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CIC meeting

September 6, 2011

Ms. Cynthia Oshita
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS-19B
Sacramento, CA 95812-4010

Dear Ms. Oshita:

Please accept this public input for consideration by the Carcinogen Identification Committee (CIC) at its next meeting on October 12-13, 2011.

Evidence supporting prioritizing fluoride for carcinogenicity hazard identification

Submitted to the California OEHHA and Carcinogenicity Identification Committee
September 6, 2011.

Having reviewed the literature and evidence for fluoride carcinogenicity for the last year, including books, journal articles, research publications, and public testimony of fluoride researchers, I accept and fully adopt the comments submitted to this committee by Chris Neurath, American Environmental Health Studies Project, and Paul Connett, Fluoride Action Network, dated May 5, 2009 (copy attached).

The attached Appendix A, is from comments submitted to the US EPA Office of Water: Dose and Exposure documents, dated April 19, 2011. These selected studies published since the release of the National Research Council report, *Fluoride in Drinking Water: A Scientific Review of EPA's Standards* in March 2006, illustrates the bounty of studies documenting the ill health effects of fluoride. Given the weight of evidence in Appendix A documenting the ill health effects caused by Fluoride it is illogical to think that Fluoride is not carcinogenic.

The best evidence of carcinogenicity of fluoride is from Elise B. Bassin et.al. cited in your report, *Evidence on the Carcinogenicity of Fluoride and Its Salts*, July 2011, described on page 5. Your study of the literature was correct to state, "By itself this study seems to provide evidence of an association between fluoride in water and osteosarcoma in young males."

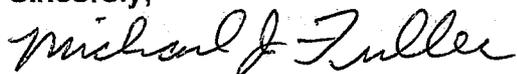
Given the weight of this study, which withstood full peer review, you then cite a letter from Chester Douglass and K. Joshipura warning that the findings of this study should be interpreted with caution. This letter lacks any weight whatsoever when you consider Mr. Douglass suffers from a serious lack of credibility when considering much of his research funding for years has been funded by dental product manufacturers. This conflict has been well documented and one must conclude Mr. Douglass' research funding would be seriously impaired by any findings of ill health effects from fluoride. His political agenda, and that of the OEHHA by association with his non-academic

comments, become abundantly clear. I urge you to consider the weight of the research and evidence in Bassin's study versus the political agenda of Chester Douglass.

I am also curious why your report gives very little effort to identify research regarding the ill effects of fluoride on reproductive health. The attached Appendix A (page 47-48) also cites several studies in this area you could have and should have reviewed, including the exposure to pregnant females and developing infants and toddlers.

Thank you for considering this input. I hope you will consider the health and protection of young children through your actions in this matter.

Sincerely,



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Disclaimer: The views expressed in this letter do not in any way reflect the views, opinions, or policies of First 5 California, its management, staff, or First 5 California Children and Family Commissioners and are solely the views and opinions of the author.

Evidence supporting prioritizing fluoride for carcinogenicity hazard identification

by

Chris Neurath, Paul Connett

American Environmental Health Studies Project and Fluoride Action Network

Submitted to the California OEHHA and Carcinogenicity Identification Committee

May 5, 2009

Fluoride and its salts (abbreviated "F" hereafter) are being assessed for priority in conducting a Hazard Identification by your committee. The most recent and authoritative review of the toxicology and potential carcinogenicity of F was conducted by the US National Research Council (NRC) and published in 2006.

The NRC 2006 review concluded:

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. [NRC 2006, p 286]

The strongest positive epidemiological study to date, a case-control study by Bassin et al 2006, was not considered in this review because it was not published until several months after the NRC review was finalized. Most of the questions the NRC had about an early unpublished version of Bassin's work were answered in her 2006 paper, further shifting the weight of evidence toward a conclusion that F is a carcinogen.

A letter to the editor from Douglass raised unspecified cautions about Bassin's results [Douglass 2006]. The only reason offered for questioning Bassin's results was because they differed from preliminary results in Douglass' own Phase 2 study. But Douglass gave insufficient details to assess the comparability or validity of his study. Douglass has a long history of issuing preliminary announcements about his F-osteosarcoma studies, all of which claim no association has been found [McGuire 1995, Douglass 1998, Douglass 2002, Douglass 2004]. Funding for his study began in 1992 and today,

17 years later, he has yet to publish a single paper on F and osteosarcoma. It is also important to understand that the data Bassin used in her analyses was gathered by Douglass during a Phase 1 of his study. In a conference abstract in 1995 Douglass had claimed that his "preliminary" analysis of this same Phase 1 data found no association between F and osteosarcoma [McGuire 1995]. So, Douglass' preliminary analyses have not been born out in later full analyses by others, using the same data

Reference is often made to the 2000 York Review for the UK [NHS Centre for Reviews 2000]. This review is weaker than the NRC's because it excluded all animal and *in vitro* evidence and predated several important positive studies. A recent Australian government review essentially summarized the findings of the York Review and added a cursory discussion of more recent evidence [Yueng 2008]. Prominent attention is paid to Douglass' letter to the editor, with the implication that this unsubstantiated letter counterbalances the weight of Bassin's peer-reviewed paper.

It is worth noting that both the York Review and the Australian review were commissioned by government agencies which strongly promote fluoridation. In contrast, the NRC Review was commissioned by the US EPA, which does not have any official policy of promoting fluoridation.

Comments on OEHHA screening results

Results of OEHHA's initial evidence screening summary for F are shown below. We provide some details on the strength of the identified evidence, along with additional evidence that may have been missed by the screens. The **X's** in black mark OEHHA's screening conclusions. Below those, we have added a line of red **X's** to indicate where we believe additional evidence exists. Details are provided below.

Exposure				Human Data				Animal Data				Other Relevant Data					
Widespread	High in frequent consumers	Limited / occupational	High in infrequent consumers	Analytical	Descriptive	Case series / reports	Analytical: mixed / poorly defined exposures	Two or more studies	One study w/ unusual incidence, site/type, age at onset	One study and second study with benign tumors only	One study	Tumor initiation / promotion or co-carcinogenicity studies	Genotoxicity	Carcinogenic metabolites	Structural similarity with tumorigens or P65 carcinogens	Hormonal activity / disruption	Other mechanistic studies
X				X					X				X				
X	X			X	X				X	X			X			X	X

From: http://www.oehha.ca.gov/prop65/CRNR_notices/state_listing/prioritization_notices/pdf/Chemicals030509.pdf - page=5

Exposure screen

Very widespread and unavoidable exposure

Human exposure to fluoride is probably more widespread and unavoidable than any of the other 38 proposed substances. In the USA 60% of the population has drinking water where F has been added with the intention of reducing dental decay. In CA, 27% of residents on public water systems in 2006 drank fluoridated water, and with recent state fluoridation decisions, the level is expected to increase substantially [CDC 2009]. But even people whose home tap water is not fluoridated can not easily avoid fluoride, because any beverages or processed foods they consume in fluoridated areas or that originate in fluoridated areas will contain fluoride. Most of the major metropolitan areas of CA including Los Angeles and San Francisco/Oakland are fluoridated. Many beverage bottling and food processing plants use fluoridated municipal water so the F becomes incorporated into their products [USDA 2005]. Unlike most other proposed chemicals which are unintended contaminants from industrial pollution or pesticide residues, fluoride is purposely added to drinking water and makes its way through foods and beverages into virtually all consumers. It is very difficult to avoid exposure.

Infants fed formula reconstituted with fluoridated water at 1 mg/L will receive approximately 250 times more fluoride than a breast fed infant. [NRC, 2006, p.33 and Table 2-6, p.40]

Additional exposures occur through dental products, many of which contain very high levels of F. For example, over 95% of the toothpaste sold is fluoridated with F levels of 1000-1500 mg/kg. Both children and adults typically swallow some of their toothpaste, even if not intentionally.

Two registered pesticides, cryolite and sulfuryl fluoride, yield F residues in agricultural products and processed foods. The F tolerances in common foods such as wheat flour and "all processed foods" are 70 mg/kg [EPA 2005, EPA 2004, FAN 2005]. Sulfuryl fluoride is a recently approved fumigant on foods so it is not clear how much additional F exposure it will produce in the general population and amongst specific groups consuming foods high in F residues.

Tea and iced tea from powder both contain elevated F levels, estimated by USDA to be about 3 times more than fluoridated water [USDA 2005b]. Tea drinkers may receive substantial F exposure even if they do not have fluoridated tap water.

The most direct exposure assessment for F comes from surveys of childhood dental fluorosis, a biomarker for fluoride exposure [Brunelle 1987]. Large-scale national surveys have found that even children growing up with unfluoridated water have a 22% rate of fluorosis and as many as 48% with fluoridated water exhibit this overexposure [Heller 1997, Beltran 2007]. Dental fluorosis occurs when exposure is more than

approximately 0.05 mg/kg-bodyweight/day during childhood. In surveys conducted before widespread fluoridation of water began, only about 1% of children in uncontaminated areas had dental fluorosis, so there is a 20-fold increase in high exposure cases even amongst those today who do not have fluoridated tap water.

“Frequent consumers” constitute a large portion of the population

The exposure screen should also be modified to indicate that “frequent consumers” will get especially high F exposures. For F, the description “frequent consumer” would apply to anyone who drinks more water than average. There is a very wide range of water consumption per bodyweight with top consumers drinking many times more water than the average. All exposure assessments except NRC 2006 have considered only average water consumption, so they have seriously underestimated exposure in the group of “frequent consumers”.

As mentioned, tea has naturally high F, so the large number of tea drinkers should also be classified as “frequent consumers”.

Human metabolism and tissue-specific exposure

Although there is no exposure screening criteria that addresses internal tissue exposure levels, it is relevant to point out that F is unusual in the extent that it partitions internally into skeletal tissues. F is a strongly “bone-seeking” chemical. The bone tissue level of F is typically tens of thousands of times higher than the serum and soft tissue levels. F has a biological half-life in bones estimated as long as 20 years, so bone F concentration rises steadily with age [NRC 2006, p 92]. About 50% of ingested F will be retained in the body, with most concentrated in the skeleton. The remainder is excreted by the kidneys. But for those with impaired kidney function due to disease or simply age over 50, F excretion is reduced so bone levels reach even higher levels.

Human data screen

Analytical study evidence

The leading analytical study providing positive evidence of carcinogenicity is Bassin 2006. This was a careful case-control study with a relatively large sample size and controlling for a number of potential confounders. The adjusted odds ratio (OR) for osteosarcoma in young males for exposure during the most susceptible time window was 5.46 (95% CI 1.50, 19.90).

The only other relatively large published case-control study of osteosarcoma [Gelberg 1995] had several potentially serious problems which may have led to underestimation of the risk of osteosarcoma from drinking water F. The authors concluded that the observed elevated risks were not large enough or consistent enough to be considered

evidence for a positive association between F and osteosarcoma. However, the NRC 2006 review was not as dismissive of the evidence.

We have examined Gelberg's study closely and have recently been able to confirm that she failed to control for age in any of her analyses. Since she used age matching, and because fluoride exposure strongly correlates with age, her unadjusted results will suffer from a form of selection bias. The bias will be toward the null, or no association. A full description of why failure to control for a matching variable can result in bias toward the null can be found in Rothman & Greenland's *Modern Epidemiology*, 2nd Edition [Rothman 1998, p 151]. So, the suggestive evidence of carcinogenicity that NRC 2006 noted in the Gelberg study is likely to be stronger when the necessary age adjustment is applied. It should be noted that Bassin did report adjusting for age in all her analyses.

A very recently published case-control study lends evidence that F exposure may cause osteosarcoma and other types of bone cancers. Sandhu 2009 compared serum F levels in two sets of cases and one control group recruited at a hospital in India. The groups were: 25 osteosarcoma cases; and an age and sex matched group of 25 non-osteosarcoma bone cancer cases; and a control group of 25 patients being seen for musculo-skeletal pain but with no cancer. The province in India where the study was conducted has regions with high natural F in drinking water. The average serum F level of osteosarcoma cases was twice as high as the bone cancer cases, and 3.5 times higher than in the controls. All differences were statistically significant.

The OEHHA screening document notes that F has "analytical" study evidence for carcinogenicity, but fails to note that there are also several ecological and semi-ecological "descriptive" studies which provide evidence of human carcinogenicity. The strongest semi-ecological study (using both individual level data and group level data) is Cohn's 1992 study for the New Jersey Department of Health. It used individual data on age, sex, race, and town of residence for osteosarcoma cases from the NJ Cancer Registry. Exposure was estimated from the F level in the drinking water of the town at the time of diagnosis. This is a more accurate estimate than was used in all other ecological studies of F which relied on average F levels in entire counties or even states/provinces. Despite relatively small numbers of cases, the effect size was large with a rate ratio as high as 8.0 (95%CI 3.9-15) amongst young white males in one analysis. A number of likely confounders were controlled.

The other commonly cited ecological study of fluoride and bone cancer was by Hoover 1991. Hoover did two analyses, the first compared changes in bone cancer rates in counties after fluoridation with rates in nearby unfluoridated counties. This analysis found an almost 100% increase in rates in young males in fluoridated counties compared to unfluoridated. Hoover then conducted additional analyses which failed to confirm the first analyses. However, the additional analyses had weaknesses and errors which invalidates them, leaving his original positive findings standing.

The weaknesses occurred because stratification into numerous categories led to very small numbers in each category and unstable rates. To try to increase numbers Hoover loosened inclusion criteria to the point that counties were no longer being compared to nearby counties, but to counties in distant states.

A serious error arose because the majority of the counties Hoover classified as “non-fluoridated”, in fact had enough natural F in drinking water that they should have been classified “fluoridated” or excluded from the analysis. His first analysis was unaffected by natural F because it only looked at changes in osteosarcoma rates following artificial fluoridation. But his additional analyses were essentially geographical comparisons between different sets of counties. For these, natural F could not be ignored.

Several small case-control studies of osteosarcoma and F were conducted in the early 1990s, but all suffered from weaknesses which limit their informativeness. We have discussed these in more detail in an accompanying document.

Similarly, our accompanying document discusses a number of ecological studies conducted in the 1990s, which also are relatively uninformative due to various limitations.

A newer ecological study looking at rates of osteosarcoma in provinces of Kenya should also be considered [Neurath 2005]. The measure of F exposure in this study was average rate of dental fluorosis by province. Dental fluorosis is a reliable biomarker of childhood F overexposure from all sources of F, not just drinking water. Osteosarcoma rates by province came from a national tumor registry maintained by Kenya’s main central hospitals. Linear regression showed a strong correlation between rate of dental fluorosis and rate of osteosarcoma incidence. Age and sex distribution data was unavailable.

Additional human analytical evidence exists from occupational cohort studies. In a very long running series of studies looking at mortality amongst workers at a cryolite factory in Denmark, Grandjean found evidence that F may be a risk factor for both bladder and lung cancer [Grandjean 2004, Grandjean 1992, Grandjean 1982]. The cohort was followed for more than 50 years until almost all had died. Their workplace exposures to cryolite dust resulted in well-documented high F exposures, but no other exposures to any known carcinogens. No information was available on smoking history, but the pattern of mortality suggested that smoking was no more common amongst the worker cohort than amongst the reference population of all Copenhagen residents. Deaths from respiratory disease were no more common in workers than the residents, suggesting that smoking probably did not account for the increases in lung and bladder cancer seen. Both tissues are sites where the F exposure would have been relatively high, since exposure was largely by inhalation and F is concentrated in the urine during excretion. Bone cancer was considered too rare for increases to have been detected in this cohort study.

Grandjean also reviews occupational cancer studies on aluminum workers who often receive high F exposure. A number of aluminum worker cohort studies have found increased risk of lung and bladder cancers, but rarely have the studies been able to distinguish risks from F compared to other chemicals common in the aluminum industry. Nevertheless, Grandjean considered it possible that the F could have played a role in the aluminum worker cancers.

Animal data screen

The main animal study showing evidence of carcinogenicity was the National Toxicology Program (NTP) 1990 study in male rats [Bucher 1990]. Although only one sex seemed to be affected, there are biologically plausible mechanisms for this gender-specific effect, and human epidemiological studies have shown the same result.

F reaches tissue concentrations in the skeleton that are tens of thousands of times higher than in serum or soft tissues. So, the finding of an association between osteosarcoma and F fits closely with both plausible biological mechanisms and tissue-specific exposures. Osteosarcoma is a very rare tumor, especially in the animal models used.

Another significant point is that the exposure levels which appeared to cause osteosarcomas in the rat bioassay were, in comparison to most chemical cancer bioassays, very close to the actual human exposure levels. Measured as concentration in drinking water, there was an increased rate of osteosarcoma found in the exposure group which received only 45 mg/L F in drinking water. 1 mg/L is the standard level of F in fluoridated public drinking water. But humans are also less efficient at excreting and sequestering F than rats. Drinking the same concentration of F, humans will reach serum F levels 5-20 times higher than rats. On a tissue-specific exposure basis, even the highest dose rats in the NTP study had bone F levels that are reached by some people.

