Fluoride doped hydroxyapatite in soft tissues and cancer. A literature review.

TECHNICAL REPORT · FEBRUARY 2015

READS
53

1 AUTHOR:

Geoff Pain

119 PUBLICATIONS **787** CITATIONS

SEE PROFILE

Fluoride doped Hydroxyapatite in Soft Tissues and Cancer – A Literature Review

Geoff Pain

October 2015

Abstract

Inorganic Fluorides are potent bio-accumulative poisons with no nutritional value and there is abundant evidence from the published literature that they are genotoxic carcinogens affecting numerous organs. Fluoride interferes with the tumour suppression by Melatonin. Fluoride will increase the deposition of Hydroxyapatite crystals in the tissues and these crystals accelerate malignant cancer growth.

Keywords: Bone, Brain, Breast, Cancer, Cervix, Clastogen, Colon, DNA Damage, Endocrine Disruptor, Fluoride, Fluoridation, Genotoxin, Hydroxyapatite, IGF, Kidney, Liver, Lung, Melanoma, Melatonin, Micronuclei, Oral, Pituitary adenoma, Pharynx, Prostate, Rectum, Stomach, Thyroid, Uterus

Introduction

Fluorides are so highly toxic that a single truckload of the industrial waste from the phosphate fertilizer industry, used to fluoridate public drinking water, is sufficient to kill the whole Australian populace outright. The largest recorded knock down of humans, animals and crops by Fluoride was the eruption of Lakagígar in Iceland over an eight-month period between 1783 and 1784, where a mixture of Hydrogen Fluoride and Sulfur Dioxide is estimated to have claimed up to 6 million lives directly or indirectly (through starvation due to loss of livestock and crops) in the Northern Hemisphere [Wikipedia 2015].

Humans and farm animals have not evolved to deal with Fluoride intoxication as have some other organisms [Li 2013] and recent studies have shown how the cells of these organisms can eject the toxin through specific ion channels [Stockbridge 2015]. It is a general rule that such highly toxic elements are carcinogenic and this review looks at the evidence that has been published with an emphasis on more recent findings.

The literature found on Fluoride includes descriptive terms including:

- Cytotoxin
- Clastogen
- Mitogen
- Genotoxin
- Carcinogen
- Mutagen
- Low-dose Endocrine Disruptor

Weight of Evidence for Fluoride as a Carcinogen

In order to assess the plausibility of inorganic Fluoride compounds as carcinogens, it is necessary to study Fluoride toxicology details at all levels:

Molecular – how does Fluoride act on your hormones, enzymes, DNA, RNA?

Organelle – e.g. how are mitochondria affected by Fluoride?

Cellular – How do cells transport, metabolize and eject Fluoride, *in vivo* and *in vitro*?

Organ – How are organs damaged by Fluoride?

Animal studies – Essential to measure chronic disease, death.

Case studies – Individual exposure, acute and chronic, genetic sensitivity, vulnerability

Clinical trials – adverse outcomes, side effects

Bioaccumulation – Autopsies and detailed examination of tumours

Epidemiology – Correlations and associations, hints of causes, time progression and industrial exposure.

The literature on Fluoride toxicology is a huge resource, growing at about 500 peer-reviewed papers per year. Therefore this brief review is intended as a pointer for those interested to read in detail the output of the hundreds of scientists who have addressed the cancer associations using one or more of the above approaches.

Excellent reviews of Fluoride Toxicology and Fluoridation with reference to cancer are available [Bryson 2004, Burk 1977, Cohn 1992, Connett 2010, Doull 2006, Hirzy 2013, Ozsvath 2009, Prystupa 2001, Thiessen 2011, 2014, Waugh 2014, Yiamouyiannis 1977, 1993].

The greatest and most easily accessed source is the online encyclopaedia established by the Fluoride Action Network and readers are encouraged to use the search function there for in-depth discussion of material summarized here [www.fluoridealert.org].

An important variable in all cancer studies, often not determined, is total dietary intake of Fluoride, with tea and toothpaste as major contributors.

A significant exposure route, often overlooked, is the direct absorption of Fluoride through the oral cavity tissues, i.e. it is not necessary to swallow toothpaste or mouth rinse to be poisoned.

A mortality and malignant neoplasm analysis found no significant increase due to fluoridation [Erickson 1978].

More recently an analysis of cancer incidence rates and water fluoridation status of 21.8 million Americans found Fluoridated drinking water was positively associated with cancer of oral cavity and pharynx, colon, rectum, hepato-biliary and urinary organs [Takahashi 2001]. Further details of this important study will be mentioned in the following description of literature found for each organ.

DNA Damage by Fluoride

Recent studies have revealed great genetic differences in the ability of organisms to excrete fluoride, making comparison of genotoxic tests at different concentrations of this toxin difficult [Crespi 1990, Rivedal 2000, Li 2013, Stockbridge 2015]. Ape and human cells show greater susceptibility to Fluoride's mutagenic effects than rodent cells [Kishi 1993, Manivanan 2012].

Extensive *in vivo* and *in vitro* studies of DNA damage by Fluoride are available [Tazhibaev 1977, Pati 1987, Jones 1988, Lasne 1988, Suzuki 1989, NAS 1993, Oguro 1995, Wu 1995, Gadhia 1997, Erciyas 2009, Flora 2012].

Some evidence that Stannous Fluoride is mutagenic was found as early as 1976 [Gocke 1981].

Fluoride increases the frequency of mutations at the thymidine kinase locus in cultured mouse lymphoma and human lymphoblastoid cells [Caspary 1987, Cole 1986, Crespi 1990]. A significant increase in micronucleated polychromatic erythrocytes was observed [Suzuki 1991].

Fluoride was found to be clastogenic to cultured human diploid cell (IMR-90) [Hayashi 1993, Oguro 1995]. Increased sister-chromatid exchange is observed in high fluoride exposed human communities [Sheth 1994, Wu 1995, Meng 1995, Meng 1997, Lazutka 1999, Joseph 2000].

Significant increases in the frequencies of chromosome aberrations were induced by Fluoride in cultured rat vertebral cells [Mihashi 1996]. Even at low doses, chromosome aberrations were observed in cultured rat bone marrow cells treated with fluorides [Khalil 1995]. DNA damage, apoptosis and cell cycle changes are induced by fluoride in rat oral mucosal cells and hepatocytes [He 2006].

Mechanisms for DNA damage by Fluoride have been discussed [Aardema 1989, Aardema 1995].

Studies using human cell lines *in vitro* are available [Lestari 2005, Zhang 2009].

Fluoride and Insulin-like Growth Factor

Fluoride treatment increases serum insulin-like growth factor IGF-1 [McClintock 1997].

Recombinant human insulin-like growth factor (IGF) binding protein-3 has been found to stimulate prostate carcinoma cell proliferation via an IGF-dependent mechanism [Angelloz-Licoud 1996].

Fluoride and Melatonin Suppression

Melatonin, produced in the Pineal Gland and many other organs, maintains the circadian rhythm, is protective against oxidative stress by scavenging free radicals, binds Calmodulin and blocks activation of oestrogen receptor-alpha [Kearney 2015]. It has been shown to suppress tumor growth in cancers of the bone [Koyama 2002], the breast [Blask 1988, Lenoir 2005] and liver [Rahman 2003].

Melatonin inhibition of cancer growth *in vivo* involves suppression of tumor fatty acid metabolism via melatonin receptor mediated signal transduction [Blask 1999].

Melatonin has been found to be an endogenous-specific inhibitor of estrogen receptor via Calmodulin [del Río 2004].

Melatonin has been found to reduce fluoride-induced genotoxicity in human peripheral blood lymphocyte cells [Rao 2006, Rao 2013, Thakur 2014].

Fluoride is bio-accumulative in the Pineal Gland via calcification with formation of Fluoride doped Hydroxyapatite $Ca_3(PO_4)_2 \cdot Ca(OH,F)_2$ [Luke 1998]. Evidence suggests that this calcification by Fluoride reduces Melatonin production with age, thereby increasing malignant cancer growth [NRC 2006].

Bladder Cancer

The bladder is one of the organs exposed to high Fluoride concentrations as the human body ejects most of the toxin via the kidneys in urine.

Significantly higher rate of bladder cancer was found in fluoridated communities [Takahashi 2001, Yang 2000].

Industrial exposure to airborne Fluoride is associated with elevated bladder cancer rates [Romunstad 1999, 2000, Grandjean 2004]. The Republic of Ireland (fluoridated) has a higher incidence of bladder cancer than Northern Ireland (not fluoridated) [Waugh 2014].

