy NJ, et al. (2004). Biochemical effects of sodium fluoride and arsenic trioxide toxicity and their reversal in the brain of mice. Fluoride 37: 80-87.

50. "The histology of the cerebral hemisphere was altered by NaF and/or Arsenic trioxide [As2O3] treatment for 30 days, wherein the effect by As2O3 was greater than by NaF treatment. This result is in agreement with others... The reduced brain acetylcholinesterase (AChE) enzyme activity observed in the present study corroborates data of others in rats exposed for three months to arsenic trioxide and in the brain of NaF-treated mice and rats as compared to controls... The DNA and RNA levels in the cerebral hemisphere were significantly lower in NaF and/or As2O3-treated mice in the present study, which could affect brain function. The ingestion of the antidotes vitimans C and E as well as calcium phosphate, either indivdually or in combination, during the 30-day withdrawal period resulted in significant recovery, probably due to the antioxidant-properties of vitamins C and E and modulation of fluoride-induced toxicity in rats by calcium."
SOURCE: Shah SD, Chinoy NJ. (2004). Adverse effects of fluoride and/or arsenic on the cerebral hemisphere of mice and recovery by some antidotes. Fluoride 37: 162-171.

51. "Superoxide dismutase (SOD) activity and the malondialdehyde (MDA) content in the brain of the combined high fluoride and low iodine group were significantly higher during and at the end of the 90-day period than in the control group, but the SOD/MDA ratio in this high fluoride and low iodine group was consistently lower than in the control group. These results suggest that [oxidative] stress from high fluoride and low iodine is one of the causes of reduction in learning and memory in offspring rats."
SOURCE: Wang J, Ge Y, Ning H, Wang S. (2004). Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats. Fluoride 37: 201-208.

52. "Brain protein was decreased by low iodine and even more by the combined interaction of high fluoride and low iodine. The activity of cholinesterase (ChE) in the brain was affected to some extent by high fluoride and low iodine but was especially affected by high fluoride and low iodine together."
SOURCE: Wang J, et al. (2004). Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats. Fluoride 37: 201-208.

53. "Recently, we have detected the alterations of nicotinic acetylcholine receptors (nAChRs) in rat brains and PC12 cells affected by fluoride toxicity... [O]xidative stress, including protein oxidation of the receptors and lipid peroxidation in cellular membrane, might be a mechanism of the deficit of the receptors."
SOURCE: Shan KR, Qi XL, Long YG, Wang YN, Nordberg A, Guan ZZ. (2004). Decreased nicotinic receptors in PC12 cells and rat brains influenced by fluoride toxicity—a mechanism relating to a damage at the level in post-transcription of the receptor genes. Toxicology 200: 169–177.

54. "Fluorosis had obvious influence on phospholipid and fatty acid composition in brain cells of rats, and its mechanism might be associated with action of lipid peroxidation, and 0.03 mg/L KI (potassium iodine) is the optimal concentration for the antagonistic action with this influence from fluorosis."
SOURCE: Shen X, Zhang Z, Xu X. (2004). [Influence of combined iodine and fluoride on phospholipid and fatty acid composition in brain cells of rats] Wei Sheng Yan Jiu. 33:158-61.

55. "These findings suggest that selective decreases in the number of nAChRs may play an important role in the mechanism(s) by which fluoride causes dysfunction of the central nervous system."
SOURCE: Chen J, Shan KR, Long YG, Wang YN, Nordberg A, Guan ZZ. (2003). Selective decreases of nicotinic acetylcholine receptors in PC12 cells exposed to fluoride. Toxicology 183: 235-42.

56. "These neurotoxic changes in the brain suggested that there was a direct action of fluoride upon the nerve tissue which was responsible for central nervous system problems such as tremors, seizures, and paralysis indicating brain dysfunction seen at the two highest doses."
SOURCE: Shashi A. (2003). Histopathological investigation of fluoride-induced neurotoxicity in rabbits. Fluoride 36: 95-105.