The only agents known to cause osteosarcoma in any mammalian species are high-energy ionizing radiation, especially from internal bone-seeking radionuclides, and chemical alkylating agents.

Most of the work on osteosarcoma and internal radionuclides has been on dogs, which are considered a more suitable model for osteosarcoma than rodents. Domestic dogs, especially larger breeds, get osteosarcoma at rates considerably higher than humans. To our knowledge, no experimental study of F and bone cancer in dogs has ever been published. Thus, the relative lack of animal evidence may be due to the fact that the most appropriate studies have not yet been done.

The OEHHA screen seems to have missed the existence of a second animal study which found clear evidence that F caused benign bone tumors, but not malignant bone tumors. This was the Maurer/Procter & Gamble 1993 study in mice where large

numbers of osteomas were found in a dose dependent relationship to F exposure. Osteomas are considered non-malignant tumors.

Other relevant data screen (genotoxicity etc.)

The NRC 2006 review found evidence that fluoride disrupts hormone function so the screening category "hormonal activity/disruption" should be considered positive. Here is the NRC's conclusion:

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. [NRC 2006, p223]

Fluoride is also well known as a potent disruptor of enzyme activity in many enzyme systems, some of which may affect hormones [Adamek 2005].

In addition, fluoride ion in the presence of the aluminum ion (Al^{3+}) forms a complex AlF_4^- which is about the same size and shape as the phosphate ion. This aluminum fluoride complex is able to switch on G-proteins (see review Li, 2003) thus interfering with the trans-membrane messaging systems of water-soluble hormones and growth factors. In fact aluminum fluoride has been used in countless biochemical experiments to mimic the effect of certain hormones and deliver the signals without the hormone being present. Caverzasio has suggested fluoride stimulates bone growth (i.e. acts as an anabolic factor via AlF_4^- switching on G-protein normally activated by a growth factor.) [Caverzasio 1998].

The stimulation of bone growth; concentration in the bone and possible mutagenic activity of F all contribute to F being a highly plausible carcinogenic agent for bone.

The evidence that F is a hormone disruptor combined with the sex-specific risks of osteosarcoma from F in animal and human studies suggest that fluoride's carcinogenic potential may occur through its affects on hormones. Bone growth and turnover is partially controlled by endocrine activity, so effects of F on the controlling endocrine systems may increase the risk of bone cancer.

The NRC 2006 review and most other recent reviews have concluded that there is sufficient evidence to judge F genotoxic. Details of the genotoxicity evidence are provided in an accompanying document.

A recent study found F effects in osteoblast cells on cell proliferation and apoptosis [Yan 2009].

A very recent paper confirms the genotoxic potential of F, but was additionally able to show genotoxicity at much lower levels than previous studies. Zhang 2009 used a new method to test genotoxicity in 20 known genotoxic agents including F, as well as 4 chemically similar but known non-genotoxic agents. All known agents including F tested positive and all known non-genotoxic tested negative. The detection level for F genotoxicity was as low as 0.5 mg/L. This level is far exceeded in bone tissues and can be reached even in serum after large exposures to F.

The NRC 2006 made estimates of intracellular fluid F concentration in the vicinity of osteoblast and osteoclast cells in bones. These are the cells thought to be involved in initiation of human osteosarcoma. The NRC estimated that the F concentration in these cells could reach over 1000 mg/L for osteoclasts and over 100 mg/L for osteoblasts. These concentrations are well above levels found to be genotoxic in *in vitro* studies. They are also above the levels (20-200 mg/L) typically used in experiments where aluminum fluoride switches on G-proteins.

Summary

Based on the evidence described, we believe fluoride and its salts qualify for highest priority to conduct a Hazard Identification by OEHHA and CIC, as the next step toward possible listing as a carcinogen.

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Selected studies published since the release of the National Research Council report, *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*, in March 2006.

Also available at <http://www.fluoridealert.org/since-nrc.html>

Year	Rough Category	Study	Journal
2011	Apoptosis	<p>Wang Z, et al. 2011. Sodium fluoride suppress proliferation and induce apoptosis through decreased insulin-like growth factor-I expression and oxidative stress in primary cultured mouse osteoblasts.</p> <p>"All the tested NaF inhibited proliferation and arrested cell cycle at S phase in osteoblasts, and further demonstrated to induce apoptosis in osteoblasts. On the other hand, we found that NaF increased oxidative stress and decreased protein expression of IGF-I. Our study herein suggested that NaF caused proliferation suppression, and apoptosis may contribute to decrease IGF-I expression and increased oxidative stress damage by NaF in the primary mouse osteoblasts."</p>	Arch Toxicol. 2011 Apr 2. [Epub ahead of print] Abstract
2011	Apoptosis	Rocha RA, et al. 2011. Arsenic and fluoride induce neural progenitor cell apoptosis.	Toxicol Lett. Mar 22. [Epub ahead of print] Abstract
2011	Apoptosis	Sun Z, et al. 2011. Fluoride-induced apoptosis and gene expression profiling in mice sperm in vivo .	Arch Toxicol. 2011 Feb 22. [Epub ahead of print] Abstract
2011	Apoptosis	Andrade-Vieira LF, et al. 2011. Spent Pot Liner (SPL) induced DNA damage and nuclear alterations in root tip cells of <i>Allium cepa</i> as a consequence of programmed cell death.	Ecotoxicol Environ Saf. 2011 Jan 11. [Epub ahead of print] Abstract
2011	Apoptosis	Yan X, et al. 2011. Fluoride induces apoptosis and alters collagen I expression in rat osteoblasts .	Toxicol Lett. 200(3):133-8. Feb 5. Abstract
2011	Apoptosis	Xu B, et al. 2011. Effects of the Fas/Fas-L pathway on fluoride-induced apoptosis in SH-SY5Y cells .	Environ Toxicol. 26(1):86-92. Feb. Abstract
2011	Apoptosis	<p>Madusudan Rao S, et al. 2011. Morphometry of buccal mucosal cells in fluorosis - a new paradigm.</p> <p>"Conclusions: Fluorosis induces oxidative stress, DNA damage and apoptosis which can be the reasons for the increase in the nuclear</p>	Hum Exp Toxicol. Mar 15. [Epub ahead of print] Abstract

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		size and decrease in the cell size."	
2010	Apoptosis	Gutiérrez-Salinas J, et al. 2010. Exposure to sodium fluoride produces signs of apoptosis in rat leukocytes .	Int J Mol Sci. 11(9):3610-22. Sept. 27. Full Text Article
2010	Apoptosis	Jacinto-Alemán LF, et al. 2010. In vitro effect of sodium fluoride on antioxidative enzymes and apoptosis during murine odontogenesis .	J Oral Pathol Med. 39(9):709-14. Oct. Abstract
2010	Apoptosis	Gutowska I, et al. 2010. Fluoride as a pro-inflammatory factor and inhibitor of ATP bioavailability in differentiated human THP1 monocytic cells. "The incubation of macrophages in fluoride solutions significantly decreased the amount of synthesized cellular ATP and increased formation of ROS and apoptosis in a dose-dependent pattern. "	Toxicology Letters 196: 74-9. Abstract
2010	Apoptosis	Lu J, et al. 2010. Proteomics analysis of liver samples from puffer fish Takifugu rubripes exposed to excessive fluoride: an insight into molecular response to fluorosis. "... Consistent with their previously known functions, these identified proteins seem to be involved in apoptosis and other functions associated with fluorosis . These results will greatly contribute to our understanding of the ... toxicological mechanism of fluoride causing fluorosis in both fish and human. "	J Biochem Mol Toxicol. 24(1):21-8. Jan-Feb. Abstract
2010	Apoptosis	Salgado-Bustamante M, et al. 2010. Pattern of expression of apoptosis and inflammatory genes in humans exposed to arsenic and/or fluoride .	Sci Total Environ. 408(4):760-7. Jan 15. Abstract
2009	Apoptosis	Karube H, et al. 2009. NaF activates MAPKs and induces apoptosis in odontoblast-like cells .	J Dent Res. 88(5):461-5. May. Abstract
2009	Apoptosis	Yan X, et al. 2009. Effects of sodium fluoride treatment in vitro on cell proliferation, apoptosis and caspase-3 and caspase-9 mRNA expression by neonatal rat osteoblasts .	Arch Toxicol. 83(5):451-8. May. Abstract
2009	Apoptosis	Herai M, et al. 2009. Induction of apoptosis in human gingival epithelial cells by sodium fluoride.	Fluoride 42(1):3-8. Jan-March. Full Report

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2009	Apoptosis	Wang H, et al. 2009. Effects of dietary protein and calcium on thymus apoptosis induced by fluoride in female rats (Wistar rats).	Environ Toxicol. 24(3):218-24. June. Abstract
2008	Apoptosis	Lee JH, et al. 2008. Involvement of both mitochondrial- and death receptor-dependent apoptotic pathways regulated by Bcl-2 family in sodium fluoride-induced apoptosis of the human gingival fibroblasts .	Toxicology 243(3):340-7. Jan 20. Abstract
2008	Apoptosis	Tsai CL, et al. Wu PC. 2008. Induction of apoptosis in rabbit oral mucosa by 1.23% acidulated phosphate fluoride gel.	Arch Toxicol. 82(2):81-7. Feb. Abstract
2008	Apoptosis	Chouhan S, et al. 2008. Effects of fluoride on the tissue oxidative stress and apoptosis in rats : biochemical assays supported by IR spectroscopy data.	Toxicology 5;254(1- 2):61-7. Dec. Abstract
2007	Apoptosis	Yan Q, Zhang Y, Li W, Denbesten PK. 2007. Micromolar fluoride alters ameloblast lineage cells in vitro.	J Dent Res. 86(4):336-40. April. Abstract
2007	Apoptosis	Liu K, et al. 2007. Fluoride-mediated apoptosis and disordering of cell cycle distributions during in vitro organ culture of mouse fetal long bones .	Fluoride 40(1):19-23. Jan-March. Full Report
2007	Apoptosis	Guney M, et al. 2007. Effect of fluoride intoxication on endometrial apoptosis and lipid peroxidation in rats: role of vitamins E and C.	Toxicology. 231(2- 3):215-23. March 7. Abstract
2007	Apoptosis	Huang C, et al. 2007. Toxic effects of sodium fluoride on reproductive function in male mice .	Fluoride 40(3):162-8. July-Sept. Full Report
2007	Apoptosis	Matsui H, et al. 2007. Some characteristics of fluoride-induced cell death in rat thymocytes : Cytotoxicity of sodium fluoride.	Toxicol in Vitro 21(6):1113-20. Sept. Abstract
2007	Apoptosis	Zhang M, et al. 2007. Effects of fluoride on the expression of NCAM, oxidative stress, and apoptosis in primary cultured hippocampal neurons .	Toxicology 236(3):208-16. July 17. Abstract
2006	Apoptosis	Yu RA, et al. 2006. Effects of selenium and zinc on renal oxidative stress and apoptosis induced by fluoride in rats.	Biomed Environ Sci. 19(6):439-44. Dec. Abstract

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2006	Apoptosis	Xu H, et al. 2006. Effect of sodium fluoride on the expression of bcl-2 family and osteopontin in rat renal tubular cells .	Biol Trace Elem Res. 109(1):55-60. Jan. Abstract
2006	Apoptosis	He LF, Chen JG. 2006. DNA damage, apoptosis and cell cycle changes induced by fluoride in rat oral mucosal cells and hepatocytes .	World J Gastroenterol. 12(7):1144-8. Feb 21. Full Report
2006	Apoptosis	Ge Y, et al. 2006. Apoptosis in brain cells of offspring rats exposed to high fluoride and low iodine.	Fluoride 39(3);173-8. July-Sept. Full Report
2005	Apoptosis	Otsuki S, et al. 2005. Possible link between glycolysis and apoptosis induced by sodium fluoride.	J Dent Res. 84(10):919-23. Oct. Abstract
2005	Apoptosis	Sun G, Zhang Y, Sun X. 2005. Experimental study of fluoride toxicity on osteoblasts during bone formation . Paper presented at the XXVth. ISFR conference in Wiesbaden, Germany.	Fluoride 38(3). Sept. See Abstract No. 48.
2005	Apoptosis	Jiang CX, et al. 2005. [Relationship between spermatogenic cell apoptosis and serum estradiol level in rats exposed to fluoride]	Wei Sheng Yan Jiu. 34(1):32-4. January. [Article in Chinese] Abstract
2011	Asthma	Donoghue AM, et al. 2011. Occupational asthma in the aluminum smelters of Australia and New Zealand: 1991-2006. "RESULTS: The incidence of occupational asthma across all smelters combined was highest in 1992 at 9.46/1,000/year, declining to 0.36/1,000/year in 2006; a 96.2% reduction. The incidence of occupational asthma was correlated with geometric mean total fluoride concentration , measured as personal samples from employees undertaking anode changing (r(s) = 0.497, P < 0.001)."	Am J Ind Med. 54(3):224-31. Mar. Abstract
2010	Asthma	Abramson MJ, et al. 2010. Is potroom asthma due more to sulphur dioxide than fluoride? An inception cohort study in the Australian aluminium industry. "... SO(2) exposure was significantly associated with these symptoms, bronchial hyper-responsiveness (BHR) to methacholine (a feature of asthma), airflow limitation (reduced forced expiratory volume in 1 second/forced	Occup Environ Med. Oct;67(10):679-85. Abstract

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		vital capacity ratio) and longitudinal decline in lung function. Fluoride exposure was associated with the same outcomes, but less strongly... further modelling suggested that of the known respiratory irritants, SO(2) was more likely than fluoride to be primarily responsible for the symptoms observed. Fluoride, inhalable dust and SO(2) were the most important airborne contaminants associated with effects on lung function."	
2006	Asthma	Taiwo OA, et al. 2006. Incidence of asthma among aluminum workers .	J Occup Environ Med. 48(3):275-82. March. Abstract
2011	Blood	Amini H, et al. 2011. Drinking Water Fluoride and Blood Pressure? An Environmental Study. "... Statistically significant positive correlations were found between the mean concentrations of F in the GWRs [ground water resources] and the hypertension prevalence of males (r = 0.48, p = 0.007), females (r = 0.36, p = 0.048), and overall (r = 0.495, p = 0.005). Also, statistically significant positive correlations between the mean concentrations of F in the GWRs and the mean SBP [systolic blood pressure] of males (r = 0.431, p = 0.018)..."	Biol Trace Elem Res. Apr 12. [Epub ahead of print] Abstract
2010	Blood	Sawan RMM, et al. 2010. Fluoride increases lead concentrations in whole blood and in calcified tissues from lead-exposed rats.	Toxicology 271(1-2): 21-6. April 30. Abstract
2010	Blood	Gutiérrez-Salinas J, et al. 2010. Exposure to sodium fluoride produces signs of apoptosis in rat leukocytes .	Int J Mol Sci. 11(9):3610-22. Sept 27. Abstract
2010	Blood	Feng P, et al, 2010. Influence of selenium and fluoride on blood antioxidant capacity of rats. " Fluorosis could induce the decline of blood antioxidant capacity and the fluidity of erythrocyte membrane, as evident in this study, and Se at different levels possess some antagonistic effects on blood induced by fluoride. "	Exp Toxicol Pathol. Dec 10. [Epub ahead of print] Abstract
2009	Blood	Gutowska I, et al. 2009. Changes in the concentration of fluoride and biogenic elements in the serum and bones of female	Fluoride 42(1):9-16. Jan-March. Full Report

		<p>rats with streptozotocin-induced diabetes.</p> <p>"In our research we observed a statistically significant increase in the concentration of F in the bones of the diabetic rats, with a simultaneous decrease in the concentration of this element in serum."</p>	
2007	Blood	<p>Grucka-Mamczar E, et al. 2007. Influence of extended exposure to sodium fluoride and caffeine on the activity of carbohydrate metabolism enzymes in rat blood serum and liver.</p> <p>"... Glycolysis in extra-hepatic tissues (serum), under the influence of F, was slightly inhibited; however, it was markedly intensified by caffeine. Overall, a more profound influence by caffeine on carbohydrate enzyme activity was observed in blood serum (extra-hepatic tissues) than in the liver."</p>	<p>Fluoride 40(1):62-66. Jan-March. Full Report</p>
2006	Blood	<p>Opydo-Szymaczek J, et al. 2006. Variations in concentration of fluoride in blood plasma of pregnant women and their possible consequences for amelogenesis in a fetus.</p> <p>"... Mean value of fluoride concentration in the samples of blood plasma from the 28th week of pregnancy was lower than the mean concentration detected in the 33rd week of pregnancy (3.29 and 3.73 $\mu\text{mol/l}$, respectively). These values suggest that apart from drinking water, there were other important sources of fluoride in the examined sample. The results indicate that a reliable assessment of fluoride exposure in a given population cannot be based solely on the concentration of fluoride in drinking water..."</p>	<p>Homo. 57(4):295-307. Abstract</p>
2006	Blood	<p>Shanthakumari D, et al. 2006. Antioxidant defense systems in red blood cell lysates of men with dental fluorosis living in Tamil Nadu, India.</p>	<p>Fluoride 39(3):231-9. July-Sept. Full Report</p>
2005	Blood	<p>Connett M. 2005. Blood fluoride levels as a tool for assessing risk of fluoride toxicity. Paper presented at the XXVIth. ISFR conference in Wiesbaden, Germany, September.</p>	<p>Fluoride 38(3):226. See Abstract Number 9</p>
2005	Blood	<p>Ruiz-Payan A, et al. 2005. Chronic effects of</p>	<p>Fluoride 38(3):246.</p>