Bone Cancer

The association between Fluoride and the relatively rare bone cancers (including Ewing sarcoma and osteosarcoma) has received considerable study, perhaps because of the obvious unwanted damaging cell proliferation that results in dental fluorosis [Wergedal 1988, Mahoney 1991, Cohn 1992, Lee 1993, Comber 1995, Khalil 1995, Rao 1995, Hsu 1999, Takahashi 1999, Ramesh 2001, Koyama 2002, Zhang 2006, Eyre 2009, Ottaviani 2009, Mirabello 2009 and 2011, Podder 2011, Sandhu 2011, Pathi 2011, Kharb 2012, Levy 2012, Huo 2013, Blakey 2014, Loder 2015].

Fluoride causes osteoblast proliferation and malignant transformation [Wergedal 1988, Zhang 2006].

A very useful set of articles on Fluoride and bone cancer is available [Lee 1993 and others]. Problems identified with this rare cancer include reclassification of body sites to cell types in the 1970s, making it impossible to compare some sets of incidence statistics.

A dose-dependent increase of osteosarcoma was seen in the bones of fluoride-treated male rats [NTP 1990] and mice [Maurer 1990]. Significantly higher rate of bone cancer was found for males in fluoridated communities [Yiamouyiannis 1993, Takahashi 2001]. Increased osteosarcoma in young males was reported in fluoridated areas [Bassin 2001, 2006]. The sex-dependent variability was also examined and 15-19 year-old males were at higher risk to osteosarcoma than females in the same age group ($p<0.001$) but no association with water fluoridation status was found [Levy 2012]. Dietary Fluoride intake was not examined.

A study of osteosarcoma and Ewing sarcoma found that both are more prevalent in males, but did not find evidence of increased rates in fluoridated areas [Blakey 2014]. The authors point out the difficulties of dealing with such rare cancers and the lack of information on total dietary intake of Fluoride and the widespread use of fluoridated toothpaste over the study period of 1980 to 2005.

A significant association between Fluoride in drinking water and osteosarcoma was found [Kharb 2012, Sandhu 2011]. Examination of osteosarcomas found no significant elevation of Fluoride within

the tumours [Kim 2011], suggesting that Fluoride simply initiates the cancer. A study based on only 130 subjects claimed to have found a protective effect of Fluoride against osteosarcoma [Gelberg 1995]. Difficulty with small numbers of cases was also found in Ireland [Comber 2011].

Induction of apoptosis by sodium fluorosilicate has been demonstrated in human osteogenic sarcoma [Song 2005].

Many of the studies of bone cancers do not mention exposure to bone-seeking radionuclides which are known contaminants in the industrial fluoride waste used to fluoridate water.

Brain and Pituitary Gland Cancer

Significantly higher rate of brain cancer was found in fluoridated US communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of central nervous system cancer than Northern Ireland (not fluoridated) [Waugh 2014].

Fluoride impact via DNA damage, S-phase cell-cycle arrest and the expression of NF-kappaB in primary cultured rat hippocampal neurons has been studied [Zhang 2008]. Sodium Fluoride induction of stress response and differential expression of 70 kDa stress proteins in HeLa and rat brain tumor 9L cells has been reported [Cheng 1998].

Various agents have been investigated to ameliorate brain damage by Fluoride [Pal 2014].

Anecdotal evidence of increased brain cancer from industrial Fluoride exposure requires further investigation [Gasser 2011].

A cluster of pituitary adenomas in workers in the aluminum industry exposed to Fluoride has been reported [Cullen 1996].

Breast Cancer

Breast cancer is the second leading cause of cancer death among women, causing almost 40,000 deaths in USA in 2011.

It is an open question to determine how human mothers largely succeed in preventing delivery of toxic Fluoride to their babies through breast milk, given that the placenta provides no barrier. One probable explanation is bio-accumulation of Fluoride in breast tissue in the form of Fluoride doped Hydroxyapatite. The deposition of Hydroxyapatite in abnormal locations has been recognized as a major health issue for some time [Garcia 2003].

One significant feature of breast cancer diagnosis is the presence of calcium deposits (averaging 0.3 mm^3 in size) detected via mammograms [Castronovo 1998, Cooke 2003].

Both Calcium Oxalate and Calcium Hydroxyapatite have been detected in breast tissue, however only the Hydroxyapatite is associated with malignancy [Wilson 2014].

Calcium Hydroxyapatite promotes mitogenesis and matrix metalloproteinase expression in human breast cancer cell lines [Morgan 2001, 2005].

A significant study followed up 61,433 women who were cancer free at baseline in 1987-1990.

Over a mean follow-up of 17.4 years, there were 2,952 incident cases of invasive breast cancer identified. Coffee consumption was not associated with risk of overall breast cancer (multivariate relative risk (RR) for ≥ 4 cups/day versus <1 cup/day = 1.02; 95% CI, 0.87-1.20) or with any subtype defined by ER and PR status. Black tea (containing large amounts of Fluoride) consumption was significantly positively associated with risk of overall breast cancer (RR 1.22 95% CI 1.05-1.40) and ER+/PR+ tumors (RR 1.36 95%CI 1.09-1.69) [Larsson 2009].

A recent meta-analysis of prospective studies involving over 3 million subjects and 49,000 cancer cases also found an increased risk of breast cancer associated with drinking 3 cups or more of black tea (RR 1.18 95%CI 1.05 -1.32) [Yu 2014].

Humoral bone morphogenetic protein 2 (BMP2) has been shown to induce breast cancer microcalcification [Liu 2008]. BMP expression has been shown to be increased by Fluoride [Huo 2013].

Hydroxyapatite enhances the mitogenesis of mammary cells, amplifying the malignant process and resulting in accelerated tumor growth [Wilson 2014]. Synthetic Hydroxyapatite nanoparticle-containing scaffolds have been used to study induction of breast cancer bone metastasis [Pathi 2011].

Due to rapid surface substitution of hydroxyl groups of Hydroxyapatite by Fluoride under mild conditions, breast cancer diagnosis has been demonstrated via PET imaging of microcalcifications caused Fluoride by using radioactive 18F-NaF [Wilson 2014].

Extracellular calcium has been shown to promote the migration of breast cancer cells through the activation of the calcium sensing receptor [Saidak 2009].

Melatonin suppression of breast cancer has been studied [Lenoir 2005] and as mentioned above, Fluoride suppression of Melatonin will increase breast cancer incidence.

Cervical and Endometrial Cancer

Factors involved in cervical and endometrial cancer include calcium uptake, Vitamin D and hypoxia [McCullough 2008, Moreno-Merlo 1999]. The Republic of Ireland (fluoridated) has a higher incidence of cervical cancer than Northern Ireland (not fluoridated) [Waugh 2014].

Colon and Rectum Cancer

Significantly higher rate of colon and rectum cancer was found in fluoridated communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of colon cancer than Northern Ireland (not fluoridated) [Waugh 2014]. High tea consumption (i.e. high Fluoride intake) showed increased risk of colorectal cancer (RR 1.28 95% CI 1.02-1.61) [Zhang 2010].

Oesophagus Cancer

Significantly higher rate of oesophagus cancer was found in fluoridated communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of oesophagus cancer than Northern Ireland (not fluoridated) [Waugh 2014]. Generation of HF gas in the stomach is a likely contributor to increase incidence of this cancer.

Gallbladder Cancer

Significantly higher rate of gallbladder cancer was found for males in fluoridated communities [Takahashi 2001].

Hodgkin's Disease

Significantly higher rate of Hodgkin's Disease was found in fluoridated communities [Takahashi 2001].

Kidney Cancer

Significantly higher rate of kidney cancer was found for females in fluoridated communities [Takahashi 2001].

Leukaemia

Significantly higher rate of monocytic Leukaemia was found for males in fluoridated US communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of Leukaemia than Northern Ireland (not fluoridated) [Waugh 2014].

Liver Cancer

An increased risk of liver cancer mortality was observed as a function of fluoride concentration in drinking water Okinawa [Tohyama 1995].

Significantly higher rate of liver cancer was found in fluoridated US communities [Takahashi 2001].

DNA damage, apoptosis and cell cycle changes are induced by fluoride in rat hepatocytes [He 2006].

Significant differences in enzyme systems were observed in liver cancer samples and the ability to metabolize fluorocarbons [Chen 1997].

Fluoride has been shown to cause lipid peroxidation, DNA damage, and apoptosis in the human embryo hepatocyte L-02 cell experimental model [Wang 2004].

Human HepG2 cell (perpetual liver cell) DNA damage by Sodium Fluoride (NaF) has been confirmed [Zhang 2009].

Researchers have investigated Melatonin in treatments that seek to ameliorate liver cancer induction [Rahman 2003]. As discussed in the present article, Melatonin, a natural cancer defence mechanism, is depressed Fluoride.