57. "CONCLUSION: Fluoride may go through the blood-brain barrier and accumulate in rat hippocampus, and inhibit the activity of cholinesterase."
SOURCE: Zhai JX, et al. (2003). [Studies on fluoride concentration and cholinesterase activity in rat hippocampus]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 21:102-4.

58. "Light microscopic study of hippocampal sub-regions demonstrated significant number of degenerated nerve cell bodies in the CA3, CA4 and dentate gyrus(Dg) areas of sodium fluoride administered adult female mice. Ultrastructural studies revealed neurodegenerative characteristics like involution of cell membranes, swelling of mitochondria, clumping of chromatin material etc, can be observed in cell bodies of CA3, CA4 and dentate gyrus (Dg)."
SOURCE: Bhatnagar M, et al. (2002). Neurotoxicity of fluoride: neurodegeneration in hippocampus of female mice. Indian Journal of Experimental Biology 40: 546-54.

59. "The DNA damage in pallium neurons in rats of the fluoride group was much more serious compared with those of the control group...Sodium fluoride could induce DNA damage and apoptosis in rats brain."
SOURCE: Chen J, Chen X, Yang K, Xia T, Xie H. (2002). [Studies on DNA damage and apoptosis in rat brain induced by fluoride]. Zhonghua Yu Fang Yi Xue Za Zhi 36: 222-224.

60. "In order to investigate the molecular mechanism(s) underlying brain dysfunction caused by chronic fluorosis, neuronal nicotinic acetylcholine receptors (nAChRs) in the brain of rats receiving either 30 or 100 ppm fluoride in their drinking water for 7 months were analyzed in the present study employing ligand binding and Western blotting... Since nAChRs play major roles in cognitive processes such as learning and memory, the decrease in the number of nAChRs caused by fluoride toxicity may be an important factor in the mechanism of brain dysfunction in the disorder."
SOURCE: Long YG, Wang YN, Chen J, Jiang SF, Nordberg A, Guan ZZ. (2002). Chronic fluoride toxicity decreases the number of nicotinic acetylcholine receptors in rat brain. Neurotoxicology and Teratology 24:751-7.

61. "These results suggest that fluoride enhances oxidative stress in the brain, thereby disturbing the antioxidant defense of rats. Increased oxidative stress could be one of the mediating factors in the pathogenesis of fluoride toxicity in

the brain."
SOURCE: Shivarajashankara YM , et al. (2002). Brain lipid peroxidation and antioxidant systems of young rats in chronic fluoride intoxication. Fluoride 35: 197-203.

62. "Rats exposed to 100 ppm fluoride showed significant neurodegenerative changes in the hippocampus, amygdala, motor cortex, and cerebellum... These histological changes suggest a toxic effect of high-fluoride intake during the early developing stages of life on the growth, differentiation, and subcellular organization of brain cells in rats."
SOURCE: Shivarajashankara YM , et al. (2002). Histological changes in the brain of young fluoride-intoxicated rats. Fluoride 35: 12-21.

63. "The extent of DNA damage in the fluoride + selenium + zinc group was significantly slighter than that in the fluoride group ($P < 0.05$). It suggested that fluoride and selenium could induce DNA damage in pallium neural cells of rats respectively."
SOURCE: Chen J, Chen X, Yang K. (2000). [Effects of selenium and zinc on the DNA damage caused by fluoride in pallium neural cells of rats]. Wei Sheng Yan Jiu. 29: 216-7.

64. "This study therefore shows that both brain and muscle are affected by fluoride with inhibition of some enzymes associated with free-radical metabolism, energy production and transfer, membrane transport, and synaptic transmission, but with an enhanced activity of XOD."
SOURCE: Lakshmi Vani M, Pratap Reddy K. (2000). Effects of fluoride accumulation on some enzymes of brain and gastrocnemius muscle of mice. Fluoride 33: 17-26.