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		fluoride on growth, blood chemistry , and thyroid hormones in adolescents residing in northern Mexico. Paper presented at the XXVIth Conference of the International Society for Fluoride Research (September 26-29).	Full Article (see Abstract Number 37)
2005	Blood	Xiang Q, et al. 2005. Serum fluoride and skeletal fluorosis in two villages in Jiangsu Province, China.	Fluoride 38(3):178-84. Full Report
2011	Bone	Chen L, et al. 2011. Medication-induced periostitis in lung transplant patients: periostitis deformans revisited. " We report five cases of diffuse periostitis resembling hypertrophic osteoarthropathy and perostitis deformans in lung transplantation patients on chronic voriconazole, a fluoride-containing compound... "	Skeletal Radiol. 40(2):143-8. Feb. Abstract
2011	Bone	Wang Z, et al. 2011. Sodium fluoride suppress proliferation and induce apoptosis through decreased insulin-like growth factor-I expression and oxidative stress in primary cultured mouse osteoblasts. "All the tested NaF inhibited proliferation and arrested cell cycle at S phase in osteoblasts, and further demonstrated to induce apoptosis in osteoblasts. On the other hand, we found that NaF increased oxidative stress and decreased protein expression of IGF-I. Our study herein suggested that NaF caused proliferation suppression, and apoptosis may contribute to decrease IGF-I expression and increased oxidative stress damage by NaF in the primary mouse osteoblasts."	Arch Toxicol. 2011 Apr 2. [Epub ahead of print] Abstract
2011	Bone	Yan X, et al. 2011. Fluoride induces apoptosis and alters collagen I expression in rat osteoblasts .	Toxicol Lett. 200(3):133-8. Feb 5. Abstract
2010	Bone	Sawan RMM, et al. 2010. Fluoride Increases Lead Concentrations in Whole Blood and in Calcified Tissues from Lead-Exposed Rats .	Toxicology 271(1-2): 21-26. Abstract
2010	Bone	Itai K, et al. 2010. Serum ionic fluoride concentrations are related to renal function and menopause status but not to age in a Japanese general population.	Clinica Chimica Acta 411: 263-266. Abstract

		<p>"Conclusion: SIF [serum ionic fluoride] concentrations in middle-aged healthy subjects were increased with an age-related degeneration in renal function. SIF concentrations in post-menopausal women arise from the increased fluoride release from bone after menopause. Age is not related to SIF concentrations."</p>	
2010	Bone	<p>Tu J, et al. 2010. Interactive effect of fluoride burden with calcitonin receptor gene polymorphisms on the risk of F bone injury.</p> <p>"In this case-control study, a total of 119 cases and 126 controls were enrolled from 2 aluminum plants in Hubei province. F burden (UF) was measured by F ion-selective electrode method... RESULTS: The odds of developing F bone injury for participants in the moderate F burden group versus the mild F burden group were 4.1 (95% CI: 1.9, 8.7); the heavy F burden group versus the mild F burden group were 14.1 (95% CI: 6.5, 30.6). The odds of developing F bone injury for participants with the TC & TT genotypes versus the CC genotype were 2.6 (95% CI: 1.4, 4.7). The interactions between TC & TT genotypes and moderate, heavy F burden were significant (OR = 14.4; OR = 40.3). CONCLUSION: The interactive effect of F burden and CTR genotype was significant, which increased the F bone injury risk."</p>	<p>Int Arch Occup Environ Health. Nov 25. [Epub ahead of print] Abstract</p>
2010	Bone	<p>Song YE, et al. 2010. Effect of fluoride exposure on bone metabolism indicators ALP, BALP, and BGP.</p>	<p>Environ Health Prev Med. 2010 Oct 2. [Epub ahead of print] Abstract</p>
2010	Bone	<p>Shalina TI, Vasil'eva LS. 2010. [Femoral bone morphogenesis in human fetuses in the area of environmental fluoride pollution].</p> <p>"... In the town of Shelekhov, located closely to the pollution source, the growth of bones in both length and width, is delayed. The bone growth was active till week 16, however, during weeks 18-29, osteoresorption prevailed over the osteosynthesis, the bone thickness decreased, while the activity of their growth in length remained reduced."</p>	<p>Morfologija. 137(1):54-7. [Article in Russian] Abstract</p>
2010	Bone	<p>Xu H, et al. 2010. Activation of PERK signaling</p>	<p>Toxicology 277(1-3):1-5.</p>

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		through fluoride-mediated endoplasmic reticulum stress in OS732 cells. "... This study proved that PERK signaling play major roles in action of fluoride on osteoblast , and suggested that bone response in skeletal fluorosis may be due in part to PERK signaling pathway."	Nov 9. Abstract
2009	Bone	Levy SM, et al. 2009. Associations of fluoride intake with children's bone measures at age 11. "... In gender-stratified, and body size- and Tanner stage-adjusted linear regression analyses, associations between girls' bone outcomes and fluoride intake for girls were almost all negative; associations for boys were all positive and none was statistically significant when using an alpha = 0.01 criterion... "	Community Dent Oral Epidemiol. 37(5):416-26. Oct. Abstract
2009	Bone	Gutowska I, et al. 2009. Changes in the concentration of fluoride and biogenic elements in the serum and bones of female rats with streptozotocin-induced diabetes. "In our research we observed a statistically significant increase in the concentration of F in the bones of the diabetic rats, with a simultaneous decrease in the concentration of this element in serum. "	Fluoride 42(1):9-16. Jan-March. Full Report
2008	Bone	Qu W, et al. 2008. Sodium fluoride modulates caprine osteoblast proliferation and differentiation.	J Bone Miner Metab 26(4):328-34. July. Abstract
2007	Bone	Tamer MN, et al. 2007. Osteosclerosis due to endemic fluorosis.	Sci Total Environ. 373(1):43-8. Feb 1. Abstract
2007	Bone	Tang Q, et al. 2007. Effect of fluoride on expression of <i>pura</i> gene and <i>CaM</i> gene in newborn rat osteoblasts.	Fluoride 40(1):31-6. Jan-March. Full Report
2007	Bone	Chavassieux P, et al. 2007. Insights into material and structural basis of bone fragility from diseases associated with fractures: how determinants of the biomechanical properties of bone are compromised by disease. " fluorosis and osteomalacia "	Endocrine Reviews 28(2):151-64. Abstract

2007	Bone	<p>Hallanger Johnson JE, et al. 2007. Fluoride-related bone disease associated with habitual tea consumption.</p> <p>Figure 1. <u>Lateral lumbar spine showing advanced osteosclerosis of the vertebral bodies, with absence of usual marrow space radiolucency</u></p>	<p>Mayo Clin Proc. 82(6):719-24. June.</p> <ul style="list-style-type: none"> • Erratum in: Mayo Clin Proc. 2007 Aug;82(8):1017. dosage error in text. <p><u>Full Text</u></p>
2007	Bone	<p>Kakei M, et al. 2007. Effect of fluoride ions on apatite crystal formation in rat hard tissues.</p>	<p>Ann Anat. 189(2):175-81.</p> <p><u>Abstract</u></p>
2006	Bone	<p>Bouletreau PH, et al. 2006. Fluoride exposure and bone status in patients with chronic intestinal failure who are receiving home parenteral nutrition.</p> <ul style="list-style-type: none"> • TABLE 3. <u>Spinal bone status</u> • TABLE 4. <u>Femoral neck bone mineral density (BMD)</u> • TABLE 5. <u>Frequency of osteopenia and osteoporosis at the beginning and the end of the survey</u> <p>"CONCLUSIONS: In chronic intestinal failure, high intakes of fluoride are frequent because of the beverages ingested to compensate for stool losses. Hyperfluoremia has an effect on bone metabolism and may increase skeletal fragility. The consumption of fluoride-rich beverages for extended periods is therefore not advisable."</p>	<p>Am J Clin Nutr. 83(6):1429-37. June.</p> <p><u>Full Article</u></p>
2006	Bone	<p>Claassen H, et al. 2006. Extracellular matrix changes in knee joint cartilage following bone-active drug treatment.</p>	<p>Cell Tissue Res. 324(2):279-89. May.</p> <p><u>Abstract</u></p>
2006	Bone	<p>Harinarayan CV, et al. 2006. Fluorotoxic metabolic bone disease: an osteo-renal syndrome caused by excess fluoride ingestion in the tropics.</p>	<p>Bone 39(4):907-14. Oct.</p> <p><u>Abstract</u></p>
2006	Bone	<p>Clarke E, et al. 2006. Fluorosis as a probable cause of chronic lameness in free ranging eastern grey kangaroos (<i>Macropus giganteus</i>).</p> <p>"... The significant lesions observed were: osteophytosis of the distal tibia and fibula, tarsal bones, metatarsus IV, and proximal coccygeal vertebrae; osteopenia of the femur,</p>	<p>J Zoo Wildl Med. Dec;37(4):477-86.</p> <p><u>Abstract</u></p>

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		tibia, and metatarsus IV; incisor enamel hypoplasia; stained, uneven, and abnormal teeth wear; abnormal bone matrix mineralization and mottling; increased bone density; and elevated bone fluoride levels. Microradiography of affected kangaroos exhibited " black osteons ," which are a known manifestation of fluorosis. Collectively, these lesions were consistent with a diagnosis of fluorosis."	
2005	Bone	Nyman JS, et al. 2005. Effect of ultrastructural changes on the toughness of bone.	Micron 36(7-8):566-82. Abstract
2005	Bone	Roos J, Dumolard A, Bourget S, Grange L, Rousseau A, 2005. [Osteofluorosis caused by excess use of toothpaste.] [Article in French].	Presse Med. 34(20 Pt 1):1518-20. Nov. Abstract
2011	Brain: <i>Animal Studies</i>	Ge Y, et al. 2011. Proteomic Analysis of Brain Proteins of Rats Exposed to High Fluoride and Low Iodine.	Archives of Toxicology Arch Jan;85(1):27-33. Abstract
2011	Brain: <i>Animal Studies</i>	Pereira M, et al. 2011. Memory Impairment Induced by Sodium Fluoride Is Associated with Changes in Brain Monoamine Levels.	Neurotoxicity Research 19(1):55-62. Jan. Abstract
2011	Brain: <i>Animal Studies</i>	Zhu W, et al. 2011. Effects of Fluoride on Synaptic Membrane Fluidity and PSD-95 Expression Level in Rat Hippocampus.	Biological Trace Element Research 139, no 2, 197-203. Feb. Abstract
2010	Brain: <i>Animal Studies</i>	Narayanaswamy M, et al. 2010. Effect of maternal exposure of fluoride on biometals and oxidative stress parameters in developing CNS of rat. "The results confirm that the fluoride provoked oxidative stress and biometal deformations are synergistic that successively governs the neuronal damage and developing CNS no longer prevents exacerbations of fluoride... A series of active or receptor mediated transport systems inherent to the BBB [blood brain barrier] vasculature fails to control the entry of fluoride into the brain... In cerebral cortex on fluoride exposure, SOD showed significance and high correlation with F; similarly, in cerebellum, catalase (100 ppm group) showed significance and high correlation with F whereas in spinal cord GSH-	Biol Trace Elem Res. 133(1):71-82. Jan. Abstract

		Px (100 ppm group) showed significance and high correlation with copper.”	
2010	Brain: <i>Animal Studies</i>	Basha PM, et al. 2010. Evaluation of Fluoride-Induced Oxidative Stress in Rat Brain: A Multigeneration Study .	Biol Trace Elem Res. Jul 24. [Epub ahead of print] Abstract
2010	Brain: <i>Animal Studies</i>	Basha PM, et al. 2010. Pre and Post Natal Exposure of Fluoride Induced Oxidative Macromolecular Alterations in Developing Central Nervous System of Rat and Amelioration by Antioxidants.	Neurochemical Research, 1017–28. Mar. Abstract
2010	Brain: <i>Animal Studies</i>	Bouaziz H, et al. 2010. Fluoride-Induced Brain Damages in Suckling Mice .	Pesticide Biochemistry and Physiology 96: 24–29.
2010	Brain: <i>Animal Studies</i>	Chouhan S, et al. 2010. Fluoride-induced Changes in Haem Biosynthesis Pathway, Neurological Variables and Tissue Histopathology of Rats. “... changes were accompanied by depletion in GSH:GSSG ratio, whole brain biogenic amine levels and a dose-dependent increase in fluoride concentration. Interestingly and most significantly, these changes were more pronounced at lower concentrations of fluoride compared with higher fluoride dose... ”	Journal of Applied Toxicology 30(1): 63–73. Abstract
2010	Brain: <i>Animal Studies</i>	Gui C Z, et al. 2010. Changes of Learning and Memory Ability and Brain Nicotinic Receptors of Rat Offspring with Coal Burning Fluorosis.	Neurotoxicology and Teratology 32(5):536-41. Sep-Oct. Abstract
2010	Brain: <i>Animal Studies</i>	Kaoud H and Kalifa B. 2010. Effect of Fluoride, Cadmium and Arsenic Intoxication on Brain and Learning-Memory Ability in Rats .	Toxicology Letters 196, suppl. 1 (2010): S53 (abstract from the XII International Congress of Toxicology).
2010	Brain: <i>Animal Studies</i>	Li H, et al. 2010. Toxic Effects of Fluoride on Rat Cerebral Cortex Astrocytes in Vitro.	Wei Sheng Yan Jiu 39(1): 86–88. Abstract (Article in Chinese)
2010	Brain: <i>Animal Studies</i>	Liu YJ, et al. 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(3): 324–29. Abstract

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2010	Brain: <i>Animal Studies</i>	Zhang J, et al. 2010. Effect of Fluoride on Calcium Ion Concentration and Expression of Nuclear Transcription Factor Kappa-B Rho65 in Rat Hippocampus .	Experimental and Toxicologic Pathology [in press; available online March 19, 2010].
2009	Brain: <i>Animal Studies</i>	Bharti VK and Srivastava RS. 2009. Fluoride-induced Oxidative Stress in Rat's Brain and Its Amelioration by Buffalo (<i>Bubalus Bubalis</i>) Pineal Proteins and Melatonin.	Biological Trace Element Research 130(2): 131–40. Abstract
2009	Brain: <i>Animal Studies</i>	Flora SJ, et al. 2009. Co-exposure to Arsenic and Fluoride on Oxidative Stress , Glutathione Linked Enzymes, Biogenic Amines and DNA Damage in Mouse Brain.	Journal of the Neurological Sciences 285(1–2): 198–205. Abstract
2009	Brain: <i>Animal Studies</i>	Gao Q, et al. 2009. Decreased Learning and Memory Ability in Rats with Fluorosis: Increased Oxidative Stress and Reduced Cholinesterase Activity .	Fluoride 42(4): 277–85. Full Report
2009	Brain: <i>Animal Studies</i>	Kaur T, et al. 2009. Effect of Concurrent Chronic Exposure of Fluoride and Aluminum on Rat Brain .	Drug and Chemical Toxicology 32(3):215–21. Abstract
2009	Brain: <i>Animal Studies</i>	Madhusudhan N, et al. 2009. Fluoride-induced Neuronal Oxidative Stress Amelioration by Antioxidants in Developing Rats.	Fluoride 42(3):179–87. Full Report
2009	Brain: <i>Animal Studies</i>	Niu R, et al. 2009. Decreased Learning Ability and Low Hippocampus Glutamate in Offspring Rats Exposed to Fluoride and Lead .	Environmental Toxicology and Pharmacology 28:254–58.
2009	Brain: <i>Animal Studies</i>	Whitford GM, et al. 2009. Appetitive-based Learning in Rats: Lack of Effect of Chronic Exposure to Fluoride. Note: This is the only study reported “no significant effect on appetitive-based learning.”	Neurotoxicology and Teratology 31(4):210–15. Abstract
2008	Brain: <i>Animal Studies</i>	Chioca LR, et al. 2008. Subchronic Fluoride Intake Induces Impairment in Habituation and Active Avoidance Tasks in Rats.	European Journal of Pharmacology 579(1–3):196–201. Abstract
2008	Brain: <i>Animal Studies</i>	Chouhan S, et al. 2008. Effects of Fluoride on the Tissue Oxidative Stress and Apoptosis in Rats: Biochemical Assays Supported by IR Spectroscopy Data.	Toxicology 254(1–2):61–67. Abstract
2008	Brain:	Niu R, et al. 2008. Effects of Fluoride and Lead	Fluoride 41(4):276–82.