Lung Cancer

Elevated lung cancer was reported for fluorspar miners [Parsons 1964]. Significantly higher rate of lung cancer was found for males in fluoridated communities [Takahashi 2001]. It has been suggested that the Fluoride in cigarette smoke might contribute to lung cancer [Sutton 1986].

Hydrogen Fluoride gas is generated in the stomach and can readily be absorbed into the blood. However there is little recognition in the literature that the HF gas can readily travel through the

airways, destroying tissue wherever it lands. Repeated tissue damage by acid or alkali is a known cause of cancer.

Lymphoma

Significantly higher rate of Non-Hodgkin lymphoma was found for females in fluoridated communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of Non-Hodgkin lymphoma than Northern Ireland (not fluoridated) and the highest incidence of all 27 EU members [Waugh 2014].

Myeloma

Significantly higher rate of multiple myeloma was found for women in fluoridated communities [Takahashi 2001]. Chromosome aberrations were observed in cultured rat bone marrow cells treated with inorganic fluorides [Khalil 1995].

Nasal and Sinus Cancer

Significantly higher rate of nose and sinus cancer was found for males in fluoridated communities [Takahashi 2001]. Everyone using fluoridated water for showers, garden irrigation or cleaning inhales an aerosol of the toxin. In hot communities, some of the aerosol will evaporate to produce Fluoride nanoparticles that will penetrate to the deepest airways.

Oral Cavity Cancer

Significantly higher rate of larynx, mouth, hypopharynx, nasopharynx, oropharynx and tongue cancer was found in fluoridated communities [Takahashi 2001]. DNA damage, apoptosis and cell cycle changes are induced by fluoride in rat oral mucosal cells [He 2006]. Genotoxic oral damage by Fluoride was observed in human volunteers [Vazquez-Alvarado 2012].

Ovarian Cancer

Significantly higher rate of ovarian cancer was found in fluoridated communities [Takahashi 2001]. This was thought to possibly be associated with the increased levels of gonadotropin, also seen due to Fluoride intoxication of cryolite workers [Tokar 1977]. Further evidence is the observation that gonadotropin down-regulates Estrogen receptor-β so that the ratio of Estrogen receptor-α/ Estrogen receptor-β mRNA ratio is altered [Beyers 1997]. A high Estrogen receptor-α/ Estrogen receptor-β mRNA ratio is associated with increase ovarian cancer malignancy [Pujol 1998].

Pancreatic Cancer

Significantly higher rate of pancreas cancer was found in fluoridated communities [Takahashi 2001]. The Republic of Ireland (fluoridated) has a higher incidence of pancreas cancer than Northern Ireland (not fluoridated) [Waugh 2014].

Prostate Cancer

Data for 1978-1982 found lower rate of prostate cancer in fluoridated communities [Takahashi 2001]. This was thought to be possibly associated with the depression of testosterone by Fluoride.

However increased hypoxia correlates with increased expression of the angiogenesis marker vascular endothelial growth factor in human prostate cancer [Cvetkovic 2001, Movsas 2000].

The Republic of Ireland (fluoridated) has a higher incidence of prostate cancer than Northern Ireland (not fluoridated) [Waugh 2014]. Low teas consumption showed no elevated risk [Ellison 2000], however evidence of a dose-response increase of prostate cancer with high tea consumption (i.e. high Fluoride intake) has been found in meta-analysis [Yu 2014, Figure 7].

Skin Cancer

Melanotic tumours were found in test species exposed to Fluoride in 1963 [Herskowitz]. Significantly lower rate of lip cancer and melanoma was found in fluoridated communities [Takahashi 2001].

Stomach Cancer

Surface changes in rat gastric mucosa are induced by Sodium Fluoride [Easmann, Pashley 1984]. Human volunteers suffered terrible damage to their stomach on ingestion of a single dose of Fluoride with the lesions taking weeks to heal [Spak 1989].

Testicular Cancer and Progesterone Synthesis

The expression of steroidogenic acute regulatory protein (StAR) mRNA and cytochrome P450 cholesterol side-chain cleavage enzyme (P450scc) mRNA is suppressed in Leydig cells [Guan 2012].

Thyroid Cancer

Significantly lower rate of thyroid cancer was found in fluoridated communities [Takahashi 2001]. Fluoride induces thyroid cell apoptosis [Liu 2014].

Uterus Cancer

An increased risk of uterine cancer mortality was observed as a function of fluoride concentration in drinking water Okinawa [Tohyama 1996].

Conclusion

Fluoride is genotoxic and causes cancer via a number of mechanisms. Fluoride directly damages DNA, affects levels of IGF and related proteins and suppresses Melatonin. Precipitates of Fluoride doped Hydroxyapatite crystals in various organs have been demonstrated to increase malignancy.

Two fundamental principles must apply:

1] The Precautionary Principle

2] The medical ethic of “Do No Harm”

Consumers should be made aware of the high Fluoride content of tea and associated increased cancer risk.

Given the overwhelming weight of evidence, continued deliberate exposure of the human population to Fluoride via fluoridation is criminal negligence.

Selected References

Those marked * were deliberately excluded from the 2007 NHMRC review

Aardema, M.J., Gibson, D.P. and R.A. LeBoeuf. 1989. Sodium fluoride-induced chromosome aberrations in different stages of the cell cycle: A proposed mechanism. Mutation Research 223, 191-203.

Aardema, M.J. and T. Tsutsui. 1995. Sodium fluoride-induced chromosome aberrations in different cell cycle stages. Mutation Research 331, 171-172

Albanese, R. 1987. Sodium fluoride and chromosome damage (in vitro human lymphocyte and in vivo micronucleus assays). Mutagenesis 2, 497-9.

Angelloz-Nicoud, P., Harel, L. and Binoux, M. 1996. Recombinant human insulin-like growth factor (IGF) binding protein-3 stimulates prostate carcinoma cell proliferation via an IGF-dependent mechanism. Role of serine proteases. Growth Regulation, 6(3) 130-136 *

Bassin, E.B. 2001. Association between fluoride in drinking water during growth and development and the incidence of osteosarcoma for children and adolescents. D.M.S. Thesis, Harvard School of Dental Medicine, Boston, Massachusetts

Bassin, E.B., Wypij, D., Davis, R.B. and Mittleman, M.A. 2006. Age-specific fluoride exposure in drinking water and osteosarcoma (United States). Cancer Causes and Control 17(4) 421-8.

Begley, S. 2005. Fluoridation, cancer: did researchers ask the right questions? Wall Street Journal (Eastern ed.) p. B1. *

Blakey, K., Feltbower, R.G., Parslow, R.C., James, P.W., Gómez Pozo, B., Stiller, C., Vincent, T.J., Norman, P., McKinney P.A., Murphy M.F., Craft A.W., McNally R.J. 2014. Is fluoride a risk factor for bone cancer? Small area analysis of osteosarcoma and Ewing sarcoma diagnosed among 0-49-year-olds in Great Britain, 1980-2005. International Journal of Epidemiology 43(1) 224-234

Blask, D.E., Sauer, L.A. Dauchy, R.T., Holowachuk, E.W., Ruhoff, M.S. and H.S. Kopff. 1999. Melatonin Inhibition of Cancer Growth in Vivo Involves Suppression of Tumor Fatty Acid Metabolism via Melatonin Receptor-mediated Signal Transduction Events Cancer Research 59, 4693–4701

Blask, D.E., Hill, S.M., Pelletier, D.B. 1988. Oncostatic signaling by the pineal gland and melatonin in the control of breast cancer. In: Gupta D, Attanasio A, Reiter RJ (eds.) The Pineal Gland and Cancer. Brain Research Promotion, London, UK, pp. 195–206.

Bonavita, J.A., Dalinka, M.K. and H.R. Schumacher, Jr. 1980. Hydroxyapatite deposition disease Radiology 134(3) 621-625

Bryson, C. 2004. The Fluoride Deception. New York: Seven Stories Press; paperback edition, 2006.

Burgstahler, A.W., Freeman, R.F., Jacobs, P.N. 2008. Toxic effects of silicofluoridated water in chinchillas, caimans, alligators, and rats held in captivity Fluoride 41(1) 83-88

Burk, D. and Yiamouyiannis, J. 1977. Fluoridation and Cancer: Age Dependence of Cancer Mortality Related to Artificial Fluoridation, 10 Fluoride 123

Burk, D. et al. 1988. A Current Restatement and Continuing Reappraisal Concerning Demographic Variables in American Time-Trend Studies on Water Fluoridation and Human Cancer, 61 Proc. Pa. Acad. of Sci. 138

Byers, M., Kuiper, G.J., Gustafsson, J.A., and Park-sarge, O.K. 1997. Estrogen receptor-α mRNA Expression in rat ovary: down-regulation by gonadotropins. Mol. Endocrinol. 11, 172-182

Campbell-Thompson, M., Lynch, I.J. and Bhardwaj, B. 2001. Cancer Res. 61, 632–640

Cantor, K.P. 1997. Drinking water and cancer. Cancer Causes and Control, 8(3) 292-308. *

Caspary, W.J., Myhr, B., Bowers, L., McGregor, D., Riach, C., Brown, A. 1987. Mutagenic activity of fluorides in mouse lymphoma cells. Mutation Research 187, 165-80.