65. "There is a tendency for neurone apoptosis in chronic fluorosis in rats. It is most evident with changes in pathology. It is not likely that only one form of neurone damage exist in the process of chronic fluorosis. There are recessive changes and apoptosis in the process at the same time."
SOURCE: Lu XH, et al. (2000). Study of the mechanism of neurone apoptosis in rats from the chronic fluorosis. Chinese Journal of Epidemiology 19: 96-98.

66. "Over uptake of fluoride for a long term could cause potential increase in the level of oxidative stress in the brain tissue."
SOURCE: Shao Q, Wang Y, Guan Z. (2000). [Influence of free radical inducer on the level of oxidative stress in brain of rats with fluorosis]. Zhonghua Yu Fang Yi Xue Za Zhi 34:330-2.

67. "It was concluded that aluminium interferes with the metabolism of the neuronal cytoskeleton and that this interference is potentiated by fluoride."
SOURCE: van der Voet GB, et al. (1999). Fluoride enhances the effect of aluminium chloride on interconnections between aggregates of hippocampal neurons. Archives of Physiology and Biochemistry 107:15-21.

68. "[T]he thickness of post-synaptic density (PSD) was decreased, and the width of synaptic cleft was remarkably increased. The results suggested that the impairment on the learning capability induced by fluorosis may be closely related with the pathological changes of synaptic structure in the brain of mice."
SOURCE: Zhang Z, et al. (1999). [Effect of fluoride exposure on synaptic structure of brain areas related to learning-memory in mice] [Article in Chinese]. Wei Sheng Yan Jiu 28:210-2.

69. "The results demonstrate that the contents of phospholipid and ubiquinone are modified in brains affected by chronic fluorosis and these changes of membrane lipids could be involved in the pathogenesis of this disease."
SOURCE: Guan ZZ, Wang YN, Xiao KQ, Dai DY, Chen YH, Liu JL, Sindelar P, Dallner G. (1998). Influence of chronic fluorosis on membrane lipids in rat brain. Neurotoxicology and Teratology 20: 537-542.

70. "While the small amount of AlF in the drinking water of rats required for neurotoxic effects is surprising, perhaps even more surprising are the neurotoxic results of NaF at the dose given in the present study [1.0 ppm F]... The results of the present study indicate that more intensive neuropathological evaluations of F effects on brain may prove to be of value... In summary, chronic administration of AlF and NaF in the drinking water of rats resulted in distinct morphological alterations in the brain, including effects on neurons and cerebrovasculature."
SOURCE: Varner JA, et al. (1998). Chronic administration of aluminum-fluoride and sodium-fluoride to rats in drinking water: Alterations in neuronal and cerebrovascular integrity. Brain Research 784: 284-298.

71. "These results indicate that fluoride may penetrate the blood brain barrier, interact with AChE located on cell membranes, and interfere with their physiological functions and thus induce the neurotoxicities."
SOURCE: Zhao XL, Wu JH. (1998). Actions of sodium fluoride on acetylcholinesterase activities in rats. Biomedical and Environmental Sciences 11(1):1-6.

72. "The metabolism of brain phospholipid might be interfered by fluoride accumulated in brain tissue, which is related with the degeneration of neuron. The changes of brain phospholipid could be involved in the pathogenesis of chronic fluorosis."
SOURCE: Guan Z, Wang Y, Xiao K. (1997). [Influence of experimental fluorosis on phospholipid content and fatty acid composition in rat brain]. Zhonghua Yi Xue Za Zhi. 77: 592-6.

73. "Neuronal abnormalities were observed in the NaF treated animals- especially in the deeper cell layers... The NaF treatment also produced distortions of cells and, in some rats, cell losses could be demonstrated in particular brain regions. Both AlF3 and NaF induced vascular inclusions, although of a different character..."
SOURCE: Issacson R, et al. (1997). Toxin-induced blood vessel inclusions caused by the chronic administration of aluminum and sodium fluoride and their implications for dementia. Annals of the New York Academy of Science 825: 152-166.