	<i>Animal Studies</i>	on Locomotor Behavior and Expression of Nissl Body in Brain of Adult Rats.	<u>Full Report</u>
2008	Brain: <i>Animal Studies</i>	Sun ZR, et al. 2008. Effects of High Fluoride Drinking Water on the Cerebral Functions of Mice.	Fluoride 41(2):148–51 . <u>Full Report</u>
2008	Brain: <i>Animal Studies</i>	Wu N, et al. 2008. Behavioral Teratology in Rats exposed to Fluoride. "Brain slices in the 25 mg/L group also showed a significantly lower average cerebral cortex thickness than in the control group (10.97 μm vs. 11.70 μm).]"	Fluoride 41(2):129–133 <u>Full Report</u>
2008	Brain: <i>Animal Studies</i>	Zhang M, et al. 2008. Effects of Fluoride on DNA Damage, S-phase Cell-cycle Arrest and the Expression of NF-KappaB in Primary Cultured Rat Hippocampal Neurons .	Toxicology Letters 179(1):1–5. <u>Abstract</u>
2008	Brain: <i>Animal Studies</i>	Zhang Z, et al. 2008. Effect of Fluoride Exposure on Synaptic Structure of Brain Areas Related to Learning-memory in Mice .	Fluoride 41(2):139–43. <u>Full Report</u>
2007	Brain: <i>Animal Studies</i>	Bera I, et al. 2007. Neurofunctional Effects of Developmental Sodium Fluoride Exposure in Rats.	European Review for Medical and Pharmacological Sciences 11(44):211–24. <u>Abstract</u>
2007	Brain: <i>Animal Studies</i>	Chirumari K and Reddy PK. 2007. Dose-Dependent Effects of Fluoride on Neurochemical Milieu in the Hippocampus and Neocortex of Rat Brain.	Fluoride 40(2):101–10. <u>Full Report</u>
2007	Brain: <i>Animal Studies</i>	Ge Y, et al. 2007. Apoptosis in Brain Cells of Offspring Rats Exposed to High Fluoride and Low Iodine .	Fluoride 39(3):173–78. <u>Full Report</u>
2007	Brain: <i>Animal Studies</i>	Xia T, et al. 2007. Effects of Fluoride on Neural Cell Adhesion Molecules mRNA and Protein Expression Levels in Primary Rat Hippocampal Neurons .	Zhonghua Yu Fang Yi Xue Za Zhi 41(6):475–78. (Article in Chinese) <u>Abstract</u>
2007	Brain: <i>Animal Studies</i>	Zhang M, et al. 2007. Effects of Fluoride on the Expression of NCAM, Oxidative Stress, and Apoptosis in Primary Cultured Hippocampal Neurons [rat].	Toxicology 236(3):208–16. <u>Abstract</u>
2006	Brain: <i>Animal Studies</i>	Bhatnagar M, et al.. 2006. Biochemical Changes in Brain and Other Tissues of Young Adult Female Mice from Fluoride in their	Fluoride 39(4):280–84. <u>Full Report</u>

		Drinking Water.	
2005	Brain: <i>Animal Studies</i>	Ge Y, Ning H, Wang S, and Wang J. 2005. Comet Assay of DNA Damage in Brain Cells of Adult Rats Exposed to High Fluoride and Low Iodine.	Fluoride 38(3):209–14. <u>Full Report</u>
2005	Brain: <i>Animal Studies</i>	Krechniak J and Inkielewicz I. 2005. Correlations Between Fluoride Concentration and Free Radical Parameters in Soft Tissues of Rats.	Fluoride 38(4):293–96. <u>Full Report</u>
2005	Brain: <i>Animal Studies</i>	Tsunoda M, et al. 2005. Changes in Fluoride Levels in the Liver, Kidney, and Brain and in Neurotransmitters of Mice after Subacute Administration of Fluorides.	Fluoride 38(4):284–92. <u>Full Report</u>
2008	Brain: <i>Human Fetal Studies</i>	Du L, et al. 2008. The Effect of Fluorine on the Developing Human Brain.	Fluoride 41(4):327–30. <u>Full Report</u>
2008	Brain: <i>Human Fetal Studies</i>	He H, et al. 2008. Effects of Fluorine on the Human Fetus.	Fluoride 41(4):321–26. <u>Full Report</u>
2008	Brain: <i>Human Fetal Studies</i>	Yu Y, et al. 2008. Neurotransmitter and Receptor Changes in the Brains of Fetuses from Areas of Endemic Fluorosis.	Fluoride 41(2):134–38. <u>Full Report</u>
2009	Brain: <i>Children Study</i>	Rocha-Amador D, et al. 2009. Use of the Rey-Osterrieth Complex Figure Test for neurotoxicity evaluation of mixtures in children. “...The highest proportion of children (89%) with Copy performance below <u>1 SD</u> was observed in children from F–As area. Approximately 9 out of 10 children were unable to copy the ROCF as expected for their age. For example, the expected score on Copy for a 6-year-old child is 9.94 <u>2.28</u> points. A child classified in the category below <u>1 SD</u> means that his score was lower than 7.66. In the F–As area children had z-scores as low as <u>5 SD</u> (scoring only two points on the test). For Immediate Recall, the proportion of children in the lowest category was 59% and almost 6 out of 10 children were unable to draw the figure	Neurotoxicology 30(6):1149-54. Nov. <u>Abstract</u>

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		as expected for their age after 3 min had elapsed. Following the same example of a 6-year-old child, the expected value for drawing the figure from memory is 7.26 \pm 2.45. One child classified in the \pm 1 SD category had a score below 4.81 points. Fluoride correlated inversely with Copy and Immediate Recall $r = -0.29$ and $r = -0.27$ (adjusted values). In the F-As area, the mean of FU was 5.6 \pm 1.7 and the proportion of children with FU levels over 2 mg/gcrt was 97.5%. All children had some degree of dental fluorosis as an indicator of chronic exposure to fluoride... "	
2008	Brain: Infant Study	Li J, et al. 2008. Effects of High Fluoride on Neonatal Neurobehavioral Development.	Fluoride 41(2):165–70. Full Report
2008	Brain: Workers Study	Z. Guo Z, et al. 2008. Research on the Neurobehavioural Function of Workers Occupationally Exposed to Fluoride.	Fluoride 41(2):152–55. Full Report
2011	Brain: Human IQ Studies	Ding Y, et al. 2011. The relationships between low levels of urine fluoride on children's intelligence, dental fluorosis in endemic fluorosis areas in Hulunbuir, Inner Mongolia, China.	Journal of Hazardous Materials 186:1942–1946. Abstract
2010	Brain: Human IQ Studies	<ul style="list-style-type: none"> • Xiang Q, et al. 2010. Serum Fluoride Level and Children's Intelligence Quotient in Two Villages in China. <p><i>Note: this is good paper initially accepted for publication by EHP and put online Dec 17. However, EHP withdrew the report because certain data was published by the lead author in another publication.</i></p>	<p>Accepted for publication in <i>Environmental Health Perspectives</i>, and pre-published online December 17.</p> <p>- available from FAN.</p>
2008	Brain: Human IQ Studies	Chen Y, et al. 2008. Research on the Intellectual Development of Children in High Fluoride Areas.	Fluoride 41(2):120–24. Full Report
2008	Brain: Human IQ Studies	Guo X, et al. 2008. A Preliminary Investigation of the IQs of 7–13 Year Old Children from an Area with Coal Burning-Related Fluoride Poisoning.	Fluoride 41(2):125–28. Full Report
2008	Brain: Human IQ Studies	Hong F, et al. 2008. Research on the Effects of Fluoride on Child Intellectual Development Under Different Environmental Conditions.	Fluoride 41(2):156–60. Full Report
2008	Brain: Human IQ Studies	Liu S, et al. 2008. Report on the Intellectual Ability of Children Living in High-Fluoride Water Areas.	Fluoride 41(2):144–47. Full Report
2008	Brain: Human IQ	Qin L, et al. 2008. Using the Raven's Standard Progressive Matrices to Determine the Effects	Fluoride 41(2):115–19. Full Report

	<i>Studies</i>	of the Level of Fluoride in Drinking Water on the Intellectual Ability of School-Age Children.	
2008	Brain: <i>Human IQ Studies</i>	Ren D, et al. 2008. A Study of the Intellectual Ability of 8–14 Year-Old Children in High Fluoride, Low Iodine Areas.	Fluoride 41(4):319–20. Full Report
2008	Brain: <i>Human IQ Studies</i>	Wang G, et al. 2008. A Study of the IQ Levels of Four- to Seven-Year-Old Children in High Fluoride Areas.	Fluoride 41(4): 340–43. Full Report
2008	Brain: <i>Human IQ Studies</i>	Wang S, et al. 2008. The Effects of Endemic Fluoride Poisoning Caused by Coal Burning on the Physical Development and Intelligence of Children.	Fluoride 41(4): 344–48. Full Report
2007	Brain: <i>Human IQ Studies</i>	Rocha-Amador D, et al. 2007. Decreased Intelligence in Children and Exposure to Fluoride and Arsenic in Drinking Water.	Cadernos de Saúde Pública 23(suppl. 4): S579–87. Full Report
2007	Brain: <i>Human IQ Studies</i>	Seraj B, et al. 2007. Effect of High Fluoride Concentration in Drinking Water on Children’s Intelligence.	Journal of Dental Medicine 19(2):80–86. English translation (from lead author).
2007	Brain: <i>Human IQ Studies</i>	Trivedi MH, et al. 2007. Effect of High Fluoride Water on Intelligence of School Children in India.	Fluoride 40(3):178–83, Full Report
2007	Brain: <i>Human IQ Studies</i>	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):643–47. Full Report
2007	Brain: <i>Human IQ Studies</i>	Fan ZX, et al. 2007. Effect of High Fluoride Exposure on Children’s Intelligence.	Huan Jing Yu Jian Kang Za Zhi 24(10): 802–3. (Article in Chinese)
2011	Brain: Other	Xu B, et al. 2011. Effects of the Fas/Fas-L pathway on fluoride-induced apoptosis in SH-SY5Y cells.	Environ Toxicol. 26(1):86-92. Feb. Abstract
2010	Brain: Other	Lockwood G. 2010. Theoretical context-sensitive elimination times for inhalation anaesthetics. <i>Note from FAN: <u>Desflurane</u>, <u>Sevoflurane</u> and <u>Isoflurane</u> all break down to the fluoride ion in the body.</i> “After 4 h of anaesthesia, the model predicted body content to be 28 g nitrous oxide, 26 g desflurane , 14 g sevoflurane , or 15 g	Br J Anaesth. 104(5):648-55. May. Abstract

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		isoflurane, and 99.9% brain elimination times were then 9 h for nitrous oxide, 33 h for desflurane, 52 h for sevoflurane, and 71 h for isoflurane. At this stage of elimination, the whole body still retained between 4% and 13% of the absorbed dose."	
2009	Brain: Other	Wann BP, et al. 2009. Effect of Olfactory Bulbectomy on Adenylyl Cyclase Activity in the Limbic System .	Brain Research Bulletin 79(1):32-36. Abstract
2009	Brain: Other	García-Montalvo EA, et al. 2009. Fluoride Exposure Impairs Glucose Tolerance Via Decreased Insulin Expression and Oxidative Stress. "Interestingly, values of F- in soft rat tissues (kidney, liver, brain and testis) were similar to those in urine (312 μmol-1) . According to this information, urinary F- level is a good indicator of the F- concentration in soft tissues. In cases of subchronic exposure, the level of F- in the plasma probably does not reflect the levels of F- distributed in soft tissues."	Toxicology 263:75-83. Abstract
2008	Brain: Other	Gao Q, et al. 2008. Oxidative Stress Might Be a Mechanism Connected with the Decreased Alpha 7 Nicotinic Receptor Influenced by High-Concentration of Fluoride in SH-SY5Y Neuroblastoma Cells .	Toxicology in Vitro 22(4):837-43. Abstract (Corrigendum in Toxicology in Vitro 22: 1814. The concentrations of fluoride should have been given as mM, instead of μM.)
2008	Brain: Other	Liu M, et al. 2008. Effect of endemic fluorosis on children's intelligence development: a Meta analysis . [Article in Chinese]	Zhongguo Dang Dai Er Ke Za Zhi.10(6):723-5. Dec. Abstract
2009	Co-exposure: Aluminum	Kaur T, et al. 2009. Effect of Concurrent Chronic Exposure of Fluoride and Aluminum on Rat Brain. Effects were "more pronounced in animals given fluoride and aluminum together ...it can be concluded that aluminum appears to enhance the neurotoxic hazards caused by fluoride."	Drug Chem Toxicol. 32(3):215-21. Abstract
2009	Co-exposure: Aluminum	Kant V, et al. 2009. Alterations in biochemical parameters during subacute toxicity of fluoride	Biol Trace Elem Res. Jul;130(1):20-30.

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		<p>alone and in conjunction with aluminum sulfate in goats.</p> <p>"... On the basis of results, it could be concluded that sodium fluoride alone and in conjunction with aluminum sulfate produced significant alterations in the various biochemical parameters of the body."</p>	<u>Abstract</u>
2006	Co-exposure: Aluminum	<p>Lubkowska A, et al. 2006. The effect of alternating administration of aluminum chloride and sodium fluoride in drinking water on the concentration of fluoride in serum and its content in bones of rats.</p> <p>"CONCLUSIONS: ... longer exposure increased fluoride accumulation in the femur ($p < 0.001$). All groups exposed to NaF had significantly higher fluoride concentration in the femur as compared with control animals. Groups receiving NaF and AlCl₃ showed lower fluoride concentration in serum and femur compared with those exposed to NaF only and higher in comparison with controls. Fluorine content in the femur of rats exposed to NaF and AlCl₃ for four months was similar to the results obtained after one month of exposure."</p>	<p>Ann Acad Med Stetin. 52 Suppl 1:67-71. [Article in Polish] <u>Abstract</u></p>
2007	Co-exposure: Aluminum	<p>Manoharan V, et al. 2007. Interactive effects of soil acidity and fluoride on soil solution aluminium chemistry and barley (<i>Hordeum vulgare</i> L.) root growth.</p> <p><i>Note from FAN: this is relevant in regards to Dow AgroSciences 2010 proposal to use sulfuranyl fluoride as a soil fumigant.</i></p> <p>"Increasing rates of F additions to soil significantly increased the soil solution concentrations of aluminium (Al) and F irrespective of the initial adjusted soil pH, which ranged from 4.25 to 5.48... The results suggested that continuous input of F to soils, and increased soil acidification, may become an F risk issue in the future."</p>	<p>Environ Pollut. Feb;145(3):778-86. <u>Abstract</u></p>
2011	Co-exposure: Arsenic	<p>Flora SJ, et al. 2011. Interactive effect of arsenic and fluoride on cardio-respiratory disorders in male rats: possible role of reactive oxygen species.</p>	<p>Biometals. Jan 18. [Epub ahead of print] <u>Abstract</u></p>
2011	Co-exposure:	<p>Rocha RA, et al. 2011. Arsenic and fluoride</p>	<p>Toxicol Lett. Mar 22.</p>

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	Arsenic	induce neural progenitor cell apoptosis.	[Epub ahead of print] <u>Abstract</u>
2010	Co-exposure: Arsenic	Kaoud H and Kalifa B. 2010. Effect of Fluoride, Cadmium and Arsenic Intoxication on Brain and Learning-Memory Ability in Rats. "... These results suggest that learning-memory ability and brain function in rats are affected by HiF, HiCd and HiAs and that oxidative stress in the brain may be one of the causes of this damage."	Toxicology Letters 196, suppl. 1 (2010): S53 (abstract from the XII International Congress of Toxicology).
2010	Co-exposure: Arsenic	Salgado-Bustamante M, et al. 2010. Pattern of expression of apoptosis and inflammatory genes in humans exposed to arsenic and/or fluoride.	Sci Total Environ. 408(4):760-7. Jan 15. <u>Abstract</u>
2009	Co-exposure: Arsenic	Flora SJ, et al. 2009. Co-exposure to Arsenic and Fluoride on Oxidative Stress, Glutathione Linked Enzymes, Biogenic Amines and DNA Damage in Mouse Brain.	Journal of the Neurological Sciences 285(1-2): 198-205. <u>Abstract</u>
2007	Co-exposure: Arsenic	Rocha-Amador D, et al. 2007. Decreased Intelligence in Children and Exposure to Fluoride and Arsenic in Drinking Water.	Cadernos de Saúde Pública 23(suppl. 4): S579-87. <u>Full Report</u>
2007	Co-exposure: Arsenic	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):643-47. <u>Full Report</u>
2006	Co-exposure: Arsenic	Mittal M and Flora SJ. 2006. Effects of individual and combined exposure to sodium arsenite and sodium fluoride on tissue oxidative stress, arsenic and fluoride levels in male mice. "Arsenic and fluoride concentration increased significantly on exposure. Interestingly, their concentration decreased significantly on concomitant exposure for 8 weeks. However, the group which was administered arsenic for 4 weeks followed by 4 weeks of fluoride administration showed no such protection suggesting that the antagonistic effect of fluoride on arsenic or vice versa is possible only during interaction at the gastro intestinal sites. These results are new and interesting and require further exploration."	Chem Biol Interact. 25;162(2):128-39. Aug. <u>Abstract</u>
2011	Co-exposure: Lead	Leite GA, et al. 2011. Exposure to lead	Arch Oral Biol. 2011 Jan 24. [Epub ahead of print]

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		exacerbates dental fluorosis. "This study shows that lead exacerbates dental fluorosis in rodents, suggesting that co-exposure to lead may affect the degree of fluorosis. "	<u>Abstract</u>
2010	Co-exposure: Lead	Sawan RMM, et al. 2010. Fluoride increases lead concentrations in whole blood and in calcified tissues from lead-exposed rats.	Toxicology 271(1-2): 21-6. April 30. <u>Abstract</u>
2009	Co-exposure: Lead	Niu R, et al. 2009. Decreased Learning Ability and Low Hippocampus Glutamate in Offspring Rats Exposed to Fluoride and Lead.	
2008	Co-exposure: Lead	Liu H, et al. 2008. Changes caused by fluoride and lead in energy metabolic enzyme activities in the reproductive system of male offspring rats.	Fluoride 41(3):184-91. July-Sept. <u>Full Article</u>
2007	Cytotoxicity	Matsui H, et al. 2007. Some characteristics of fluoride-induced cell death in rat thymocytes: cytotoxicity of sodium fluoride.	Toxicol In Vitro. 21(6):1113-20. Sept. <u>Abstract</u>
2005	Cytotoxicity	Satoh R, et al. 2005. Changes in fluoride sensitivity during in vitro senescence of normal human oral cells.	Anticancer Res. 25(3B):2085-90. May-June. <u>Abstract</u>
2009	Dental Caries	Warren JJ, et al. 2009. Considerations on optimal fluoride intake and dental caries outcomes--a longitudinal study. "... These findings suggest that achieving a caries-free status may have relatively little to do with fluoride <i>intake</i> , while fluorosis is clearly more dependent on fluoride intake ... CONCLUSIONS: Given the overlap among caries/fluorosis groups in mean fluoride intake and extreme variability in individual fluoride intakes, firmly recommending an "optimal" fluoride intake is problematic."	J Pub Health Dent 69(2): 111-115. <u>Abstract</u>
2007	Dental Caries	Broffitt L, et al. 2007. An investigation of bottled water use and caries in the mixed	Journal of Public Health Dentistry 67(3):151-8.