Castronovo, V., Bellahcene, A. 1998. Evidence that breast cancer associated microcalcifications are mineralized malignant cells. Int J Oncol. 12(2) 305-8

Chang, C.Y., P.H. Phillips, E.B. Hart, and G. Bonstedt. 1934. The effect of feeding raw rock phosphate on the fluorine content of the organs and tissues of dairy cows. J Dairy Sci 17, 695-700 (as cited in Galletti and Joyet 1958).

Chen, T.L., Hou, W.Y., Sun, W.Z., Wu, G.J., Wang, K.C., Peng, W.L., and Lin, C.J. 1997. Metabolic characteristics and enflurane defluorination of cytochrome P450-dependent monooxygenases in human hepatocellular carcinoma, Acta Anaesthesiologica Sinica, 35(1) 7-14. *

Cheng, T.J., Chen, T.M., Chen, C.H., and Lai, Y.K. 1998. Induction of stress response and differential expression of 70 kDa stress proteins by sodium fluoride in HeLa and rat brain tumor 9L cells. Journal of Cellular Biochemistry, 69, (2) 221-231. *

Cohn, P.D. 1992. An Epidemiologic Report on Drinking Water and Fluoridation. New Jersey Department of Health, Trenton, NJ.

Cohn, P.D. 1992. A Brief Report on the Association of Drinking Water Fluoridation and the Incidence of Osteosarcoma among Young Males. New Jersey Department of Health, November 8, 1992.

Cole, J., Muuriel, W.J., Bridges, B.A. 1986. The mutagenicity of sodium fluoride to L5178Y [wild-type and TK+/- (3.7.2c)] mouse lymphoma cells. Mutagenesis 1, 157-167

Comber, H., Deady, S., Montgomery, E., Gavin, A. 2011. Drinking water fluoridation and osteosarcoma incidence on the island of Ireland. Cancer Causes Control. 22(6) 919-24

Connett, P.H., Beck, J. and H.S. Micklem. 2010. The Case against Fluoride. How Hazardous Waste ended up in our drinking water and the Bad Science and Powerful Politics keeps it there. Chelsea Green Publishing Company, White River Junction, Vermont USA

Connett, P.H. 2009. A Critique of the York Review (Fluoridation of Drinking Water: a Systematic Review of its Efficacy and Safety by the NHS Centre for Reviews and Dissemination, the University of York, York, UK)

Cook-Mozaffari, P. 1996. Cancer and fluoridation, Community Dental Health, 13 Suppl 2, 56-62. *

Cooke, M.M., McCarthy, G.M., Sallis, J.D., Morgan, M.P. 2003. Phosphocitrate inhibits calcium hydroxyapatite induced mitogenesis and upregulation of matrix metalloproteinase-1, interleukin-1beta and cyclooxygenase-2 mRNA in human breast cancer cell lines. Breast Cancer Res Treat. 79(2) 253-63

Crespi, C., Seixas, G., Turner, T., Penman, B. 1990. Sodium fluoride is a less efficient human cell mutagen at low concentrations. Environ Mol Mutagen 15, 71-77.

Cullen, M.R., Checkoway, H. and Alexander, B.H. 1996. Investigation of a cluster of pituitary adenomas in workers in the aluminum industry, Occupational and Environmental Medicine, 53(11) 782-786 *

Cvetkovic, D., Movsas, B., Dicker, A. P., Hanlon, A. L., Greenberg, R. E., Chapman, J. D., Hanks, G. E., and Tricoli, J. V. 2001. Increased hypoxia correlates with increased expression of the angiogenesis marker vascular endothelial growth factor in human prostate cancer, Urology, 57(4) 821-825. *

del Río, B., Pedrero, J.M.G., Martínez-Campa, C., Zuazua, P., Lazo, P.S. and S. Ramos. 2004. Melatonin, an Endogenous-specific Inhibitor of Estrogen Receptor via Calmodulin J. Biol. Chem., 279 (37) 38294-38302

Doull, J., Boekelheide, K., Farishian, B.G., Isaacson, R.L., Klotz, J.B., Kumar, J.V., Limeback, H., Poole, C., Puzas, J.E., Reed, N-M.R., Thiessen, K.M., Webster, T.F. National Research Council (NRC) 2006. Committee on Fluoride in Drinking Water Board on Environmental Studies and Toxicology Division on Earth and Life Studies. Fluoride in Drinking Water: A Scientific Review of EPA's Standards

Easmann, R.P., Steflik, D.E., Pashley, D.H., McKinney, R.V., Whitford, G.M. 1984. Surface changes in rat gastric mucosa induced by sodium fluoride: a scanning electron microscopic study. J Oral Pathol 13, 255–264

Ellison, L.F. 2000. Tea and other beverage consumption and prostate cancer risk: a Canadian retrospective cohort study. Eur J Cancer Prev. 9(2) 125-30

Erciyas, K., Sarikaya, R. 2009. Genotoxic evaluation of sodium fluoride in the Somatic Mutation and Recombination Test (SMART) Food and Chemical Toxicology 47(11), 2860-2

Erickson, J.D., 1978. Mortality in Selected Cities with Fluoridated and Non-Fluoridated Water Supplies. New England Journal of Medicine, 298, 1112-1116,

Eyre, R., Feltbower, R.G., Mubwandarikwa, E., Eden, T.O.B. and R.J.Q. McNally. 2009. Epidemiology of bone tumours in children and young adults. Pediatr. Blood Cancer 53, 941-952

Flora, S.J., Mittal M., Pachauri, V., Dwivedi, N. 2012. A possible mechanism for combined arsenic and fluoride induced cellular and DNA damage in mice. Metallomics 4(1) 78-90

Foley, E.F., Jazaeri, A.A., Shupnik, M.A., Jazaeri, O., and Rice, L.W. 2000. Antitumor effects on advanced breast, ovarian, and colon cancer. Cancer Res. 60, 245–248

Garcia, G.M., McCord, G.C., Kumar, R. 2003. Hydroxyapatite crystal deposition disease. Semin Musculoskelet Radiol. 7(3) 187-93

Gadhia, P.K. and S. Joseph. 1997. Sodium fluoride induced chromosome aberrations and sister chromatid exchange in cultured human lymphocytes. Fluoride 30(3) 153-156.

Gelberg, K.H., Fitzgerald, E.F., Hwang, S. and R. Dubrow. 1995. Fluoride exposure and childhood osteosarcoma: A case-control study. American Journal of Public Health 85 (12) 1678-1683.

Glasser, G. 2011. Death in the Air

Gocke, E., King, M.-T., Eckhardt, K. and D. Wild. 1981. Mutagenicity of cosmetics ingredients licensed by the European Communities. Mutat. Res. 90, 91-109

Grandjean, P. and Olsen, J.H. 2004. Extended follow-up of cancer incidence in fluoride-exposed workers [2], Journal of the National Cancer Institute, 96(10) 802-803 *

Grandjean, P., Olsen, J. H. and Juel, N. 1993. Excess cancer incidence among workers exposed to fluoride Scand. J Work Environ. Health 19(Suppl. 1) 108-109

Guan, Y., Hao, P., Tang, C., Li, P., Li, S., Cheng, X., Ba, Y., Cui, L. 2012. Effect of fluoride on the expression of StAR mRNA and P450scc mRNA in the progesterone synthesis of mouse Leydig tumor cells. Wei Sheng Yan Jiu. 41(1) 105-8.

Gutknecht, J., Walter A. 1981. Hydrofluoric acid and nitric acid transport through lipid bilayer membranes. Biochim Biophys Acta 644, 153-156 cited in Takahashi 2001.

Hayashi, N. and Tsutsui, T. 1993. Cell cycle dependence of cytotoxicity and clastogenicity induced by treatment of synchronized human diploid fibroblasts with sodium fluoride. Mutation Research 290, 293-302

Hayes, C.W. and Conway, W.F. 1990. Calcium Hydroxyapatite Deposition Disease. Radiographics 10, 1031-48

He, L.F. and Chen, J.G. 2006. DNA damage, apoptosis and cell cycle changes induced by fluoride in rat oral mucosal cells and hepatocytes. World Journal of Gastroenterology 12(7) 1144-8

Hein, J.W., Smith, F.A. and F. Brudevold. 1954. Distribution of 1 ppm fluoride as radioactively tagged NaF in soft tissues of adult female albino rats. J Dent Res 33(Oct.) 709-710.

