NRC (National Research Council). 2006. Fluoride in Drinking Water: A Scientific Review of EPA's Standards. Washington, DC: The National Academies Press. [Available at to read online for free at: <u>http://www.nap.edu/catalog/11571.html]</u>

Selected Quotes

FLUORIDE'S EFFECTS ON THE BRAIN:

"On the basis of information largely derived from histological, chemical, and molecular studies, it is apparent that fluorides have the ability to interfere with the functions of the brain and the body by direct and indirect means." p187

"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**." p186

"The possibility has been raised by the studies conducted in China that fluoride can lower intellectual abilities." p187

"Studies of populations exposed to different concentrations of fluoride should be undertaken to evaluate neurochemical changes that may be associated with **dementia**. Consideration should be given to assessing effects from chronic exposure, effects that might be delayed or occur late-in-life, and individual susceptibility." p187

"Two small studies have raised the possibility of an increased incidence of **spina bifida** occulta in fluorosis-prone areas in India; larger, well-controlled studies are needed to evaluate that possibility further." p164

FLUORIDE'S EFFECTS ON THE ENDOCRINE SYSTEM:

"In summary, evidence of several types indicates that **fluoride affects normal endocrine function or response**; the effects of the fluoride-induced changes vary in degree and kind in different individuals. **Fluoride is therefore an endocrine disruptor** in the broad sense of altering normal endocrine function or response, although probably not in the sense of mimicking a normal hormone. The mechanisms of action remain to be worked out and appear to include both direct and indirect mechanisms, for example, direct stimulation or inhibition of hormone secretion by interference with second messenger function, indirect stimulation or inhibition of hormone secretion by effects on things such as calcium balance, and inhibition of peripheral enzymes that are necessary for activation of the normal hormone." p223

FLUORIDE'S EFFECTS ON THE THYROID:

"several lines of information indicate an effect of fluoride exposure on thyroid function." p197

"Fluoride exposure in humans is associated with elevated TSH concentrations, increased goiter prevalence, and altered T4 and T3 concentrations; similar effects on T4 and T3 are reported in experimental animals.." p218

"In humans, effects on thyroid function were associated with fluoride exposures of 0.05-0.13 mg/kg/day when iodine intake was adequate and 0.01-0.03 mg/kg/day when iodine intake was inadequate." p218 Note: For a 70kg/154pounds person 0.01mg/kg is equal to 0.7mg fluoride, what one would consume after drinking 1 liter of fluoridated water.

lodine deficiency is increasing world-wide: 36% of women in USA <u>http://www.cdc.gov/nchs/products/pubs/pubd/hestats/iodine.htm</u> 70% of women in Australia <u>http://www.abc.net.au/health/thepulse/stories/2008/11/06/2399550.htm</u>

"Intake of nutrients such as calcium and iodine often is not reported in studies of fluoride effects. The effects of fluoride on thyroid function, for instance, might depend on whether iodine intake is low, adequate, or high, or whether dietary selenium is adequate." p222

FLUORIDE'S EFFECTS ON THE PINEAL GLAND:

"The single animal study of pineal function indicates that fluoride exposure results in altered melatonin production and altered timing of sexual maturity (Table 8-1)."

"Recent information on the role of the pineal organ in humans suggests that any agent that affects pineal function could affect human health in a variety of ways, including effects on sexual maturation, calcium metabolism, parathyroid function, postmenopausal osteoporosis, cancer, and psychiatric disease." p221-22

FLUORIDE'S EFFECTS ON INSULIN SECRETION/DIABETES:

"The conclusion from the available studies is that sufficient fluoride exposure appears to bring about increases in blood glucose or impaired glucose tolerance in some individuals and to increase the severity of some types of diabetes. In general, impaired glucose metabolism appears to be associated with serum or plasma fluoride concentrations of about 0.1 mg/L or greater in both animals and humans. In addition, diabetic individuals will often have higher than normal water intake, and consequently, will have higher than normal fluoride intake for a given concentration of fluoride in drinking water. An estimated 16-20 million people in the U.S. have diabetes mellitus; therefore, any role of fluoride exposure in the development of impaired glucose metabolism or diabetes is potentially significant." p. 217

FLUORIDE'S EFFECTS ON THE IMMUNE SYSTEM:

"Nevertheless, patients who live in either an artificially fluoridated community or a community where the drinking water naturally contains fluoride ... have all accumulated fluoride in their skeletal systems and potentially have very high fluoride concentrations in their bones. The bone marrow is where immune cells develop and that could affect humoral immunity and the production of antibodies to foreign chemicals." p249