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		dentition.	<u>Abstract</u>
2007	Dental Caries	<p>Cheng KK, et al. 2007. Adding fluoride to water supplies.</p> <p>“... “If fluoride is a medicine, evidence on its effects should be subject to the standards of proof expected of drugs, including evidence from randomized trials... There have been no randomized trials of water fluoridation... Although the prevalence of caries varies between countries, levels everywhere have fallen greatly in the past three decades, and national rates of caries are now universally low. This trend has occurred regardless of the concentration of fluoride in water or the use of fluoridated salt, and it probably reflects use of fluoridated toothpastes and other factors, including perhaps aspects of nutrition.”</p>	British Medical Journal 335(7622):699-702.
2007	Dental Caries	<p>Maupomé G, et al. 2007. A comparison of dental treatment utilization and costs by HMO members living in fluoridated and nonfluoridated areas.</p> <p>In the largest region examined in the study, representing over 75% of the HMO members surveyed (the Portland metro area of Oregon), fewer children and adults in the non-fluoridated areas required treatment than children and adults in the fluoridated areas. Moreover, the children and adults in the non-fluoridated area who sought treatment accrued lower total costs over the 5-year period than those in the fluoridated area. As noted by the authors, the “Portland metro had lower treatment costs for the NF (Non-Fluoridated) area...”</p>	Journal of Public Health Dentistry 67(4):224-33.
2007	Dental Caries	<p>Pizzo G, et al. 2007. Community water fluoridation and caries prevention: a critical review.</p> <p>“For the past 50 years, CWF (Community Water Fluoridation) has been considered the most cost-effective measure for the control of caries at the community level. However, it is now accepted that systemic fluoride plays a limited role in caries prevention. Several</p>	Clinical Oral Investigations 11(3):189-93.

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		epidemiologic studies conducted in fluoridated and nonfluoridated communities clearly indicated that CWF may be unnecessary for caries prevention, particularly in the industrialized countries where the caries level has [become] low."	
2006	Dental Caries	Burt BA, et al. 2006. Dietary patterns related to caries in a low-income adult population . "This population had severe caries, poor oral hygiene, and diets that are high in sugars and fats and low in fruits and vegetables... Interventions to promote oral health are unlikely to be successful without improvements in the social and physical environment. "	Caries Res. 40(6):473-80. Abstract
2005	Dental Caries	Neurath C. 2005. Tooth decay trends in nonfluoridated and fluoridated countries .	Fluoride 38(4):324-5. Nov. Full Report
2011	Dental Fluorosis	Leite GA, et al. 2011. Exposure to lead exacerbates dental fluorosis. "This study shows that lead exacerbates dental fluorosis in rodents, suggesting that co-exposure to lead may affect the degree of fluorosis. "	Arch Oral Biol. 2011 Jan 24. [Epub ahead of print] Abstract
2011	Dental Fluorosis	Riksen EA, et al. 2011. Fluoride reduces the expression of enamel proteins and cytokines in an ameloblast-derived cell line. "Conclusions. These results indicate that fluoride may impact on the expression of structural enamel proteins and the protease responsible for processing these proteins during the secretory stage of amelogenesis and go some way to explaining the mineralization defect that characterises fluorotic enamel."	Arch Oral Biol. 56(4): 324-330. April. Abstract
2011	Dental Fluorosis	Jiménez-Farfán MD, et al. 2011. Fluoride consumption and its impact on oral health. "CONCLUSIONS: Data from our study show that, despite values of excretion within an optimal fluoride intake range, the prevalence of caries was significant in both groups, and	Int J Environ Res Public Health. 8(1):148-60. Jan. Full Article

		60% of the 11- to 12-year-old children presented with dental fluorosis. In addition, variable fluoride concentrations in products frequently consumed by children were found."	
2010	Dental Fluorosis	Beltran-Aguilar ED, et al. 2010. Prevalence and severity of dental fluorosis in the United States, 1999-2004. See Table 23. Mexican-Americans and Black Americans had significantly higher levels of moderate dental fluorosis compared to White Americans and Mexican-Americans had significantly higher levels of severe dental fluorosis compared to Black or White Americans.	NCHS data brief, no 53. Hyattsville, MD: National Center for Health Statistics. Full Report (See Table 23)
2010	Dental Fluorosis	Choubisa SL, et al. 2010. Osteo-dental fluorosis in relation to age and sex in tribal districts of Rajasthan, India. "... males showed relatively a higher incidence of dental and skeletal fluorosis compared to their counterparts... "	J Environ Sci Eng. 52(3):199-204. July. Abstract
2010	Dental Fluorosis	Levy SM, et al. 2010. Associations between fluorosis of permanent incisors and fluoride intake from infant formula, other dietary sources and dentifrice during early childhood. "CONCLUSIONS: Greater fluoride intakes from reconstituted powdered formulas (when participants were aged 3-9 months) and other water-added beverages (when participants were aged 3-9 months) increased fluorosis risk, as did higher dentifrice intake by participants when aged 16 to 36 months. "	Journal of the American Dental Association 141(10):1190-1201. Abstract
2010	Dental Fluorosis	Martinez-Mier EA, et al. 2010. Differences in exposure and biological markers of fluoride among White and African American children.	Journal of Public Health Dentistry 70:234-240. Abstract
2010	Dental Fluorosis	Verkerk RH. 2010. The paradox of overlapping micronutrient risks and benefits obligates risk/benefit analysis. "Conventional risk assessment on fluoride as undertaken by European and US authorities is explored in detail, and it is shown that risk	Toxicology 278(1):27-38. Nov 28. Abstract

		management, if applied by public authorities in a manner which is consistent with that used for other nutrients, would make public drinking water fluoridation programmes unfeasible in light of dental fluorosis risk to children."	
2009	Dental Fluorosis	<p>Sohn W, et al. 2009. Fluoride ingestion is related to fluid consumption patterns.</p> <p>"...African-American children ingested significantly more fluoride than White children in bivariate analysis. This association remained significant after accounting for fluid consumption pattern and other confounding factors in the model.</p> <p>CONCLUSION: Our results raise concerns that some children are ingesting significantly more fluoride than others depending on sociodemographic factors and fluid consumption patterns. Additional research is warranted to investigate the variation in the amounts of fluoride ingestion by these factors and its impact on fluorosis prevalence in different population groups.</p>	J Public Health Dent. 2069(4):267-75. Fall. Abstract
2009	Dental Fluorosis	<p>Warren JJ, et al. 2009. Considerations on optimal fluoride intake assessing dental fluorosis and dental caries outcomes - a longitudinal study.</p> <p>"CONCLUSIONS: Given the overlap among caries/fluorosis groups in mean fluoride intake and extreme variability in individual fluoride intakes, firmly recommending an "optimal" fluoride intake is problematic."</p>	J Public Health Dent. 69(2):111-5. Spring. Abstract
2009	Dental Fluorosis	<p>Nyvad B, et al. 2009. Diagnosing dental caries in populations with different levels of dental fluorosis [in Denmark].</p> <p>"The prevalence of dental fluorosis was 45% in the 1.1 ppm fluoride area and 21% in the 0.3 ppm fluoride area."</p>	Eur J Oral Sci. 117(2):161-8. April. Abstract
2008	Dental Fluorosis	Sharma R, et al. 2008. Fluoride induces endoplasmic reticulum stress and inhibits	Environ Health Perspect. 116(9):1142-6. Sept.

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		<p>protein synthesis and secretion.</p> <p>"CONCLUSIONS: These data suggest that F(-) initiates an ER stress response in ameloblasts that interferes with protein synthesis and secretion. Consequently, ameloblast function during enamel development may be impaired, and this may culminate in dental fluorosis."</p>	<u>Full Report</u>
2008	Dental Fluorosis	<p>Dincer E. 2008. Why do I have white spots on my front teeth?</p> <p>"Because their swallowing reflex is not fully developed, children under the age of 6 can swallow between 25% and 33% of fluoridated toothpaste with each brushing. In order to better educate parents about fluorosis and its effect on children's teeth, it is worth revisiting the guidelines for toothpaste use."</p>	<p>NY State Dent J. 74(1):58-60. Jan.</p> <p><u>Abstract</u></p>
2008	Dental Fluorosis	<p>Wurtz T, et al. 2008. Fluoride at non-toxic dose affects odontoblast gene expression in vitro.</p>	<p>Toxicology 249(1):26-34. July 10.</p> <p><u>Abstract</u></p>
2007	Dental Fluorosis	<p>Xiong X, et al. 2007. Dose-effect relationship between drinking water fluoride levels and damage to liver and kidney functions in children.</p> <p>"... our results suggest that drinking water fluoride levels over 2.0 mg/L can cause damage to liver and kidney functions in children and that the dental fluorosis was independent of damage to the liver but not the kidney."</p>	<p>Environ Res. 103(1):112-6. Jan.</p> <p><u>Abstract</u></p>
2007	Dental Fluorosis	<p>Vandana KL, et al. 2007. Periodontal changes in fluorosed and nonfluorosed teeth by Scanning Electron Microscopy.</p>	<p>Fluoride 40(2):128-33. April-June.</p> <p><u>Full Report</u></p>
2007	Dental Fluorosis	<p>Waidyasekera PG, et al. 2007. Caries susceptibility of human fluorosed enamel and dentine.</p> <p>"CONCLUSIONS: Moderately fluorosed enamel showed a significant caries resistance. In contrast, mild and moderately fluorosed dentine was significantly caries susceptible in vitro."</p>	<p>J Dent. 35(4):343-9. April.</p> <p><u>Abstract</u></p>

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2007	Dental Fluorosis	Ruan JP, et al. 2007. Dental fluorosis in children in areas with fluoride-polluted air, high-fluoride water, and low-fluoride water as well as low-fluoride air: a study of deciduous and permanent teeth in the Shaanxi province, China.	Acta Odontol Scand. 65(2):65-71. April. Abstract
2006	Dental Fluorosis	Lyaruu DM, et al. 2006. Short exposure to high levels of fluoride induces stage-dependent structural changes in ameloblasts and enamel mineralization.	Eur J Oral Sci 114 (Suppl. 1):111-5. Abstract
2005	Dental Fluorosis	Bharati P, et al. 2005. Clinical symptoms of dental and skeletal fluorosis in Gadag and Bagalkot Districts of Karnataka.	J. Hum. Ecol. 18(2):105-7.
2005	Dental Fluorosis	Cunha-Cruz J, et al. 2005. Dental fluorosis increases caries risk.	Journal of Evidence Based Dental Practice 5:170-1.
2005	Dental Fluorosis	Beltran-Aguilar ED et al. 2005. Surveillance for Dental Caries, Dental Sealants, Tooth Retention, Edentulism, and Enamel Fluorosis -- United States, 1988--1994 and 1999--2002. See Table 23.	MMWR. Surveillance Summaries. 54(03);1-44. August 26. Full Article
2005	Dental Fluorosis	Heikens A, et al. 2005. The impact of the hyperacid Ijen Crater Lake: risks of excess fluoride to human health. "Based on the total daily intake, the lowest F concentration in drinking water that poses a risk of developing fluorosis is approximately 0.5 mg/l for dental fluorosis and 1.1 mg/l for skeletal fluorosis."	Sci Total Environ. 346(1-3):56-69. June 15. Abstract
2010	Developmental	Flace P, et al. 2010. Effects of developmental fluoride exposure on rat ultrasonic vocalization, acoustic startle reflex and pre-pulse inhibition.	Eur Rev Med Pharmacol Sci. 14(6):507-12. June. Abstract
2007	Developmental	Wang SX, et al. 2007. Arsenic and Fluoride Exposure in Drinking Water: Children's IQ and Growth in Shanyin County, Shanxi Province, China. "... The statistically significant differences were found in the following comparisons: Children's height in the control group was significantly higher than that in high-fluoride group ($p < 0.05$) ... It is less surprising that exposure to	Environmental Health Perspectives 115(4):643-47. Full Report

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		fluoride affected children's growth function, especially height. Previous studies have demonstrated multiple effects of exposure to high concentrations of fluoride on children's morphology, growth and development, and on bones and teeth (<u>Qian et al. 1989; Xu and Huo 2000</u>). This is because fluoride accumulates in bone and reduces calcium uptake, thereby influencing growth."	
2011	DNA	Andrade-Vieira LF, et al. 2011. Spent Pot Liner (SPL) induced DNA damage and nuclear alterations in root tip cells of <i>Allium cepa</i> as a consequence of programmed cell death .	Ecotoxicol Environ Saf. 2011 Jan 11. [Epub ahead of print] Abstract
2011	DNA	Madusudanan Rao S, et al. 2011. Morphometry of buccal mucosal cells in fluorosis - a new paradigm. "Conclusions: ... Fluorosis induces oxidative stress, DNA damage and apoptosis which can be the reasons for the increase in the nuclear size and decrease in the cell size..."	Hum Exp Toxicol. Mar 15. [Epub ahead of print] Abstract
2010	DNA	Li H, et al. 2010. [Toxic effects of fluoride on rat cerebral cortex astrocytes in vitro]. "Conclusion: NaF can induce cell cycle arrest from S to G2/M and inhibit activities of 5'-NT,SDH and ACP in astrocytes. "	Wei Sheng Yan Jiu. 39(1):86-8. Jan. [Article in Chinese] Abstract
2010	DNA	Shashi A, et al. 2010. Histochemical pattern of gastrocnemius muscle in fluoride toxicity syndrome. "Conclusions: The findings of present study demonstrate that certain concentrations of fluoride can induce muscle lesions and damage DNA, RNA, and protein in muscle cells and excessive intake and accumulation of fluoride is therefore a serious risk factor for muscular abnormalities in fluorosis."	Asian Pacific Journal of Tropical Medicine 3(2):136-140. Feb.
2009	DNA	Zhang R, et al. 2009. A stable and sensitive testing system for potential carcinogens based on DNA damage-induced gene expression in human HepG2 cell . "The results showed that all 20 [including sodium fluoride] tested known carcinogenic	Toxicol In Vitro. 23(1):158-65. Feb. Abstract