Hein, J.W., Bonner, J.F., Brudevold, F., et al. 1956. Distribution in the soft tissue of the rat of radioactive fluoride administered as sodium fluoride. Nature 178 (4545) 1295–1296.

Herskowitz, I. and Norton, I. 1963. Increased Incidence of Melanotic Tumors in two strains of Drosophila Melanogaster Following Treatment with Sodium Fluoride. Genetics, 48, 307-310

Hirzy, J.W., Carton, R.J., Bonanni, C.D., Montanero, C.M., Nagle, M.F. 2013. Comparison of hydrofluorosilicic acid and pharmaceutical sodium fluoride as fluoridating agents—A cost–benefit analysis. Environmental Science and Policy 38, 282-284

Hirzy, J.W. 1999. Why the EPA's Headquarters Union of Scientists Opposes Fluoridation. Press release from National Treasury Employees Union, May 1, 1999. http://www.fluoridealert.org/hpepa.htm)

Hirzy, J.W. 2000. Statement of Dr. J. William Hirzy, National Treasury Employees Union Chapter 280, before the Subcommittee on Wildlife, Fisheries and Drinking Water, United States Senate, June 29, 2000. Available at http://www.nteu280.org/Issues/Fluoride/629FINAL.htm or http://www.fluoridealert.org/HirzyTestimony.pdf.

Hoover, R.N., Devesa, S.S. Cantor, K.P. Lubin, J.H. and J.F. Fraumeni. 1991. Fluoridation of drinking water and subsequent cancer incidence and mortality. Appendix E in: Review of Fluoride Benefits and Risks. Report of the Ad Hoc Subcommittee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs. U.S. Public Health Service.

Hsu, H., Lacey, D.L., Dunstan, C.R., Solovyev, I., Colombero, A., Timms, E., Tan, H.L., Elliott, G., Kelley, M.J., Sarosi, I., Wang, L., Xia, X.Z., Elliott, R., Chiu, L., Black, T., Scully, S., Capparelli, C., Morony, S., Shimamoto, G., Bass, M.B., Boyle, W.J. 1999. Tumor necrosis factor receptor family member RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand. Proc Natl Acad Sci USA 96, 3540–3545.

Huo, L., Liu, K., Pei, J., Yang, Y., Ye, Y., Liu, Y., Sun, J., Han, H., Xu, W. And Y. Gao. 2013. Fluoride Promotes Viability and Differentiation of Osteoblast-Like Saos-2 Cells Via BMP/Smads Signaling Pathway. Biological Trace Element Research. 155(1) 142-149

Jachimczak, D. and Skotarczak, B. 1978. The Effect of Fluorine and Lead Ions on the Chromosomes of Human Leucocytes in Vitro. Genetica Poloncia 19, 353

Jedrychowski, W., Maugeri, U., and Bianchi, I. 1997. Environmental pollution in central and eastern European countries: A basis for cancer epidemiology. Reviews on Environmental Health, 12(1) 1-23 *

Jensen, P.S. 1988. Chondrocalcinosis and other calcifications. Radiol. Clin. North Am. 26 (6) 1315-25

Jones, C.A. et al. 1988. Sodium fluoride promotes morphological transformation of Syrian hamster embryo cells. Carcinogenesis 9, 2279-84

Joseph, S., Gadhia, P.K. 2000. Sister chromatid exchange frequency and chromosome aberrations in residents of fluoride endemic regions of South Gujarat. Fluoride 33, 154-158

Kearney, R. 2015. Melatonin in Health and Disease – Effects of Fluoride. Presented at the Australian Conference on Water Fluoridation, Sydney.

Kesse-Guyot, E., Bertrais, S., Duperray, B., Arnault, N., Bar-Hen, A., Galan, P., Hercberg, S. 2007. Dairy products, calcium and the risk of breast cancer: results of the French SU.VI.MAX prospective study. Ann Nutr Metab. 51(2) 139-45. Epub 2007 May 29

Khalil, A.M. 1995. Chromosome aberrations in cultured rat bone marrow cells treated with inorganic fluorides. Mutation Research 343, 67-74.

Kharb, S., Sandhu, R. and Kundu, Z.S. 2012. Fluoride levels and osteosarcoma. South Asian J Cancer, 1(2) 76-77

Kim, F.M., Hayes C., Williams, P.L., Whitford, G.M., Joshipura, K.J., Hoover, R.N., Douglass C.W. 2011. An assessment of bone fluoride and osteosarcoma Journal of Dental Research 90(10) 1171-6

Kishi, K., and T. Ishida. 1993. Clastogenic activity of sodium fluoride in great ape cells. Mutation Research 301, 183-188.

Knox, E.G. (Chairman). 1985. Fluoridation of water and cancer- A review of the epidemiological evidence (Report of the working party), Her Majesty's Stationery Office, UK pp. 76-83, 100-103. Cited in Takahashi 2001.

Koyama, H., Nakade, O., Takada, Y., Kaku, T. and K.-H. W. Lau. 2002. Melatonin at Pharmacologic Doses Increases Bone Mass by Suppressing Resorption Through Down-Regulation of the RANKL-Mediated Osteoclast Formation and Activation. J Bone Miner Res 17, 1219 –1229

Larsson, S.C., Bergkvist, L. and Wolk, A. Division of Nutritional Epidemiology, The National Institute of Environmental Medicine, Karolinska Institute, Sweden. 2009. Coffee and black tea consumption and risk of breast cancer by estrogen and progesterone receptor status in a Swedish cohort. Cancer Causes and Control, 20(10) 2039-2044

Lasne, C., Lu, Y.-P. and I. Chouroulinkov. 1988. Transforming activities of sodium fluoride in cultured Syrian hamster embryo and BALB/3T3 cells. Cell Biology and Toxicology 4(3) 311-324.

Lazutka, J.R., et al. 1999. Chromosomal aberrations and sister-chromatid exchanges in Lithuanian populations: effects of occupational and environmental exposures. Mutation Research 445, 225-229

Lee, J.R. 1993. Fluoridation and Bone Cancer, Fluoride, Vol.26. No.2 http://www.fluorideresearch.org/262/files/FJ1993_v26_n2_p079-164.pdf

Lenoir, V., de Jonage-Canonico, M.B.Y., Perrin, M.-H., Martin, A., Scholler, R. and B. Kerdelhué. 2005. Preventive and curative effect of melatonin on mammary carcinogenesis induced by dimethylbenz[a]anthracene in the female Sprague–Dawley rat. Breast Cancer Research 7, R470-R476

Lestari, F., Hayes, A.J., Green, A.R. and B. Markovic. 2005. In vitro cytotoxicity of selected chemicals commonly produced during fire combustion using human cell lines. Toxicology in Vitro 19, 653-663

Levy, M., Leclerc, B.S. 2012. Fluoride in drinking water and osteosarcoma incidence rates in the continental United States among children and adolescents. Cancer Epidemiology 36(2) e83-8

Li, S., Smith, K.D., Davis, J.H., Gordon, P.B., Breaker, R.R. and S.A. Strobel. 2013. Eukaryotic resistance to fluoride toxicity mediated by a widespread family of fluoride export proteins. Proceedings of the National Academy of Sciences. 110(47) 19018-19023

Liu, H.L., Zeng, Q., Cui, Y.S., Zhang, L., Fu, G., Hou, C.C., Zhao, L., Wang, A. 2014. Fluoride-induced thyroid cell apoptosis. Fluoride 47(2) 161-69

Liu, F., Bloch, N., Bhushan, K.R., De Grand, A.M., Tanaka, E., Solazzo, S., Mertyna, P.M., Goldberg, N., Frangioni, J.V., Lenkinski, R.E. 2008. Humoral bone morphogenetic protein 2 is sufficient for inducing breast cancer microcalcification. Mol. Imaging. 7(4) 175-86

Loder, R. and Sabatino, M. 2015. The Time of the Insult/Triggering Event in Primary Osteosarcoma and Ewing's Sarcoma of Bone as Determined by Incubation Period Modeling and Age Distribution of Such Malignancies. Epidemiology Research International pp.1-9

Luke, J. 1998. Effects of Fluoride on the Physiology of the Pineal Gland. Fluoride, Vol. 31(3) 129-174

Mahoney, M.C., Nasca P.C., Burnett W.S., Melius J.M. 1991. Bone cancer rates in New York State: time trends and fluoridated drinking water. Am J Pub Health 81, 475–479.