74, "Coenzyme Q content of brain tissue in rats fed with fluorine-containing water decreased at early stage of fluorosis, but increased significantly at late stage. It is speculated that changes in content of coenzyme Q could correlate with changes in free radical levels induced by fluorine."
SOURCE: Wang Y, Guan Z, Xiao K. (1997). [Changes of coenzyme Q content in brain tissues of rats with fluorosis]. Zhonghua Yu Fang Yi Xue Za Zhi. 31: 330-3.

75. "Excessive fluoride intake decreased 5-hydroxy indole acetic acid and increased norepinephrine in rat brain."
SOURCE: Li Y, et al. (1994). [Effect of excessive fluoride intake on mental work capacity of children and a preliminary study of its mechanism] Hua Hsi I Ko Ta Hsueh Hsueh Pao. 25(2):188-91.

76. "The results reported here indicate that fluoride has a specific effect on the synthesis of proteins in the brain which may lead to degenerative changes in the form of ballooning degeneration of neurons, various degrees of loss of nisal substance, and changes in the purkinje cells of the cerebellar cortex. Such changes would provide a plausible explanation for some of the diverse neruological complaints in arms and legs such as numbness, muscle spasms and pains, tenaniform convulsions, and spastic paraplegia, encountered in patients with skeletal fluorosis."
SOURCE: Shashi A, et al. (1994). Effect of long-term administration of fluoride on levels of protein, free amino acids and RNA in rabbit brain. Fluoride 27: 155-159.

77. "The neurotoxic effect of fluoride on lipid content of brain was assessed in rabbits during experimental fluorosis... Fluoride exerts an inhibitory effect on the free fatty acids in brain of both sexes. The relevance of these results in experimental fluorosis is discussed."
SOURCE: Shashi A. (1992). Studies on alterations in brain lipid metabolism following experimental fluorosis. Fluoride 25:77-84.

Water with fluoride at 1 ppm is only part of the total fluoride exposure. The Board of Health needs to keep in mind, although studies often have fluoride concentrations higher than fluoridated water, the total exposure is well within levels received by many people.

Plenty of studies have been published finding risks to the brain and neurological system for the Board of Health to provide the public with warning. Those di
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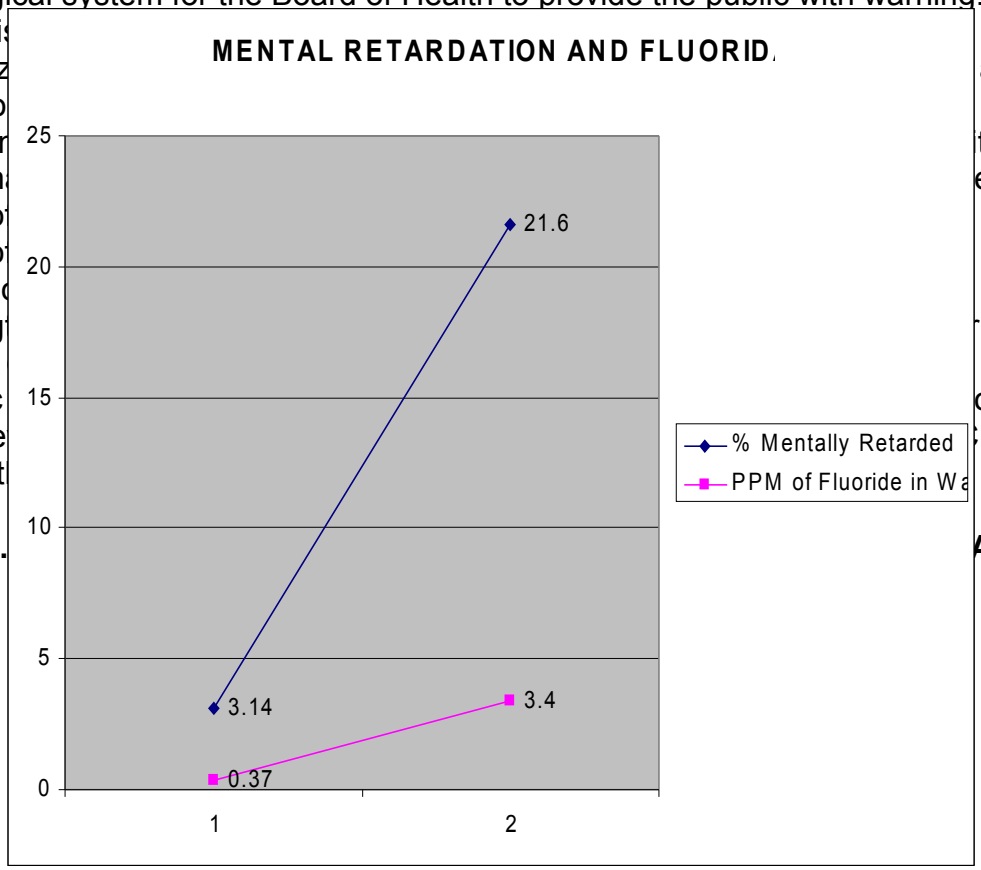