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		and genotoxic agents were able to induce gadd153-Luc expression at a sublethal dose.”	
2008	DNA	Jia L, et al. 2008. DNA damage induced by fluoride in rat kidney cells.	Fluoride 41(4):297-300. October-December. Full Report
2008	DNA	Zhang M, et al. 2008. Effects of fluoride on DNA damage, S-phase cell-cycle arrest and the expression of NF- B in primary cultured rat hippocampal neurons .	Toxicology Letters 179(1):1-5. Abstract
2006	DNA	He LF, Chen JG. 2006. DNA damage, apoptosis and cell cycle changes induced by fluoride in rat oral mucosal cells and hepatocytes .	World J Gastroenterol. 12(7):1144-8. February 21. Full Report
2006	DNA	Zhang Y, et al. 2006. DNA damage induced by fluoride in rat osteoblasts .	Fluoride 39(3)191-4. July-Sept. Full Report
2005	DNA	Ge Y, et al. 2005. Comet assay of DNA damage in brain cells of adult rats exposed to high fluoride and low iodine.	Fluoride 38(3):209-14. Full Report
2005	DNA	Ge Y, et al. 2005. DNA damage in thyroid gland cells of rats exposed to long-term intake of high fluoride and low iodine.	Fluoride 38(4):318-23. November. Full Report
2008	Dyspepsia	Spittle B. 2008. Dyspepsia associated with fluoridated water.	Fluoride 41(1):89-92. Jan-March. Full Report
2008	Enzymes	Moolenburgh H. 2008. Fluoride and serum cholinesterase . Letter.	Fluoride 41(3): 227. July-Sept. Full Report
2005	Enzymes	Adamek E, et al. 2005. In vitro and in vivo effects of fluoride ions on enzyme activity.	Ann Acad Med Stetin. 51(2):69-85.
2011	Exposure	Vernacchio L, et al. 2011. Vitamin, Fluoride, and Iron Use among US Children Younger than 12 Years of Age : Results from the Slone Survey 1998-2007. “...Between February 1998 and April 2007, there were 2,857 children 0 to 11 years of age enrolled from the 48 contiguous United States ... The response rate to the survey was 61%... Overall, fluoride was used by 3.3% of participants and iron by 9.7%... Use of each was highest in the 2- to 5-year-old age group	J Am Diet Assoc. 111:285-289.

		for both (4.3% for fluoride and 12.4% for iron).	
2010	Exposure	<p>Lockwood G. 2010. Theoretical context-sensitive elimination times for inhalation anaesthetics.</p> <p><i>Note from FAN: <u>Desflurane, Sevoflurane and Isoflurane</u> all break down to the fluoride ion in the body.</i></p> <p>"After 4 h of anaesthesia, the model predicted body content to be 28 g nitrous oxide, 26 g desflurane, 14 g sevoflurane, or 15 g isoflurane, and 99.9% brain elimination times were then 9 h for nitrous oxide, 33 h for desflurane, 52 h for sevoflurane, and 71 h for isoflurane. At this stage of elimination, the whole body still retained between 4% and 13% of the absorbed dose."</p>	Br J Anaesth. 104(5):648-55. May. <u>Abstract</u>
2010	Exposure	<p>Mansfield P. 2010. Fluoride consumption: the effect of water fluoridation.</p> <p>Mansfield re-analyzed data from the 2000-2003 UK National Diet and Nutrition Survey. 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.</p>	Fluoride 43(4): 223-231. <u>Full Report</u>
2010	Exposure	<p>Mason SC, et al. 2010. Evaluation of salivary fluoride retention from a new high fluoride mouthrinse.</p> <p>Single-use treatment with the new mouthrinse containing 450 ppm fluoride resulted in statistically significantly higher salivary fluoride levels throughout the 120 min test period. Total fluoride retention (AUC₀₋₁₂₀) was also statistically significantly greater versus comparator rinse treatments.</p>	J Dent. 38(Suppl 3):S30-S36. Nov. <u>Abstract</u>
2009	Exposure	Rodrigues MH, et al. 2009. Dietary fluoride	J Dent Res. 88(2):142-5.

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		<p>intake by children receiving different sources of systemic fluoride.</p> <p>“The aim of this study was to estimate the dietary F intake by children receiving F from artificially fluoridated water (AFW-Brazil, 0.6-0.8 mg F/L), naturally fluoridated water (NFW-Brazil, 0.6-0.9 mg F/L), fluoridated salt (FS-Peru, 180-200 mg F/Kg), and fluoridated milk (FM-Peru, 0.25 mg F). Children (n=21-26) aged 4-6 yrs old participated in each community. A non-fluoridated community (NoF) was evaluated as the control population... The results indicate that the dietary F intake must be considered before a systemic method of fluoridation is implemented.”</p>	<p>Feb. <u>Abstract</u></p>
2009	Exposure: Children	<p>Sohn W, et al. 2009. Fluoride ingestion is related to fluid consumption patterns.</p> <p>“There was substantial variation in the estimated amount of fluoride ingestion depending on the children's fluid consumption patterns as well as age, gender, and race/ethnicity. African-American children ingested significantly more fluoride than White children in bivariate analysis. This association remained significant after accounting for fluid consumption pattern and other confounding factors in the model.</p> <p>CONCLUSION: Our results raise concerns that some children are ingesting significantly more fluoride than others depending on sociodemographic factors and fluid consumption patterns. Additional research is warranted to investigate the variation in the amounts of fluoride ingestion by these factors and its impact on fluorosis prevalence in different population groups.</p>	<p>J Public Health Dent. 2069(4):267-75. Fall. <u>Abstract</u></p>
2007	Exposure	<p>Opydo-Szymaczek J, et al. 2007. Transplacental passage of fluoride in pregnant Polish women assessed on the basis of fluoride concentrations in maternal and cord blood plasma.</p>	<p>Fluoride 40(1):46-50. <u>Full Report</u></p>
2007	Exposure	<p>Kanbak M, et al. 2007. Renal safety and extrahepatic defluorination of sevoflurane in</p>	<p>Transplant Proc.</p>

		hepatic transplantations.	39(5):1544-8. June.
2006	Exposure	<p>Hong L, et al. 2006. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars.</p> <p>"... As part of the longitudinal Iowa Fluoride Study, subjects were followed from birth to 36 months... Cumulatively from birth to 36 months, average daily intake of 0.04 mg F/kg BW or less carried relatively low risk for fluorosis (12.9% for maxillary central incisors, 6.8% for first molars). Average daily intake of 0.04-0.06 mg F/kg BW showed a significantly elevated risk for fluorosis (23.0% for maxillary central incisors, 14.5% for first molars), while fluorosis risk was even higher for average intake above 0.06 mg F/kg BW (38.0% for maxillary central incisors, 32.4% for first molars)."</p>	Caries Res. 40(6):494-500. <u>Abstract</u>
2006	Exposure	<p>Hong L, et al. 2006. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors.</p> <p>"... The first two years of life were most important to fluorosis development in permanent maxillary central incisors; however, this study also suggests the importance of other individual years."</p>	Community Dent Oral Epidemiol. 34(4):299-309. <u>Abstract</u>
2006	Exposure	Krook LP, Justus C. 2006. Fluoride poisoning of horses from artificially fluoridated drinking water.	Fluoride 39(1)3-10. Jan-Mar. <u>Full Report</u>
2006	Exposure	ADA (American Dental Association). 2006. Interim Guidance on Reconstituted Infant Formula . 2006.	American Dental Association, ADA, eGRAM. Nov 9.
2005	Exposure	Erdal S, et al. 2005. A quantitative look at fluorosis, fluoride exposure, and intake in children using a health risk assessment approach.	Environ Health Persp 113:111-7. <u>Full Report</u>
2006	Exposure	Pagliari AV, et al. 2006. Analysis of fluoride concentration in mother's milk substitutes .	Braz Oral Res. 20(3):269-74. <u>Abstract</u>
2005	Exposure	Zuanon ACC, Aranha AMF. 2005. Mouthwash	J Clin Pediatr Dent

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		ingestion by preschool children.	30(1):15-18.
2010	Exposure: Tea	Pehrsson PR, et al. 2010. The fluoride content of select brewed and microwave-brewed black teas in the United States. "Conclusions: ... on average, the dry tea contributes 3–4 times as much fluoride to the brewed tea as does the water. The fluoride provided by brewed tea may contribute significantly amounts of F, and should be considered when assessing total daily intake. "	Journal of Food Composition and Analysis. Published ahead of print. Dec 27.
2010	Exposure: Tea	Joshi S, et al. 2010. Skeletal fluorosis due to excessive tea and toothpaste consumption.	Osteoporos Int. Oct 9. [Epub ahead of print] Abstract
2010	Exposure: Tea	Cressey P, et al. 2010. Estimated dietary fluoride intake for New Zealanders. "Intake of fluoride was driven by consumption of dietary staples (bread, potatoes), beverages (particularly tea , soft drinks, and beer), and the fluoride status of drinking water."	J Public Health Dent. 70(4):327-36. Fall. Abstract
2009	Exposure: Tea	de Lourdes Azpeitia-Valadez M, et al. 2009. [Risk factors for dental fluorosis in children between 6 and 15 years old]. "Prepared gaseous drink and tea consumption , age in relation to the exhibition of periodic applications of fluoride and the area of residence are the main risk factors for dental fluorosis. "	Rev Med Inst Mex Seguro Soc. May-47(3):265-70. June. [Article in Spanish] Abstract
2008	Exposure: Tea	Whyte MP, et al. 2008. Skeletal fluorosis from instant tea. "CONCLUSIONS: SF [skeletal fluorosis] from habitual consumption of large volumes of extra strength instant tea calls for recognition and better understanding of a skeletal safety limit for this modern preparation of the world's most popular beverage. "	J Bone Miner Res. 23(5):759-69. May. Abstract
2008	Exposure: Tea	Yi J, Cao J. 2008. Tea and fluorosis. "... Long-term consumption of high fluoride tea could result in chronic fluoride intoxication. This review summarized those data of the fluoride content in various tea commodities, and estimated the risk of	Journal of Fluorine Chemistry 129:76-81.

		fluorosis caused by high fluoride tea commodities. We also introduced fluorosis caused by tea from case reports, epidemiology observations and animal models... it is urgent that governmental and international agencies adopt safe standards of fluoride content in tea commodities."	
2007	Exposure: Tea	Hallanger Johnson JE, et al. 2007. Fluoride-related bone disease associated with habitual tea consumption. Figure 1. <u>Lateral lumbar spine showing advanced osteosclerosis of the vertebral bodies, with absence of usual marrow space radiolucency</u>	Mayo Clin Proc. 82(6):719-24. June. • Erratum in: Mayo Clin Proc. 2007 Aug;82(8):1017. dosage error in text. Full Text
2006	Exposure: Tea	Whyte MP. 2006. Fluoride Levels in Bottled Teas . Letter to Editor.	American Journal of Medicine, 119(2):189-90. February.
2005	Exposure: Tea	Whyte MP, et al. 2005. Skeletal fluorosis and instant tea. "CONCLUSIONS: SF [skeletal fluorosis] from habitual consumption of large volumes of extra strength instant tea calls for recognition and better understanding of a skeletal safety limit for this modern preparation of the world's most popular beverage. "	Am J Med. 118(1):78-82. Jan. Abstract
2005	Exposure: Tea	Pehrsson P et al. 2005. The fluoride content of brewed and microwave brewed black teas .	U.S. Department of Agriculture. Full Article
2005	Exposure: Tea	Sun DJ et al. 2005. Dose-response relationship between dental fluorosis and fluoride in brick tea . Presented at the 26th International Society for Fluoride Research in Wiesbaden, Germany (September).	Fluoride 38(3):253. Full Article (see Abstract 47)
2006	Fetotoxicity	Helal M, El Dakdoky M. 2006. Fetotoxicity of fluoride in rats alleviated by some antioxidants.	Fluoride 39(3):202-10. July-Sept. Full Report
2007	Fluoridation	Cheng KK, et al. 2007. Adding fluoride to water supplies . "...If fluoride is a medicine, evidence on its effects should be subject to the standards of proof expected of drugs, including evidence	British Medical Journal 335(7622):699-702. Full Report

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		from randomized trials... In the case of fluoridation, people should be aware of the limitations of evidence about its potential harms and that it would be almost impossible to detect small but important risks (especially for chronic conditions) after introducing fluoridation... "	
2007	Fluoridation	Limeback H, Thiessen K, Isaacson R, Hirzy W. 2007. The EPA MCLG for fluoride in drinking water: new recommendations. "Our results indicated that in all calculations the new MCLG for fluoride in drinking water should be at most one tenth (0.4 mg/L) of the current MCLG of 4 mg/L, suggesting that the practice of fluoridation should be re-evaluated."	Society of Toxicology 46th Annual Meeting, Charlotte, North Carolina, March 25-29.
2007	Free Radicals	Shanthakumari D, et al. 2007. Effect of fluoride intoxication on the levels of intestinal antioxidants studied in rats.	Methods Find Exp Clin Pharmacol. 29(2):93-9. Abstract
2005	Free Radicals	Krechniak J, Inkielewicz I. 2005. Correlations between fluoride concentrations and free radical parameters in soft tissues of rats.	Fluoride 38(4):293-6. Nov. Full Report
2011	Genotoxicity	Podder S, et al. 2011. Reduction in fluoride-induced genotoxicity in mouse bone marrow cells after substituting high fluoride-containing water with safe drinking water.	J Appl Toxicol. 2011 Mar 5. doi: 10.1002/jat.1644. Abstract
2010	Genotoxicity	Podder S, et al. 2010. Fluoride-induced genotoxicity in mouse bone marrow cells : effect of buthionine sulfoximine and N-acetyl-l-cysteine.	J Appl Toxicol. 2010 Dec 10. doi: 10.1002/jat.1605. [Epub ahead of print] Abstract
2008	Genotoxicity	Podder S, et al. 2008. Differential <i>in vivo</i> genotoxic effects of lower and higher concentrations of fluoride in mouse bone marrow cells.	Fluoride 41(4):301-7. Oct-Dec. Full Report
2008	Genotoxicity	Podder S, et al. 2008. <i>In vivo</i> suppression by fluoride of chromosome aberrations induced by mitomycin-C in mouse bone marrow cells.	Fluoride 41(1):40-3. Jan-March.
2005	Genotoxicity	Velazquez-Guardarrama, et al. 2005. Genotoxic evaluation of sodium fluoride and sodium perborate in mouse bone marrow	Bull Environ Contam and Toxicol. 74: 566-72.

		cells.	
2010	Haem Biosynthesis Pathway	<p>Chouhan S, et al. 2010. Fluoride-induced changes in haem biosynthesis pathway, neurological variables and tissue histopathology of rats.</p> <p>"This study intended to determine the effects of various concentrations of fluoride (1, 10, 50 and 100 ppm) in drinking water for a period of 12 weeks on changes in haem biosynthesis pathway, oxidative stress and neurological variables supported by histopathological observations and fluoride in rats... Interestingly and most significantly, these changes were more pronounced at lower concentrations of fluoride compared with higher fluoride dose...These changes support our earlier findings regarding the role of decreased ionic mobility of fluoride ion at higher concentrations, leading to less pronounced toxicity."</p>	<p>J Appl Toxicol. 30(1):63-73. Jan. Abstract</p>
2011	Heart: <i>Study on children</i>	<p>Karademir S, et al. 2011. Effects of fluorosis on QT dispersion, heart rate variability and echocardiographic parameters in children - Original Investigation.</p> <p>"... We found statistically significant low T4 levels, hypocalcemia and hyponatremia, increased QT and QTc interval in children with dental fluorosis. Our results show that fluorosis might increase risk of arrhythmia indirectly, due to its hypocalcemic, hypernatremic, and hypothyroidism effects... Further studies concerning cardiovascular effect of fluorosis in both adults and children are needed."</p>	<p>Anadolu Kardiyol Derg. 11(2):150-5. Full Report</p>
2011	Heart	<p>Flora SJ, et al. 2011. Interactive effect of arsenic and fluoride on cardio-respiratory disorders in male rats: possible role of reactive oxygen species.</p>	<p>Biometals. Jan 18. [Epub ahead of print] Abstract</p>
2010	Heart	<p>Varol E, et al. 2010. Impact of chronic fluorosis on left ventricular diastolic and global functions.</p>	<p>Science of the Total Environment 408(11): 2295-8. Abstract</p>
2010	Heart	<p>Varol E, et al. 2010. Aortic elasticity is</p>	<p>Biol Trace Elem Res. 133:121-7.</p>