Maity, A., Sall, W., Koch, C. J., Oprysko, P.R., and Evans, S.M. 2001. Low pO2 and beta-estradiol induce VEGF in MCF-7 and MCF-7-5C cells: relationship to in vivo hypoxia, Breast Cancer Research and Treatment, 67(1) 51-60 *

Makhoul, I. Harvey, H. Souba, W. and H. Makhoul. 2006. Breast Cancer. Emedicine from WebMD

Manivannan, J., Sinha, S., Ghosh, M., Mukherjee, A. 2012. Evaluation of multi-endpoint assay to detect genotoxicity and oxidative stress in mice exposed to sodium fluoride. Mutation Research 18, 751(1) 59-65

Marcus, W. 1990. Memorandum from Dr. William Marcus, to Alan B. Hais, Acting Director, Criteria and Standards Division ODW, US EPA, DATED MAY 1, 1990, and subsequent memos.

Maurer, J.K., Cheng, M.C., Boysen, B.G., Anderson, R.L. 1990. Two-year carcinogenicity study of sodium fluoride in rats. J Natl Cancer Inst 82, 1118–1126

McCullough, M.L., Bandera E.V., Moore D.F., Kushi L.H. 2008. Vitamin D and calcium intake in relation to risk of endometrial cancer: a systematic review of the literature. Prev. Med. 46(4) 298-302. Epub 2007 Nov 28

Medina, N., Douglass, C. W., Whitford, G. M., Hoover, R. N., and Fears, T. R. 2006. A reproducibility study for a fluoride assay in bone. Cancer Epidemiology Biomarkers and Prevention, 15(5) 1035-1037. *

Meiers, P. 2000. Fluoridation and cancer: Does water fluoridation have negative side effects? A Critique of the New York Review

Mendoza-Schulz, A., Solano-Agama, C., Arreola-Mendoza, L., Reyes-Márquez, B., Barbier, O., Del Razo, L.M., Mendoza-Garrido, M.E. 2009. The effects of fluoride on cell migration, cell proliferation, and cell metabolism in GH4C1 pituitary tumour cells. Toxicology Letters 190(2) 179-86

Meng, Z., Meng, H. and X. Cao. 1995. Sister-chromatid exchanges in lymphocytes of workers at a phosphate fertilizer factory. Mutation Research 334, 243-246.

Meng, Z. and B. Zhang. 1997. Chromosomal aberrations and micronuclei in lymphocytes of workers at a phosphate fertilizer factory. Mutation Research 393, 283-288.

Mihashi, M. and T. Tsutsui. 1996. Clastogenic activity of sodium fluoride to rat vertebral body-derived cells in culture. Mutation Research 368, 7-13.

Mirabello, L., Troisi, R.J. and Savage, S.A. 2009. International osteosarcoma incidence patterns in children and adolescents, middle ages and elderly persons, Int. J. Cancer 125, 229–234

Mirabello, L., Yu, K., Berndt, S.I., Burdett, L., Wang, Z., Chowdhury, S., Teshome, K., Uzoka, A., Hutchinson, A., Grotmol, T., Douglass, C., Hayes, R.B., Hoover, R.N., Savage, S.A. and for the National Osteosarcoma Etiology Study Group. 2011. A comprehensive candidate gene approach identifies genetic variation associated with osteosarcoma. BMC Cancer 11, 209

Moreno-Merlo, F., Nicklee, T., and Hedley, D. W. 1999. Association between tissue hypoxia and elevated non-protein sulphydryl concentrations in human cervical carcinoma xenografts. British Journal of Cancer, 81(6) 989-993 *

Morgan, M.P., Cooke M.M., McCarthy G.M. 2005. Microcalcifications associated with breast cancer: an epiphenomenon or biologically significant feature of selected tumors? J Mammary Gland Biol Neoplasia. 10(2) 181-7.

Morgan M.P., Cooke M.M., Christopherson P.A., Westfall P.R., McCarthy G.M. 2001. Calcium hydroxyapatite promotes mitogenesis and matrix metalloproteinase expression in human breast cancer cell lines. Mol Carcinog. 32(3) 111-7.

Morin, P. et al. 1985. Fluorides, Water Fluoridation, Cancer, and Genetic Diseases, Science and Public Policy 12, 36

Morshed, S.R., Tokunaga, T., Otsuki, S., Takayama, F., Satoh, T., Hashimoto, K., Yasui, T., Okamura, M., Shimada, J., Kashimata, M., and Sakagami, H. 2003. Effect of Antitumor Agents on Cytotoxicity Induction by Sodium Fluoride, Anticancer Research, vol. 23, no. 6 C, pp. 4729-4736. *

Movsas, B., Chapman, J.D., Greenberg, R.E., Hanlon, A.L., Horwitz, E.M., Pinover, W.H., Stobbe, C., and Hanks, G.E. 2000. Increasing levels of hypoxia in prostate carcinoma correlate significantly with increasing clinical stage and patient age: An Eppendorf pO2 study, Cancer, vol. 89(9) 2018-2024. *

Moyad, M.A. 2002. Complementary therapies for reducing the risk of osteoporosis in patients receiving luteinizing hormone-releasing hormone treatment/orchiectomy for prostate cancer: A review and assessment of the need for more research, Urology, 59(4 SUPPL. 1) 34-40 *

Mukherjee, R.N., Sobels F.H. 1968. The effects of sodium fluoride and iodoacetamide on mutation induction by x-irradiation in mature spermatozoa of drosophila. Mutat Res 6, 217-25.

Nagakawa, T., Kayahara, M., Ohta, T., Kitagawa, H., Mikami, K., Kurata, T., and Otsuji, S. 2000. Dihydropyrimidine dehydrogenase activity in human pancreatic tumor tissues. Cancer Investigation, 18(6) 516-520 *

National Academy of Sciences. 1977. Drinking Water and Health. National Academy Press, Washington, DC., pp. 388-389.

National Academy of Sciences. 1993. Health Effects of Ingested Fluoride. National Academy Press, Washington, DC. Chapter 6.

Needham, B. 2010. “Killer Smile” Report to Minister for Health and Human Services. Water Fluoridation and Ill Health of at Risk Groups in the Tasmanian Population in 2010.

NTP. National Toxicology Program [NTP]. 1990. Toxicology and Carcinogenesis Studies of Sodium Fluoride in F344/N Rats and B6C3f1 Mice. Technical report Series No. 393. NIH Publ. No 91-2848.

Oguro, A., Cervenka, J. and K. Horii. 1995. Effect of sodium fluoride on chromosomal ploidy and breakage in cultured human diploid cells (IMR-90): An evaluation of continuous and short-time treatment. Pharmacology and Toxicology 76, 292-296

O’Neill, V. J. and Cassidy, J. 2005. Capecitabine in the treatment of colorectal cancer, Future oncology (London), 1(2) 183-190 *

Osmunson B. and A. Adams. 2015. Nomination for the Office of the Report on Carcinogens: Fluoride

Ottaviani G., Jaffe, N. 2009. The epidemiology of osteosarcoma. Cancer Treat Res. 152, 3-13

Ozsvath, D.L. 2009. Fluoride and Environmental Health: a Review. Reviews in Environmental Science and Biotechnology 8(1) 59-79.

Pal, S., Sarkar, C. 2014. Protective effect of resveratrol on fluoride induced alteration in protein and nucleic acid metabolism, DNA damage and biogenic amines in rat brain. Environ Toxicol Pharmacol. 38(2) 684-99.

Palmieri, M.J., Luber, J., Andrade-Vieira, L.F., Davide, L.C. 2014. Cytotoxic and phytotoxic effects of the main chemical components of spent pot-liner: A comparative approach. Mutation Research 763, 30-35

Parsons, W.D., De Villiers, A.J., Bartlett, L.S., Becklake, M.R. 1964. Lung cancer in fluorspar mining community. II. Prevalence of respiratory symptoms and disability. Br. J. Industr. Med. 21, 10

Pashley, D.H., Allison, N.B, Easmann, R.P., McKinney, R.V., Horner, J.A., Whitford, G.M. 1984. The effects of fluoride on the gastric mucosa of the rat. J Oral Pathol 13, 535–545.

Pathi, S.P., Lin, D.D.W., Dorvee, J.R., Estroff, L.A. and C. Fischbach. 2011. Hydroxyapatite nanoparticle-containing scaffolds for the study of breast cancer bone metastasis Biomaterials 32(22), 5112–5122

Pati, P.C., Bhunya S.P. 1987. Genotoxic effect of an environmental pollutant, sodium fluoride, in mammalian in vivo test system. Caryologia 40, 79-87.