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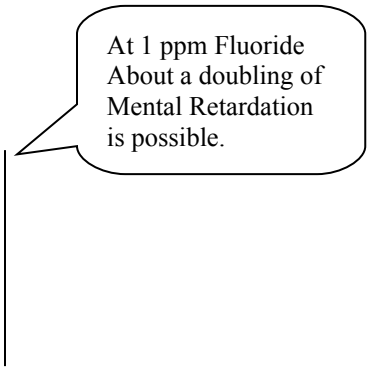

Graph A

Tianjin reported a 21.6% mental retardation rate with water containing 3.14ppm of fluoride and a decrease to 3.4% mental retardation at 0.37 ppm of fluoride concentration,[1] illustrated in "Graph A" above. Assuming a linear increase of mental retardation with increase in concentration of fluoride in water, an estimate of perhaps a doubling of the mental retardation at 1 ppm is possible.

"Graph B" ranks the US states in order of their whole population on fluoridated water using CDC and USGS data.[2] The graph visually illustrates increasing mental retardation with increase in the percentage of the population on fluoridated water and is consistent with the citations above.

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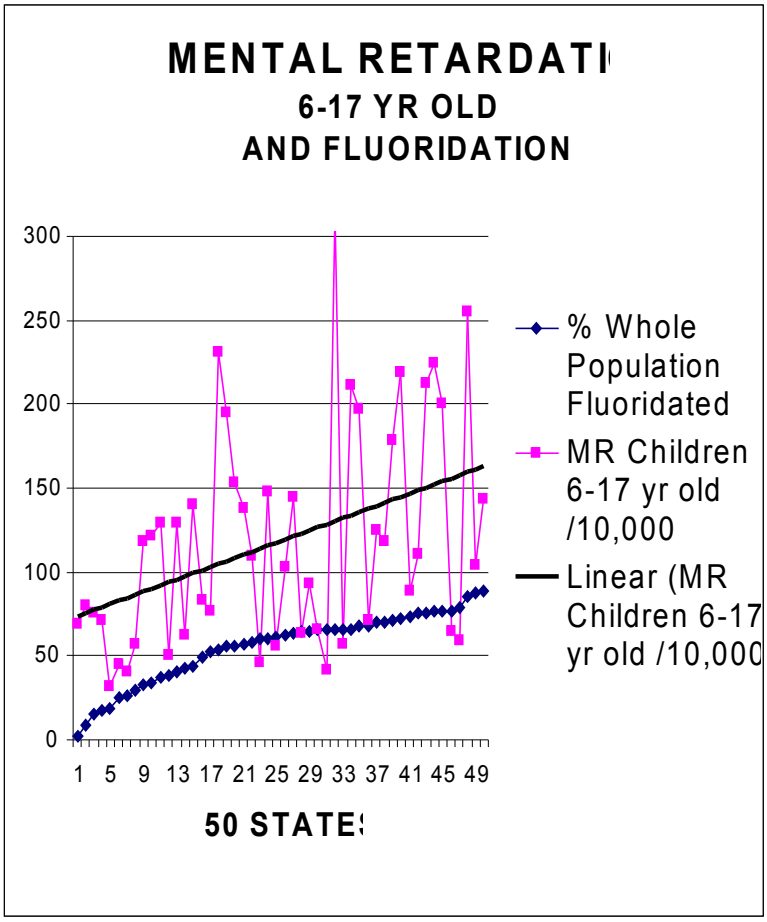
[1] Tianjin, Fluoride Vol. 33 No. 2 49052 2000, Editorial 49 Fluoride 33 (2) 2000 http://www.fluoride-journal.com/00-33-2/332-49.pdf