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		impaired in patients with endemic fluorosis.	<u>Abstract</u>
2010	Heart	Yang E, et al. 2010. Fluoride induces vascular contraction through activation of RhoA/Rho kinase pathway in isolated rat aortas.	Environ Toxicol Pharmacol. 29(3):290-296. May.
2006	Heart	Jeon SB, et al. 2006. A role for Rho kinase in vascular contraction evoked by sodium fluoride.	Biochem Biophys Res Commun. 343(1):27-33. April 28. <u>Abstract</u>
2005	Heart	Cicek E, et al. 2005. Effects of chronic ingestion of sodium fluoride on myocardium in a second generation of rats.	Hum Exp Toxicol. 24(2):79-87. Feb. <u>Abstract</u>
2011	Immune System / Human study	Hernández-Castro B, et al. 2010. Effect of fluoride exposure on different immune parameters in humans. "Context: T regulatory (Treg) cells play an important role in the modulation of the immune response, and are implicated in the pathogenesis of autoimmune diseases... Conclusion: Our data suggest that F exposure exerts a complex and relevant effect on Treg cells in humans."	Immunopharmacology and Immunotoxicology, 33(1):169-77. March. <u>Abstract</u>
2011	Insulin	Lupo M, et al. 2011. Effect of fluoridated water on plasma insulin levels and glucose homeostasis in rats with renal deficiency. "... It is concluded that the consumption of fluoridated water from water supply did not affect plasma glucose levels even in cases of animals with renal disease. However, a resistance to insulin action was demonstrated. "	Biol Trace Elem Res. 140(2):198-207. May. <u>Abstract</u>
2009	Insulin	García-Montalvo EA, et al. 2009. Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress.	Toxicology 263(2-3):75-83. Sept 19. <u>Abstract</u>
2008	Insulin	Chehoud KA, et al. 2008. Effects of fluoride intake on insulin sensitivity and insulin signal transduction.	Fluoride 41(4):270-5. Oct-Dec. <u>Full Article</u>
2008	Insulin	Menoyo I, et al. 2008. Fluoride- induced resistance to insulin in the rat.	Fluoride 41(4):260-9. Oct-Dec. <u>Full Article</u>
2005	Insulin	Menoyo I et al. 2005. Effect of fluoride on the	Arzneimittelforschung

		secretion of insulin in the rat.	55:455-60. <u>Abstract</u>
2011	Iodine	Ge Y, et al. 2011. Proteomic Analysis of Brain Proteins of Rats Exposed to High Fluoride and Low Iodine.	Archives of Toxicology Arch Jan;85(1):27-33. <u>Abstract</u>
2009	Iodine	Wang J, et al. 2009. Chapter 67 - DNA Damage in Brain and Thyroid Gland Cells due to High Fluoride and Low Iodine.	Comprehensive Handbook of Iodine, Pages 643-649. Edited by: Victor R. Preedy, Gerard N. Burrow and Ronald Watson. ISBN: 978-0-12-374135-6. Elsevier Inc.
2008	Iodine	Ren D, et al. 2008. A Study of the Intellectual Ability of 8–14 Year-Old Children in High Fluoride, Low Iodine Areas.	Fluoride 41(4):319–20. <u>Full Report</u>
2007	Iodine	Voronych-Semchenko NM. 2007. Characteristics of hypothyroidism correction and lipid metabolism disorder in iodine deficiency. “... It has been revealed that hypothyrosis has negative influence on lipid metabolism indexes. "Iodid-100" usage stabilized hormonal and lipid status. Excessive intake of chlorine and fluorine ions by the organism decreased the effectiveness of iodine containing drugs. ”	Fiziol Zh. 53(3):38-42. [Article in Ukrainian] <u>Abstract</u>
2006	Iodine	Ge Y, et al. 2006. Apoptosis in brain cells of offspring rats exposed to high fluoride and low iodine.	Fluoride 39(3);173-8. July-Sept. <u>Full Report</u>
2005	Iodine	Ge Y, et al. 2005. Comet assay of DNA damage in brain cells of adult rats exposed to high fluoride and low iodine.	Fluoride 38(3):209-14. <u>Full Report</u>
2005	Iodine	Ge Y, et al. 2005. DNA damage in thyroid gland cells of rats exposed to long-term intake of high fluoride and low iodine.	Fluoride 38(4):318–23. November. <u>Full Report</u>
2005	Iodine	Gas'kov Alu, et al. 2005. [The specific features of the development of iodine deficiencies in children living under environmental pollution with fluorine compounds]	Gig Sanit. Nov-Dec;(6):53-5. <u>Full Article - English Translation</u>
2011	Kidney	Yang K and Liang X. 2011. Fluoride in Drinking	Encyclopedia of Environmental Health

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		<p>Water: Effect on Liver and Kidney Function.</p> <p>"Abstract. ... high level of fluoride in drinking water is harmful to the living system. Chronic fluoride intoxication causes damages to osseous tissue (teeth and bone) and soft tissues (liver, kidney, brain, etc.). Liver and kidney are the target organs markedly attacked by excessive amount of fluoride. High doses of fluoride intake lead to changes of structure, function, and metabolism in liver and kidney."</p>	(Editor-in-Chief: Jerome O. Nriagu, Elsevier B.V.), Pages 769-775.
2011	Kidney	<p>Chattopadhyay A, et al. 2011. Fluoride-induced histopathology and synthesis of stress protein in liver and kidney of mice.</p> <p>"Selective low (15 mg sodium fluoride (NaF)/L) and relatively high (150 mg NaF/L) doses of in vivo fluoride (F) treatment to Swiss albino mice through drinking water elicited organ-specific toxicological response. All the F-exposed groups showed severe alterations in both liver and kidney architectures"</p>	Arch Toxicol. 85(4):327-35. April. <u>Abstract</u>
2011	Kidney	<p>Chandrajith R, et al. 2011. Dose-dependent Na and Ca in fluoride-rich drinking water--another major cause of chronic renal failure in tropical arid regions.</p>	Sci Total Environ. 409(4):671-5. Jan 15. <u>Abstract</u>
2010	Kidney	<p>Itai K, et al. 2010. Serum ionic fluoride concentrations are related to renal function and menopause status but not to age in a Japanese general population.</p> <p>"Conclusion: SIF [Serum ionic fluoride] concentrations in middle-aged healthy subjects were increased with an age-related degeneration in renal function. SIF concentrations in post-menopausal women arise from the increased fluoride release from bone after menopause. Age is not related to SIF concentrations."</p>	Clinica Chimica Acta 411: 263-266. <u>Abstract</u>
2010	Kidney	<p>Błaszczuk I, et al. 2011. Influence of methionine upon the activity of antioxidative enzymes in the kidney of rats exposed to sodium fluoride.</p> <p>"... Among the factors inducing intensified free</p>	Biol Trace Elem Res. 33(1):60-70. Jan. <u>Abstract</u>

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		radical processes, fluoride ions are listed, among others. One of the organs most exposed to the toxic activity of fluorides is the kidney... The studies carried out confirmed the disadvantageous effect of NaF upon the antioxidative system in rats (decrease in activity of antioxidative enzymes)."	
2010	Kidney	Al Omireeni, et al. 2010. Biochemical and histological studies on the effect of sodium fluoride on rat kidney collagen. "Abstract: The present study was carried out to study the effect of acute doses of sodium fluoride on the collagen content of the rat kidneys. Five groups of rats were studied: (i) control rats and (ii) rats divided into four subgroups according to the dose of NaF. Results showed that higher doses of sodium fluoride 10, 20 and 30 mg of NaF/kg body weight caused a significant decrease in the collagen content of the kidneys when compared to the control rats. Electron microscope studies supported these results and showed the sodium fluoride doses 10, 20 and 30 mg of NaF/kg body weight caused disruption of ordered collagen fibrils of the rat kidneys. "	J of Saudi Chemical Society. 14(4):413-416. Full Report
2009	Kidney	Kobayashi CAN, et al. 2009. Proteomic analysis of kidney in rats chronically exposed to fluoride.	Chem Biol Interact. 180(2):305-11. July 15. Abstract
2008	Kidney	Jia L, et al. 2008. DNA damage induced by fluoride in rat kidney cells .	Fluoride 41(4):297-300. Oct-Dec. Full Report
2008	Kidney	Tang Q, et al. 2008. In vitro hormesis effects of sodium fluoride on kidney cells of three-day old male rats .	Fluoride 41(4):292-6. Oct-Dec. Full Article
2007	Kidney	Xiong X, et al. 2007. Dose-effect relationship between drinking water fluoride levels and damage to liver and kidney functions in children . "... our results suggest that drinking water fluoride levels over 2.0 mg/L can cause damage to liver and kidney functions in children and that the dental fluorosis was independent of damage to the liver but not	Environ Res. 103(1):112-6. Jan. Abstract

		the kidney."	
2007	Kidney	Xu H, et al. 2007. Effects of fluoride on the intracellular free Ca ²⁺ and Ca ²⁺ -ATPase of kidney. "To sum up, the effect of fluoride on Ca ²⁺ -ATPase is a similar to a dose-effect relationship phenomenon characterized by low-dose stimulation and high-dose inhibition, and the increase of [Ca²⁺]_i probably plays a key role on the mechanism of renal injury in fluorosis. "	Biol Trace Elem Res. 116(3):279-88. June. Abstract
2006	Kidney	Bober J, et al. 2006. Fluoride aggravation of oxidative stress in patients with chronic renal failure.	Fluoride 39(4):302-9. Oct-Dec. Full Article
2006	Kidney	Bansal R, Tiwari SC. 2006. Back pain in chronic renal failure. "...Definitive diagnosis was reached with estimation of fluoride levels in blood and urine, which were 0.291 mg/l and 0.962 mg/l (15.3 and 50.6 µmol/l), respectively. Her drinking water source , ground water from a tubewell, was found to contain 3.910 mg/l (205.9 µmol/l) of fluoride."	Nephrology Dialysis Transplantation 21:2331-2. Full Article
2006	Kidney	Harinarayan CV, et al. 2006. Fluorotoxic metabolic bone disease: an osteorenal syndrome caused by excess fluoride ingestion in the tropics.	Bone 39(4):907-14. Abstract
2006	Kidney	Ayoob S, Gupta AK. 2006. Fluoride in drinking water: a review on the status and stress effects.	Critical Reviews in Environmental Science and Technology 36:433-87.
2006	Kidney	Zhan XA, et al. Toxic effects of fluoride on kidney function and histological structure in young pigs.	Fluoride 39(1):22-6. Jan-Mar. Full Report
2005	Kidney	Liu JL, et al. 2005. [The dose-effect relationship of water fluoride levels and renal damage in children] "CONCLUSION: Over 2.0 mg/L fluoride in drinking water can cause renal damage in children, and the damage degree increases with the drinking water fluoride content. Renal damage degree is not related to	Wei Sheng Yan Jiu. 34(3):287-8. May. [Article in Chinese]. Abstract

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		whether the children suffered from dental fluorosis and mainly due to water fluoride concentration."	
2005	Kidney	Grucka-Mamczar E, et al. 2005. Disturbances of kidney function in rats with fluoride-induced hyperglycemia after acute poisoning by sodium fluoride.	Fluoride 38(1):48–51. Full Report
2005	Kidney	Xu H, et al. 2005. Proteomic analysis of kidney in fluoride-treated rat.	Toxicol Lett. 60(1):69-75. Dec 30. Abstract
2010	Lipid Peroxidation	Chauhan SS, et al. 2010. Modulation of lipid peroxidation and antioxidant defense systems in rat intestine by subchronic fluoride and ethanol administration. "These findings suggest that fluoride and ethanol exposure induces considerable changes in lipid peroxidation, antioxidant defense, and morphology of rat intestine, which may affect its functions."	Alcohol, [Epub ahead of print] Abstract
2007	Lipid Peroxidation	Kalyanalakshmi P, et al. 2007. Oxidative stress in males with skeletal fluorosis in Andhra Pradesh, India.	Fluoride 40(1):42–5. Full Report
2007	Lipid Peroxidation	Oncu M, et al. 2007. Effect of long-term fluoride exposure on lipid peroxidation and histology of testes in first- and second-generation rats .	Biol Trace Elem Res. 118(3):260-8. Sept. Abstract
2006	Lipid Peroxidation	Oncu M, et al. 2006. Effect of chronic fluorosis on lipid peroxidation and histology of lung tissues in first and second generation rats .	Toxicol Ind Health. 22(9):375-80. Oct. Abstract
2005	Lipid Peroxidation	Bouaziz H, et al. 2005. Toxic effects of fluoride by maternal ingestion on kidney function of adult mice and their suckling pups . "Lipid peroxidation increased in the treated mice, as revealed by high kidney malondialdehyde levels, while plasma and urinary uric acid levels showed a significant decline."	Fluoride 38(1):23–31. Full Report
2004	Lipid Peroxidation	Karaoz E, et al. 2004. Effect of chronic fluorosis on lipid peroxidation and histology of kidney tissues in first- and second-generation rats .	Biol Trace Elem Res. 102(1-3):199-208. Winter. Abstract

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2011	Liver	<p>Yang K and Liang X. 2011. Fluoride in Drinking Water: Effect on Liver and Kidney Function.</p> <p>"Abstract. ... high level of fluoride in drinking water is harmful to the living system. Chronic fluoride intoxication causes damages to osseous tissue (teeth and bone) and soft tissues (liver, kidney, brain, etc.). Liver and kidney are the target organs markedly attacked by excessive amount of fluoride. High doses of fluoride intake lead to changes of structure, function, and metabolism in liver and kidney."</p>	<p>Encyclopedia of Environmental Health (Editor-in-Chief: Jerome O. Nriagu. Elsevier B.V.), Pages 769-775.</p>
2011	Liver	<p>Chattopadhyay A, et al. 2011. Fluoride-induced histopathology and synthesis of stress protein in liver and kidney of mice.</p> <p>"Selective low (15 mg sodium fluoride (NaF)/L) and relatively high (150 mg NaF/L) doses of in vivo fluoride (F) treatment to Swiss albino mice through drinking water elicited organ-specific toxicological response. All the F-exposed groups showed severe alterations in both liver and kidney architectures"</p>	<p>Arch Toxicol. 85(4):327-35. April. <u>Abstract</u></p>
2010	Liver	<p>Iano FG, et al. 2010. Chronic Toxicity of Fluoride in the Liver Antioxidant Defense.</p> <p>"... The enzyme CAT was significantly reduced and SOD significantly increased, respectively, in the 15 ppm F group when compared to control and 5 ppm F group. In summary, clear changes in the antioxidant parameters in relation with the level of administered F was observed. These results show that chronic F administration alters the antioxidant systems of rats."</p>	<p>Free Radical Biology and Medicine 49(Suppl 1):S221. July.</p>
2009	Liver	<p>Birkner E, et al. 2009. The Influence of rich-in-cholesterol diet and fluoride ions contained in potable water upon the concentration of malondialdehyde and the activity of selected antioxidative enzymes in rabbit liver.</p>	<p>Biol Trace Elem Res. 129(1-3):137-42. Summer. <u>Abstract</u></p>
2007	Liver	<p>Xiong X, et al. 2007. Dose-effect relationship between drinking water fluoride levels and damage to liver and kidney functions in</p>	<p>Environ Res. 103(1):112-6. Jan. <u>Abstract</u></p>

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		children.	
2007	Liver	<p>Grucka-Mamczar E, et al. 2007. Influence of extended exposure to sodium fluoride and caffeine on the activity of carbohydrate metabolism enzymes in rat blood serum and liver.</p> <p>"... Glycolysis in extra-hepatic tissues (serum), under the influence of F, was slightly inhibited; however, it was markedly intensified by caffeine. Overall, a more profound influence by caffeine on carbohydrate enzyme activity was observed in blood serum (extra-hepatic tissues) than in the liver."</p>	<p>Fluoride 40(1)62-66. Jan-March. <u>Full Report</u></p>
2005	Liver	<p>Guo X, et al. 2005. [Effect of fluoride on activities of enzyme and ultrastructure in primary cultured rat hepatocytes]</p>	<p>Wei Sheng Yan Jiu. 34(1):35-7. January. [Article in Chinese] <u>Abstract</u></p>
2009	Lung	<p>Ridley W, Matsuoka M. 2009. Fluoride-induced cyclooxygenase-2 expression and prostaglandin E(2) production in A549 human pulmonary epithelial cells.</p>	<p>Toxicol Lett. 188(3):180-5. Aug10. <u>Abstract</u></p>
2008	Lung	<p>Refsnes M, et al. 2008. Fluoride-induced IL-8 release in human epithelial lung cells: relationship to EGF-receptor-, SRC- and MAP-kinase activation.</p>	<p>Toxicol Appl Pharmacol. 227(1):56-67. Feb 15. <u>Abstract</u></p>
2006	Lung	<p>Oncu M, et al. 2006. Effect of chronic fluorosis on lipid peroxidation and histology of lung tissues in first and second generation rats.</p>	<p>Toxicol Ind Health. 22(9):375-80. Oct. <u>Abstract</u></p>
2003	Lung	<p>Aydin G, et al. 2003. Histopathological and biochemical changes in lung tissues of rats following administration of fluoride over several generations.</p> <p>"... This multigenerational evaluation of the long-term effect of different doses of fluoride intake through drinking water on lung damage shows that the lung tissues were damaged, there was emphysema and inflammation of lung parenchyma associated with loss of alveolar architecture and the degree of lung damage seemed to correlate with the increased dosage of fluoride. A similar relationship was observed between the degree of lung damage, body and lung weight and</p>	<p>J Appl Toxicol. 23(6):437-46. Nov-Dec. <u>Abstract</u></p>

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		serum fluoride levels according to the fluoride dose."	
2010	Muscle	<p>Shashi A, et al. 2010. Histochemical pattern of gastrocnemius muscle in fluoride toxicity syndrome.</p> <p>"Conclusions: The findings of present study demonstrate that certain concentrations of fluoride can induce muscle lesions and damage DNA, RNA, and protein in muscle cells and excessive intake and accumulation of fluoride is therefore a serious risk factor for muscular abnormalities in fluorosis."</p>	Asian Pacific Journal of Tropical Medicine 3(2):136-140. Feb.
2011	Oxidative Stress	<p>Madusudanan Rao S, et al. 2011. Morphometry of buccal mucosal cells in fluorosis - a new paradigm.</p> <p>"Conclusions: Fluorosis induces oxidative stress, DNA damage and apoptosis which can be the reasons for the increase in the nuclear size and decrease in the cell size."</p>	Hum Exp Toxicol. Mar 15. [Epub ahead of print] Abstract
2010	Oxidative Stress	<p>Liu H, et al. 2010. Fluoride-Induced Oxidative Stress in Three-Dimensional Culture of OS732 Cells and Rats.</p> <p>"The study provided insight into the mechanism of skeletal fluorosis. Also, this study distinguished itself by identifying oxidative stress as a potential modulator of osteogenesis in skeletal fluorosis."</p>	Biol Trace Elem Res. Oct 23. [Epub ahead of print] Abstract
2010	Oxidative Stress	<p>Basha PM, et al. 2010. Evaluation of Fluoride-Induced Oxidative Stress in Rat Brain: A Multigeneration Study.</p> <p>"Results of this study can be taken as an index of neurotoxicity in rats exposed to water fluoridation over several generations."</p>	Biol Trace Elem Res. Jul 24. [Epub ahead of print] Abstract
2010	Oxidative Stress	<p>Kaoud H and Kalifa B. 2010. Effect of Fluoride, Cadmium and Arsenic Intoxication on Brain and Learning-Memory Ability in Rats.</p> <p>"... These results suggest that learning-memory ability and brain function in rats are affected by HiF, HiCd and HiAs and that oxidative stress in the brain may be one of the causes of this</p>	Toxicology Letters 196, suppl. 1 (2010): S53 (abstract from the XII International Congress of Toxicology).