Pawar, A.C., Naik, S.J.K., Kumari, S.A. 2014. Cytogenetic analysis of human lymphocytes of fluorosis-affected men from the endemic fluorosis region in Nalgonda district of Andhra Pradesh, India. Fluoride 47(1) 78-84

Podder, S., Chattopadhyay, A., Bhattacharya, S., Ray, M.R., Chakraborty, A. 2011. Fluoride-induced genotoxicity in mouse bone marrow cells: effect of buthionine sulfoximine and N-acetyl-l-cysteine Journal of Applied Toxicology 31(7) 618-25

Podder, S., Chattopadhyay, A., Bhattacharya, S. 2011. Reduction in fluoride-induced genotoxicity in mouse bone marrow cells after substituting high fluoride-containing water with safe drinking water Journal of Applied Toxicology 31(7) 703-5

Podder, S., Chattopadhyay, A., Bhattacharya, S., Ray, M.R. 2008. Differential in vivo genotoxic effects of lower and higher concentrations of fluoride in mouse bone marrow cells. Fluoride 41(4) 301–307

Prystupa, J. 2011. Fluorine—a current literature review. An NRC and ATSDR based review of safety standards for exposure to fluorine and fluorides. Toxicology Mechanisms and Methods 21(2) 103–170

Pujol, P., Rey, J.M., Nirde, P., Roger, P., Gastaldi, M., Laffargue, F., Rochefort, H., and Maudelonde, T. 1998. Differential expression of estrogen receptor- α and –β messenger RNAs as a potential marker of ovarian carcinogenesis. Cancer Res. 58, 5367–5373

Rahman, K.M.W., Shigeyuki, S.T., Watanabe, T., Tanaka, H.M. 2003. Chemopreventive Effects of Melatonin on Diethylnitrosamine and Phenobarbital-Induced Hepatocarcinogenesis in Male F344 Rats Nutrition and Cancer 47(2) 148-155

Ramesh, N., Vuayarahavan, A.S., Desai, B.S., Natarajan, M., Murthy, P.B., Pillai, K.S. 2001. Low levels of p53 mutations in Indian patients with osteosarcoma and the correlation with fluoride levels in bone. J Environ Pathol Toxicol Oncol 20(3) 237-43

Rao, M.V., Thakur, S.B. 2013. Effects of melatonin and amla antioxidants on fluoride-induced genotoxicity in human peripheral blood lymphocyte cells Fluoride 46(3) 128–134

Rao, M.V., Tiwari, H. 2006. Amelioration by melatonin of chromosomal anomalies induced by arsenic and/or fluoride in human blood lymphocyte cultures. Fluoride 39(4) 255-60

Rao, H.V., Beliles, R.P., Whitford, G.M., Turner, C.H. 1995. A physiologically-based pharmaco-kinetic model for fluoride uptake by bone. Regul Toxicol Pharmacol 22, 30–42

Rivedal, E., et al. 2000. Morphological transformation and effect on gap junction intercellular communication in Syrian hamster embryo cells as screening tests for carcinogens devoid of mutagenic activity. Toxicology In Vitro 14(2), 185-92.

Romundstad, P., Andersen, A., and Haldorsen, T. 2000. Cancer incidence among workers in six Norwegian aluminum plants, Scandinavian Journal of Work, Environment and Health, 26 (6) 461-469 *

Romundstad, P., Haldorsen, T., and Ronneberg, A. 1999. Exposure to PAH and fluoride in aluminum reduction plants in Norway: Historical estimation of exposure using process parameters and industrial hygiene measurements. American Journal of Industrial Medicine, 35(2) 164-174. *

Romundstad, P., Haldorsen, T., and Andersen, A. 2000. Cancer incidence and cause specific mortality among workers in two Norwegian aluminum reduction plants, American Journal of Industrial Medicine, 37(2) 175-183 *

Saidak, Z., Boudot, C., Abdoune, R., Petit, L., Brazier, M., Mentaverri, R., Kamel, S. 2009. Extracellular calcium promotes the migration of breast cancer cells through the activation of the calcium sensing receptor. Exp Cell Res. 315(12) 2072-80.

Sandhu, R., Lal, H., Kundu, Z.S., Kharb, S. 2011. Serum fluoride and sialic acid levels in osteosarcoma Biological Trace Element Research 144(1-3) 1-5

Satoh, R., Kishino, K., Morshed, S. R. M., Takayama, F., Otsuki, S., Suzuki, F., Hashimoto, K., Kikuchi, H., Nishikawa, H., Yasui, T., and Sakagami, H. 2005. Changes in fluoride sensitivity during in vitro senescence of normal human oral cells. Anticancer Research, 25 (3B) 2085-2090. *

Schlesinger, E.R., et al. 1956. Newburgh-Kingston Caries-Fluorine Study XIII. Pediatric Findings after Ten Years. Journal of the American Dental Association, 52 CDC 2012 http://www.cdc.gov/fluoridation/statistics/2012stats.htm

Schmidt, K., Horneber, M., Borrelli, F., and Ernst, E. 2004. Green tea (Camellia sinensis) for the prevention of cancer. Cochrane Database of Systematic Reviews: Protocols.2004.Issue 4 John.Wiley.and Sons., Ltd. Chichester, UK *

Scott, D. 1986. Cytogenetic effects of sodium fluoride in cultured human fibroblasts. Mutagenesis 1, 69

Scott, D. and S.A. Roberts. 1987. Extrapolation from in vitro tests to human risk: Experience with sodium fluoride clastogenicity. Mutat. Res., 189, 47-58,

Sheth, F.J., et al. 1994. Sister chromatid exchanges: A study in fluorotic individuals of North Gujurat. Fluoride 27, 215-219

Slattery, M.L., West, D.W. 1993. Smoking, alcohol, coffee, tea, caffeine, and theobromine: risk of prostate cancer in Utah (United States). Cancer Causes Control. 4(6) 559-63.

Song, J.S., Park, Y.D., Hyun, J.W. and Kim, J.H. 2005. Induction of apoptosis by sodium fluorosilicate treatment in human osteogenic sarcoma (HOS) cells, Anticancer Research, 25(1 A) 391-395 *

Steiner, G.G. 2002. Cancer incidence rates and environmental factors: An ecological study, Journal of Environmental Pathology, Toxicology and Oncology, 21(3) 205-212

Steiner, D.M. and Steiner, G.G. 2004. Fluoride as an essential element in the prevention of disease. Medical Hypotheses, 62(5) 710-717

Spak, C-J., Sjostedt, S., Eleborg, L., Veress, B., Perbeck, L. and J. Ekstrand. 1989. Tissue response of gastric mucosa after ingestion of fluoride. BMJ 298, 1686-87

Srilatha K., Banji D., Banji O.J.F., Vinod, K.R. and Saidulu, A. 2013. Investigation of the anti-genotoxic effect of ocimum sanctum in fluoride induced genotoxicity. International Research Journal of Pharmacy 4(5) 160-64

Stockbridge, R.B., Kolmakova-Partensky, L., Shane, T., Koide, A., Koide, S., Miller, C. and S. Newstead. 2015. Crystal structures of a double-barrelled fluoride ion channel. Nature, 525, 548-551

Sutton, P.R.N. 1986. Lung Cancer: Is Fluoride in Cigarette Smoke an Etyological Factor? Medical Hypotheses 20, 51

Suzuki, N., Tsutsui, T. 1989. Dependence of lethality and incidence of chromosome aberrations induced by treatment of synchronized human diploid fibroblasts with sodium fluoride on different periods of the cell cycle. [Article in Japanese] Shigaku. 77(2) 436-47.

Suzuki, Y., Li, J., Shimizu, H. 1991. Induction of micronuclei by sodium fluoride. Mutation Research 253(3) 278

Takahashi, K., Akiniwa, K., and Narita, K. 2001. Regression analysis of cancer incidence rates and water fluoride in the U.S.A. based on IACR/IARC (WHO) data (1978-1992). International Agency for Research on Cancer, Journal of Epidemiology / Japan Epidemiological Association, 11(4) 170-179.

Takahashi, N, Udagawa N, Suda T. 1999. A new member of tumor necrosis factor ligand family, ODF/OPGL/TRANCE/ RANKL, regulates osteoclast differentiation and function. Biochem Biophys Res Commun 256, 449–455

Taylor, A. and N.C. Taylor. 1965. Effect of Fluoride on Tumor Growth, Proceedings of the Society of Experimental Biology and Medicine, 65, 252-255

Tazhibaev Sh.S., et al. 1977. [Modifying effect of nutrition on the mutagenic activity of phosphorus and fluorine compounds]. Vopr Pitan. Jul-Aug (4) 63-6.