"it is important to consider subpopulations that accumulate large concentrations of fluoride in their bones (e.g., renal patients). When bone turnover occurs, the potential exists for immune

system cells and stem cells to be exposed to concentrations of fluoride in the interstitial fluids of bone that are higher than would be found in serum. From an immunologic standpoint, individuals who are immunocompromised (e.g., AIDS, transplant, and bone-marrow-replacement patients) could be at greater risk of the immunologic effects of fluoride." p 258

FLUORIDE'S INTERACTIVE/SYNERGISTIC EFFECTS (aluminum, lead):

"Available information now indicates a role for aluminum in the interaction of fluoride on the second messenger system; thus, differences in aluminum exposure might explain some of the differences in response to fluoride exposures among individuals and populations." p222

"With the increasing prevalence of acid rain, metal ions such as aluminum become more soluble and enter our day-to-day environment; the opportunity for bioactive forms of AIF to exist has increased in the past 100 years. Human exposure to aluminofluorides can occur when a person ingests both a fluoride source (e.g., fluoride in drinking water) and an aluminum source; sources of human exposure to aluminum include drinking water, tea, food residues, infant formula, aluminum-containing antacids or medications, deodorants, cosmetics, and glassware." p42

"Another possible explanation for increased blood lead concentrations which has not been examined is the effect of fluoride intake on calcium metabolism; a review by Goyer (1995) indicates that higher blood and tissue concentrations of lead occur when the diet is low in calcium. Increased fluoride exposure appears to increase the dietary requirement for calcium (see Chapter 8); in addition, the substitution of tap-water based beverages (e.g., soft drinks or reconstituted juices) for dairy products would result in both increased fluoride intake and decreased calcium intake." p43

"[G]iven the expected presence of fluoride ion (from any fluoridation source) and silica (native to the water) in any fluoridated tap water, it would be useful to examine what happens when that tap water is used to make acidic beverages or products (commercially or in homes), especially fruit juice from concentrate, tea, and soft drinks. Although neither Urbansky (2002) nor Morris (2004) discusses such beverages, both indicate that at pH < 5, SiF6 2- would be present, so it seems reasonable to expect that some SiF6 2- would be present in acidic beverages but not in the tap water used to prepare the beverages. Consumption rates of these beverages are high for many people, and therefore the possibility of biological effects of SiF62-, as opposed to free fluoride ion, should be examined." p44

FLUORIDE & DOWNS SYNDROME:

"The possible association of cytogenetic effects with fluoride exposure suggests that Down's syndrome is a biologically plausible outcome of exposure." p170

"A reanalysis of data on Down's syndrome and fluoride by Takahashi (1998) suggested a possible association in children born to young mothers. A case-control study of the incidence of Down's syndrome in young women and fluoride exposure would be useful for addressing that issue. However, it may be particularly difficult to study the incidence of Down's syndrome today given increased fetal genetic testing and concerns with confidentiality." 172

FLUORIDE'S EFFECTS ON THE GASTROINTESTINAL SYSTEM:

"There are a few case reports of GI upset in subjects exposed to drinking water fluoridated at 1 mg/L.

Those effects were observed in only a small number of cases, which suggest hypersensitivity." p. 250

"Studies are needed to evaluate gastric responses to fluoride from natural sources at concentrations up to 4 mg/L and from artificial sources." p. 258

FLUORIDE'S EFFECTS ON THE KIDNEY:

"Human kidneys... concentrate fluoride as much as 50-fold from plasma to urine. Portions of the renal system may therefore be at higher risk of fluoride toxicity than most soft tissues." p236

"future studies should be directed toward determining whether kidney stone formation is the most sensitive end point on which to base the MCLG." p247

FLUORIDE & CANCER:

"Fluoride appears to have the potential to initiate or promote cancers, particularly of the bone, but the evidence to date is tentative and mixed (Tables 10-4 and 10-5). As noted above, osteosarcoma is of particular concern as a potential effect of fluoride because of (1) fluoride deposition in bone, (2) the mitogenic effect of fluoride on bone cells, (3) animal results described above, and (4) pre-1993 publication of some positive, as well as negative, epidemiologic reports on associations of fluoride exposure with osteosarcoma risk." p. 286

"Because fluoride stimulates osteoblast proliferation, there is a theoretical risk that it might induce a malignant change in the expanding cell population. This has raised concerns that fluoride exposure might be an independent risk factor for new osteosarcomas." p109

"Osteosarcoma presents the greatest a priori plausibility as a potential cancer target site because of fluoride's deposition in bone, the NTP animal study findings of borderline increased osteosarcomas in male rats, and the known mitogenic effect of fluoride on bone cells in culture (see Chapter 5). Principles of cell biology indicate that stimuli for rapid cell division increase the risks for some of the dividing cells to become malignant, either by inducing random transforming events or by unmasking malignant cells that previously were in nondividing states." p275