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		damage."	
2009	Oxidative Stress	García-Montalvo EA, et al. 2009. Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress.	Toxicology 263(2-3):75-83. Sept 19. Abstract
2008	Oxidative Stress	Chouhan S, Flora SJ. 2008. Effects of fluoride on the tissue oxidative stress and apoptosis in rats : biochemical assays supported by IR spectroscopy data.	Toxicology 254(1-2):61-7. Dec 5. Abstract
2008	Oxidative Stress	Izquierdo-Vega JA, et al. 2008. Decreased in vitro fertility in male rats exposed to fluoride-induced oxidative stress damage and mitochondrial transmembrane potential loss.	Toxicol Appl Pharmacol. 230(3):352-7. Aug 1. Abstract
2008	Oxidative Stress	Gao Q, Liu Y-J, Guan Z-Z. 2008. Oxidative stress might be a mechanism connected with the decreased alpha 7 nicotinic receptor influenced by high-concentration of fluoride in SH-SY5Y neuroblastoma cells . Corrigendum: "the concentrations of fluoride should have been given as mM, instead of 1M."	Toxicol In Vitro. 22(4):837-43. June. Abstract
2008	Oxidative Stress	Xu H, et al. 2008. Role of oxidative stress in osteoblasts exposed to sodium fluoride.	Biol Trace Elem Res. 123(1-3):109-15. Abstract
2008	Oxidative Stress	Inkielewicz I, Czarnowska W. 2008. Oxidative stress parameters in rats exposed to fluoride and aspirin.	Fluoride 41(1):76-82. Jan-March. Full Report
2007	Oxidative Stress	Jin XQ, et al. 2007. Fluoride-induced oxidative stress of osteoblasts and protective effects of baicalein against fluoride toxicity.	Biol Trace Elem Res. 116(1):81-9. April. Abstract
2007	Oxidative Stress	Jin XQ, et al. 2007. Fluoride-induced oxidative stress of osteoblasts and protective effects of baicalein against fluoride toxicity.	Biol Trace Elem Res. 116(1):81-90. April. Abstract
2007	Oxidative Stress	Bouaziz H, et al. 2007. Oxidative stress induced by fluoride in adult mice and their suckling pups .	Exp Toxicol Pathol. 58(5):339-49. April 26. Abstract
2006	Oxidative Stress	Sarkar S, et al. 2006. Fluoride-induced immunotoxicity in adult male albino rat : a correlative approach to oxidative stress.	J Immunotoxicol. Jul 1;3(2):49-55. Abstract
2009	Pancreas	Ito M, Nakagawa H, Okada T, Miyazaki S,	Arch Toxicol. 83(2):151-9.

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		Matsuo S. 2009. ER-stress caused by accumulated intracisternal granules activates autophagy through a different signal pathway from unfolded protein response in exocrine pancreas cells of rats exposed to fluoride.	February. Abstract
2011	Reproductive	Sun Z, et al. 2011. Fluoride-induced apoptosis and gene expression profiling in mice sperm in vivo .	Arch Toxicol. 2011 Feb 22. [Epub ahead of print] Abstract
2010	Reproductive	Kumar N, et al. 2010. Effect of duration of fluoride exposure on the reproductive system in male rabbits. "CONCLUSION: The present study demonstrates that fluoride hampers the reproductive functions of male rabbits and is proportional to the duration of fluoride exposure."	J Hum Reprod Sci. 3(3):148-52. Sept. Full Article
2010	Reproductive	Hao P, et al. 2010. [Effect of fluoride on human hypothalamus-hypophysis-testis axis hormones].	Wei Sheng Yan Jiu. 39(1):53-5. Jan. [Article in Chinese] Abstract
2008	Reproductive	Izquierdo-Vega JA, et al. 2008. Decreased in vitro fertility in male rats exposed to fluoride-induced oxidative stress damage and mitochondrial transmembrane potential loss.	Toxicol Appl Pharmacol. 230(3):352-7. Aug 1. Abstract
2008	Reproductive	Liu H, et al. 2008. Changes caused by fluoride and lead in energy metabolic enzyme activities in the reproductive system of male offspring rats .	Fluoride 41(3):184-91. July-Sept. Full Article
2008	Reproductive	Dvorakova-Hortova K, et al. 2008. The influence of fluorides on mouse sperm capacitation .	Anim Reprod Sci. 108(1-2):157-70. Oct. Abstract
2008	Reproductive	Huang C, et al. 2008. Effects of sodium fluoride on androgen receptor expression in male mice .	Fluoride 41(1):10-7. Jan-March. Full Article
2007	Reproductive	Huang C, et al. 2007. Toxic effects of sodium fluoride on reproductive function in male mice .	Fluoride 40(3):162-8. July-Sept. Full Report
2007	Reproductive	Gupta RS, et al. 2007. The toxic effects of sodium fluoride on the reproductive system of	Toxicol Ind Health. 23(9):507-13. Oct. Abstract

		male rats.	
2007	Reproductive	Jiang Q, Song XK, Cui QH, Chen LJ. 2007. [Effect of fluoride on expression of telomerase reverse transcriptase expression and proliferating cell nuclear antigen in germ cells of rats' testes]	Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 25(2):96-9. Feb. [Article in Chinese] Abstract
2007	Reproductive	Reddy PS, et al. 2007. Suppression of male reproduction in rats after exposure to sodium fluoride during early stages of development.	Naturwissenschaften 94(7):607-11. July. Abstract
2007	Reproductive	Oncu M, et al. 2007. Effect of long-term fluoride exposure on lipid peroxidation and histology of testes in first- and second-generation rats.	Biol Trace Elem Res. 118(3):260-8. Sept. Abstract
2006	Reproductive	Bataineh HN, Nusierb MK. 2006. Impact of 12-week ingestion of sodium fluoride on aggression, sexual behavior, and fertility in adult male rats.	Fluoride 39(4):293-301. Oct-Dec. Full Report
2006	Reproductive	Li Y, Zhu JY, et al. 2006. [Research in the relation between telomerase reverse transcriptase expression in spermatogenic cells and serum levels of estradiol of fluorotic rats.]	Wei Sheng Yan Jiu. 2006 35(5):546-8. Sept. [Article in Chinese] Abstract
2006	Reproductive	Wan S, et al. 2006. Fluoride-induced changes in the expression of epidermal growth factor and its receptor in testicular tissues of young male rats.	Fluoride 39(2):121-5. April-June. Full Article
2006	Reproductive	Wan SX, et al. 2006. Effects of high fluoride on sperm quality and testicular histology in male rats.	Fluoride 39(1):17-21. Jan-March. Full Article
2006	Reproductive	Sarkar S, et al. 2006. Management of fluoride induced testicular disorders by calcium and vitamin-E co-administration in the albino rat.	Reprod Toxicol. 22(4):606-12. Nov. Abstract
2006	Reproductive	Zhang J, et al. 2006. Effects of sodium fluoride and sulfur dioxide on sperm motility and serum testosterone in male rats.	Fluoride 39(2):126-31. April-June. Full Article
2006	Reproductive	Zhang J, et al. 2006. Changes in testes protein and metabolic enzyme activities in rats induced by sodium fluoride and sulfur dioxide.	Fluoride 39(3):179-84. July-Sept. Full Article

2005	Reproductive	Pushpalatha T, et al. 2005. Exposure to high fluoride concentration in drinking water will affect spermatogenesis and steroidogenesis in male albino rats .	Biomaterials. 18(3):207-12. June. Abstract
2010	Skeletal fluorosis	Choubisa SL, et al. 2010. Osteo-dental fluorosis in relation to age and sex in tribal districts of Rajasthan, India. “... Out of 11205 individuals of Dungarpur and 7416 of Udaipur districts, 8090 (72.1%) and 2914 (39.2%) exhibited evidence of dental fluorosis respectively... Regarding the incidence of skeletal fluorosis, 21 years of age revealed 27.6% in Dungarpur and 12.0% in Udaipur . Whereas 44 years showed maximum incidence of skeletal fluorosis, its minimum incidence was found in the age group of 21-28 years. Severity of fluorosis could be associated with the advancing of age and F concentration. Moreover, males showed relatively a higher incidence of dental and skeletal fluorosis compared to their counterparts... ”	J Environ Sci Eng. 52(3):199-204. July. Abstract
2010	Skeletal fluorosis	Joshi S, et al. 2010. Skeletal fluorosis due to excessive tea and toothpaste consumption .	Osteoporos Int. Oct 9. [Epub ahead of print] Abstract
2010	Skeletal fluorosis	Liu H, et al. 2010. Fluoride-Induced Oxidative Stress in Three-Dimensional Culture of OS732 Cells and Rats . "The study provided insight into the mechanism of skeletal fluorosis. Also, this study distinguished itself by identifying oxidative stress as a potential modulator of osteogenesis in skeletal fluorosis ."	Biol Trace Elem Res. Oct 23. [Epub ahead of print] Abstract
2008	Skeletal fluorosis	Buchancová J, et al. 2008. Skeletal fluorosis from the point of view of an occupational exposure to fluorides in former Czechoslovakia. "... The authors demonstrate cases of occupational skeletal fluorosis (currently rare in Europe) in 14 metallurgists which were all disclosed in [aluminum] foundry workers in Žiar nad Hronom as to the year 2005. The occupational disease was diagnosed after 17.7 ± 7.67 years (x±SD) of exposure in the foundry.	Interdiscip Toxicol. Sep;1(2):193-7. Full Report

		The authors describe the clinical conditions, haematological and biochemical tests (decreased level of ionising calcium was found in serum). The content of fluorides in urine was increased ($254.4 \pm 130.95 \mu\text{mol/l}$). The average age of patients at the time of recognition of the professional etiology of the disease was 57.93 ± 7.95 years..."	
2008	Skeletal Fluorosis	Srikanth R, et al. 2008. Endemic fluorosis in five villages of the Palamau district, Jharkhand, India. "A level of 2.5 mg F/L was found to be a critical threshold for manifestations of crippling skeletal fluorosis."	Fluoride 41(3):206-11. July-Sept. Full Article
2008	Skeletal Fluorosis	Shashi A, et al. 2008. Incidence of skeletal deformities in endemic fluorosis.	Trop Doct. 38(4):231-3. Oct. Abstract
2008	Skeletal Fluorosis	Younes M, et al. 2008. [Cervical myelopathy revealing bone fluorosis].	Rev Neurol (Paris) 164(2):185-8. Feb. Abstract
2007	Skeletal Fluorosis	Li W, et al. 2007. Quantification of rib COL1A2 gene expression in healthy and fluorosed Inner Mongolia cashmere goats.	Fluoride 40(1):13-8. Jan-March. Full Article
2007	Skeletal Fluorosis	Gupta RC, et al. 2007. Skeletal fluorosis mimicking seronegative arthritis.	Scandinavian Journal of Rheumatology, 36:2:154-5.
2005	Skeletal Fluorosis	Heikens A, et al. 2005. The impact of the hyperacid Ijen Crater Lake: risks of excess fluoride to human health. "Based on the total daily intake, the lowest F concentration in drinking water that poses a risk of developing fluorosis is approximately 0.5 mg/l for dental fluorosis and 1.1 mg/l for skeletal fluorosis."	Sci Total Environ. 346(1-3):56-69. June 15. Abstract
2005	Skeletal Fluorosis	Bharati P, et al. 2005. Clinical symptoms of dental and skeletal fluorosis in Gadag and Bagalkot Districts of Karnataka.	J. Hum. Ecol., 18(2):105-7.
2005	Teratogen	Krupanidhi S, Cherry KN. 2005. Teratogenicity due to fluoride.	FASEB J. 19(4):A58. March.
2008	Teratogen	Wu N, et al. 2008. Behavioral teratology in	Fluoride 41(2):129-33.

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		rats exposed to fluoride. "...differences in motor coordination, auditory reaction, pain sensitivity, and other cognitive responses, some statistically significant, varying with time and F exposure, were noted, especially among the pups in the 25 mg/L group. Brain slices in the 25 mg/L group also showed a significantly lower average cerebral cortex thickness than in the control group (10.97 μm vs. 11.70 μm).]"	April-June. Full Article
2011	Thyroid	Karademir S, et al. 2011. Effects of fluorosis on QT dispersion, heart rate variability and echocardiographic parameters in children - Original Investigation. "... We found statistically significant low T4 levels, hypocalcemia and hyponatremia , increased QT and QTc interval in children with dental fluorosis. Our results show that fluorosis might increase risk of arrhythmia indirectly, due to its hypocalcemic, hypernatremic, and hypothyroidism effects... Further studies concerning cardiovascular effect of fluorosis in both adults and children are needed."	Anadolu Kardiyol Derg. 11(2):150-5. Full Report
2010	Thyroid / Parathyroid	Koroglu BK, et al. 2010. Serum Parathyroid Hormone Levels in Chronic Endemic Fluorosis. "The results of our study demonstrate that serum PTH levels are increased in patients with endemic fluorosis. Fluoride, by interfering calcium balance, may be the cause of secondary hyperparathyroidism. "	Biol Trace Elem Res. Sep 14. [Epub ahead of print]. Abstract
2009	Thyroid	Wang H, et al. 2009. Fluoride-induced thyroid dysfunction in rats : roles of dietary protein and calcium level.	Toxicol Ind Health. 25(1):49-57. Feb. Abstract
2009	Thyroid	Zhan X, et al. 2006. Effects of fluoride on growth and thyroid function in young pigs .	Fluoride 39(2):95-100. April-June. Full Article
2009	Thyroid	Wang J, et al. 2009. Chapter 67 - DNA Damage in Brain and Thyroid Gland Cells due to High Fluoride and Low Iodine .	Comprehensive Handbook of Iodine, Pages 643-649. Edited by: Victor R. Preedy, Gerard N. Burrow and Ronald Watson. ISBN: 978-0-12-374135-6. Elsevier

			Inc.
2008	Thyroid / Parathyroid	Sharifian A, et al. 2008. Serum calcium and parathyroid hormone levels in aluminum potroom workers exposed to fluoride emissions.	Fluoride 41(4):314- 6. Oct-Dec. Full Article
2005	Thyroid	Bouaziz H, et al. 2005. Fluoride-induced thyroid proliferative changes and their reversal in female mice and their pups .	Fluoride 38(3):185-92. Full Article
2005	Thyroid	Gas'kov Alu, et al. 2005. [The specific features of the development of iodine deficiencies in children living under environmental pollution with fluorine compounds]	Gig Sanit. Nov-Dec;(6):53-5. Full Article - English Translation
2005	Thyroid	Ge Y, et al. 2005. DNA damage in thyroid gland cells of rats exposed to long-term intake of high fluoride and low iodine.	Fluoride 38(4):318-23. Nov. Full Article
2005	Thyroid	Ruiz-Payan A, et al. 2005. Chronic effects of fluoride on growth, blood chemistry, and thyroid hormones in adolescents residing in northern Mexico. Paper presented at the XXVIth Conference of the International Society for Fluoride Research (September 26-29).	Fluoride 38(3):246. Full Article (see Abstract Number 37)

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<http://www.ncbi.nlm.nih.gov/pubmed/19508423>

Sohn W, et al. 2009. Fluoride ingestion is related to fluid consumption patterns. J Public Health Dent. 2069(4):267-75. Fall.

"There was substantial variation in the estimated amount of fluoride ingestion depending on the children's fluid consumption patterns as well as age, gender, and race/ethnicity. African-American children ingested significantly more fluoride than White children in bivariate analysis. This association remained significant after accounting for fluid consumption pattern and other confounding factors in the model.

CONCLUSION: Our results raise concerns that some children are ingesting significantly more fluoride than others depending on sociodemographic factors and fluid consumption patterns. Additional research is

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warranted to investigate the variation in the amounts of fluoride ingestion by these factors and its impact on fluorosis prevalence in different population groups.