Thakur, S.B., Rao, M.V. 2014. In vitro fluoride induced genotoxic effect on human blood lymphocyte cells and its amelioration by emblica officinalis extract Molecular Cytogenetics 7 (Suppl 1) 48

Thiessen, K.M., Limeback, H., Beck, J., Micklem, H.S., Litras, S., Spittle, B., Atkin, G.M. 2014. Scientific and Critical Analysis of the 2014 New Zealand Fluoridation Report. International Critique of the Royal Society of New Zealand/Office of the Prime Minister's Chief Science Advisor's Fluoridation Report: Health effects of water fluoridation: A review of the scientific evidence. Fluoride Free New Zealand. Accessed from www.fluoridefree.org.nz

Thiessen, K.M. 2011. Comments in response to Evidence on the Carcinogenicity of Fluoride and Its Salts. July 2011 Reproductive and Cancer Hazard Assessment Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency

Tohyama, E. 1996. Relationship between fluoride concentration in drinking water and mortality rate from uterine cancer in Okinawa prefecture, Japan. Journal of epidemiology / Japan Epidemiological Association 6(4) 184-191. *

Tohyama, E. 1995. Drinking water quality and its relationship with the mortality rate in Okinawa prefecture. Japanese J of Health and Human Ecology, 61 (2) 69-82

Tokar, U.T., Savchenko, O.N. 1977. Effect of inorganic fluoride compounds on the functional state of the pituitary-testis system, Probl Endoklinol (Mosk) 23, 104-107, cited in Takahashi 2001

Tokunaga, T., Morshed, S.R.M., Otsuki, S., Takayama, F., Satoh, T., Hashimoto, K., Yasui, T., Ogawa, S., Kanegae, H., Yokote, Y., Akahane, K., Kashimata, M., Satoh, K., and Sakagami, H. 2003. Effect of Antioxidants, Oxidants, Metals and Saliva on Cytotoxicity Induction by Sodium Fluoride, Anticancer Research, 23(5A) 3719-3726 *

Torell, J.A., Knight, J.P., Marcus, P.B. 1984. Intraluminal calcium hydroxyapatite crystals in breast carcinoma: an ultrastructural study. Ultrastruct Pathol. 6(1)9-14

Tsutsui, T., Suzuki, N., Ohmori, M., and Maizumi, H. 1984. Cytotoxicity, chromosome aberrations and unscheduled DNA synthesis in cultured human diploid fibroblasts induced by sodium fluoride. Mutat. Res. 139, 193-198

Tsutsui, T. et al. 1991. Cytotoxicity and Chromosome Aberrations in Normal Human Oral Keratinocytes Induced by Chemical Carcinogens: Comparison of Inter-Individual Variations, Toxicology in Vitro 5, 353

Turner, C.H., Garetto, L.P., Dunipace, A.J., Zhang, W., Wilson, M.E., Grynpas, M.D., Chachra, D., McClintock, R., Peacock, M., and Stookey, G.K. 1997. Fluoride treatment increased serum IGF-1, bone turnover, and bone mass, but not bone strength, in rabbits. Calcif. Tissue Int. 61, 77-83

US Public Health Service. 1991. Review of fluoride: benefits and risks, Report of the Ad Hoc Subcommittee on Fluoride. Public Health Service, Atlanta, cited in Takahashi 2001.

Varner, J.A., Jensen, K.F., Horvath, W., Isaacson, R.L. 1998. Chronic administration of aluminum-fluoride or sodium-fluoride to rats in drinking water: alterations in neuronal and cerebrovascular integrity. Brain Res. 784, 284-298 cited in Takahashi 2001.

Vazquez-Alvarado P., Melendez-Ocampo A., Ortiz-Espinosa R.M., Munoz-Juarez S., Hernandez-Ceruelos A. 2012. Genotoxic damage in oral epithelial cells induced by fluoride in drinking-water on students of Tula de Allende, Hidalgo, Mexico Journal of Toxicology and Environmental Health Sciences 4(8) 123-129

Venkateswarlu, P., Zero, D.T. 1994. Report for Working Group I: strategies for improving the assessment of fluoride accumulation in body fluids and tissues. Adv Dent Res 8, 113–115.

Wang, A.-G., T. Xia, Q.-L. Chu, M. Zhang, F. Liu, X.-M. Chen, and K.-D. Yang. 2004. Effects of fluoride on lipid peroxidation, DNA damage and apoptosis in human embryo hepatocytes. Biomedical and Environmental Sciences 17, 217-222.

Waugh, D. 2014. Health impacts of water fluoridation. Presentation to Nutritional Therapists of Ireland.

Wergedal, J.E., Lau, K-H.W., Baylink, D.J. 1988. Fluoride and bovine bone extract influence cell proliferation and phosphatase activities in human bone cell cultures. Clin Orthop Relat Res 233, 274–82

Whitford, G.M. 1994. Intake and metabolism of fluoride. Adv Dent Res 8, 5–14.

Whitford, G.M., Bawden, J.W., Bowen, W.H., Brown, L.J., Ciardi, J.E., Clarkson, T.W., Imrey, P.B., Kleerekoper, M., Marthaler, T.M., McGuire, S., Ophaug, R.H., Robinson, C., Schultz, J.S., Stookey, G.K., Tochman, M.S., Whitford, G.M., Biles, E.D., Birdsong-Whitford, N.L. 1991. A comparative study of fluoride pharmacokinetics in five species. J Dent Res 70, 948–951.

Whitford, G.M. 1996. The metabolism and Toxicity of Fluoride. 2nd Rev. Ed. Monographs in Oral Science Vol. 16. New York: Karger.

Whitford, G.M. 1999. Fluoride metabolism and excretion in children. J Pub Health Dent 59, 224–228.

Whitford, G.M., Buzalaf, M.A., Bijella M.F., Waller, J.L. 2005. Plaque fluoride concentrations in a community without water fluoridation: effects of calcium and use of a fluoride or placebo dentifrice. Caries Res 39, 100–107.

Whitford, G.M., Sampaio, F.C., Arneberg, P., von der Fehr, F.R. 1999. Fingernail fluoride: a method for monitoring fluoride exposure. Caries Res 33, 462–467.

Whitford, G.M., Thomas, J.E., Adair S.M. 1999. Fluoride in whole saliva, parotid ductal saliva and plasma in children. Arch Oral Biol 44, 785–788.

Wikipedia 2015. Laki. https://en.wikipedia.org/wiki/Laki accessed October 2105.

Wilson, George H. III et al. 2014. An Approach to Breast Cancer Diagnosis via PET Imaging of Microcalcifications using 18F-NaF. The Journal of Nuclear Medicine 7, 1138-1143

Wu, D.Q., and Y. Wu. 1995. Micronucleus and sister chromatid exchange frequency in endemic fluorosis. Fluoride 28(3) 125-127.

Xie, M., Yang, D., Liu, L., Xue, B., and Yan, B. 2002. Human and rodent carboxylesterases: Immunorelatedness, overlapping substrate specificity, differential sensitivity to serine enzyme inhibitors, and tumor-related expression. Drug Metabolism and Disposition, 30(5) 541-547 *

Yang, C.Y., Cheng, M.F., Tsai, S.S., and Hung, C.F. 2000. Fluoride in drinking water and cancer mortality in Taiwan. Environmental Research, 82(3), 189-193

Yiamouyiannis, J.A. and Burk, D. 1977. Fluoridation and Cancer: Age Dependence of Cancer Mortality Related to Artificial Fluoridation, Fluoride, 10 (3) 102-123

Yiamouyiannis, J. 1993. Fluoridation and Cancer: The Biology and Epidemiology of Bone and Oral Cancer Related to Fluoridation, Fluoride 26, 83

Yu, F., Jin, Z., Jiang, H., Xiang, C., Tang, J., Li, T. and J. He. 2014. Tea consumption and the risk of five major cancers: a dose–response meta-analysis of prospective studies. BMC Cancer 14, 197

Zhang R., Niu Y., Du H., Cao X., Shi D., Hao Q., Zhou Y. 2009. A stable and sensitive testing system for potential carcinogens based on DNA damage-induced gene expression in human HepG2 cell Toxicology in Vitro 23(1) 158-65

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.

Zhang Y., Sun X., Sun G., Liu S., Wang L. 2006. DNA damage induced by fluoride in rat osteoblasts. Fluoride 30(3), 191-94

Zhang X., Albanes D., Beeson, W.L., van den Brandt P.A., Buring, J.E., Flood, A., Freudenheim, J.L., Giovannucci, E.L., Goldbohm, R.A., Jaceldo-Siegl, K., Jacobs, E.J., Krogh, V., Larsson, S.C., Marshall, J.R., McCullough, M.L., Miller, A.B., Robien, K., Rohan, T.E., Schatzkin, A., Sieri, S., Spiegelman, D., Virtamo, J., Wolk, A., Willett, W.C., Zhang, S.M., Smith-Warner, S.A. 2010. Risk of colon cancer and coffee, tea, and sugar-sweetened soft drink intake: pooled analysis of prospective cohort studies. J Natl Cancer Inst 102(11), 771–783

Ziegelbecker, R. 1987. Zur Frage eines Zusammenhanges zwischen Trinkwasserfluordierung, Krebs, und Leberzirrhose, 218 GWF Wasser/Abwasser 111