[2] **http://apps.nccd.cdc.gov/giscvh/map.aspx**
http://apps.nccd.cdc.gov/nohss/FluoridationV.asp
http://pubs.usgs.gov/circ/2004/circ1268/htdocs/table05.html
http://www.cdc.gov/mmwR/preview/mmwrhtml/00040023.htm



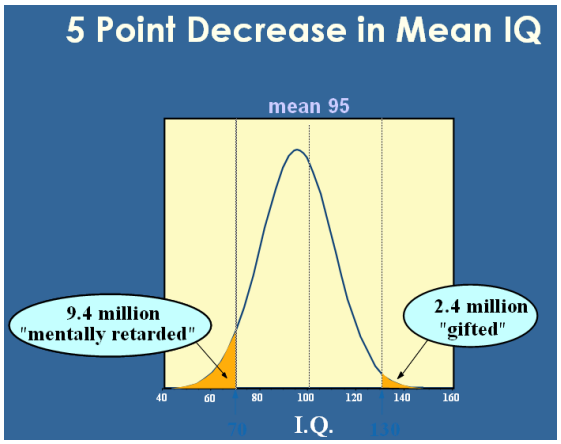
The graphical illustration cannot be extrapolated to any single state, in part because there are numerous confounding factors. And socioeconomics, culture, race and a host of variables does not make the prevalence of the data from the Tianjin study directly applicable to other specific communities. However, the trends compared within each country are remarkable and valid. The power of the graph is to illustrate to the Board of Health in an easy to understand graph that fluoridation is contributing to excess fluoride exposure and causing an increase in mental retardation.

With a risk assessment, the Board of Health can be absolutely confident there may be an increase in mental retardation with fluoridation. If the Board of Health were to seek FDA approval, there is little doubt the FDA would require a warning on the label of possible mental retardation and decrease in IQ. Remember, prescription fluoride supplements purchased at the pharmacy are not FDA approved and an appropriate label has not been reviewed and approved by the FDA for either supplements or fluoridation.

The cost to the state for special education, employment support, medical support and life-time care for persons with mental retardation is staggering and growing every year. Financial costs to the state don't come close, comparatively, to the financial cost and emotional burden to families caring for their child with mental retardation, often until their own decline or death. Further, one person with mental retardation requires many people to support them, and whether those supports are from family or government, the result is significant loss of employment, work productivity and tax revenues to the state.

Mental retardation only reviews one subpopulation. Fluoride affects everyone; however, measuring everyone's intelligence has not been done in the USA. The graphs below[3] of the "Bell Curve" illustrate the effects of toxic chemicals on a population. In theory, there should be the same number of "mentally retarded" as "gifted." In addition, when a chemical contributes to an increase in the number of mentally retarded, it is reasonable to expect a reduction in intelligence throughout the population.

Public Health Education for the safety of the public in preventing brain damage, lower IQ and increased mental retardation is reasonable and required of the Board of Health.



[3] http://www.psr.org/site/DocServer/IHWAugust08mkab.ppt?docID=5401#7