HEALTH EFFECTS: Fluoride's Mutagenicity (Genotoxicity)

Key Findings - Fluoride's Mutagenicity:

1) According to the National Toxicology Program, "the preponderance of evidence" from laboratory 'in vitro' studies indicate that fluoride is a mutagenic compound.

2) Many substances which are mutagens, are also carcinogens (i.e. they can cause cancer).

3) While the concentrations of fluoride causing mutagenic damage in the in vitro studies is higher than the concentrations found in human blood, there are certain "microenvironments" in the body (e.g. the bones) where the concentrations of fluoride can accumulate to levels comparable to, or in excess of, those causing mutagenic effects in the laboratory.

4) A study comparing fluoride's ability to cause mutagenic damage in cells from apes and humans versus cells from rodents, found that the cells from apes and human were much more sensitive to fluoride's mutagenic effects.

5) Five studies on fluoride-exposed humans, published since 1994, have reported an increased incidence of mutagenic damage when compared to comparable controls. Two studies conducted during this period did not find this effect. The primary type of mutagenic damage found in fluoride-exposed humans was sister chromatid exchange.

Excerpts from In-Vivo Human Studies - Fluoride's Mutagenicity: (back to top)

"A number of investigators have utilized the SCE (Sister Chromatid Exchange) test to study the genotoxicity of fluoride. In the present study, human populations directly exposed to fluoride in drinking water in endemic regions of North Gujarat were investigated to evaluate the possible effect of fluoride on SCE. To the best of our knowledge this is the first report on genotoxic effects following long-term fluoride intake in an endemic area in India... The results of the present investigation suggest that in fluoride-affected persons exposed to 1.95 - 2.2 ppm fluoride in drinking water chromosomal alterations as indicated by SCE frequency and chromosome aberrations were higher than in normal persons exposed to 0.6 - 1.0 ppm drinking water fluoride."


*In recent years, SCE analysis has been considered to be a sensitive method for detecting DNA damage. There is a clear relationship between a substance's ability to induce DNA damage, mutate chromosomes, and cause cancers. The SCE frequency in the human body in peripheral blood lymphocytes is very steady, and does not vary with age or sex. Any increase of the SCE frequency is primarily due to chromosome damage. Thus using a method to detect SCE for exploring the toxicity and harm caused by fluoride is of great importance. The results in this paper showed an obvious increase in the SCE frequency of the patients with fluorosis, indicating that fluoride had some mutagenic effects, and could give rise to DNA damage. The fact that the SCE frequency of the healthy people in the endemic regions was also higher than that of the controls in the non-endemic regions suggests that early harm by fluoride can be cytogenetically detected in the sub-clinical patients with fluorosis who could not be given an early diagnosis clinically. Under normal circumstances, the incidence rate of micronucleus is very low, usually 0-2%. The normal value checked in this paper is 0-2%, which agrees with that reported in the literature. The results show that the mean value of the micronucleus rate of the fluoro-toxic patients was 1.94 ± 0.86% (range 1-15%) which is 2-3 times more than that of 0.57 ± 0.44% in the controls... To sum up, the rise of SCE and MN in the peripheral blood lymphocytes of the fluoride-intoxicated patients indicates that fluoride is a mutagenic agent which can cause DNA and chromosomal damage."


*Our study here provided evidence that the air pollutants at the phosphate fertilizer factory, of which HF and SiF4 are the main chemicals, could induce SCEs in human blood lymphocytes in vivo. These results imply that even if the concentration of the chemical pollutants in the air is low (e.g.F: 0.50 - 0.80 mg/m3), it may cause damage to genetic material at the chromosomal level, although the general health of the workers in the phosphate fertilizer factory was found to be satisfactory... HF and SiF4 are the main air pollutants; however, dust containing fluoride, phosphate fog, ammonia (NH3), and sulfur dioxide (SO2) were also released in small amounts into the air during fertilizer production. These pollutants may also make a contribution to the induction of SCES. Hence, further study of the induction effect of HF or SiF4 alone on SCEs in human lymphocytes to understand the cytogenetic damage of fluoride pollution in the air would be needed."


*Our study here provides evidence that the air pollutants at the phosphate fertilizer factory, in which HF and SiF4 are the main chemicals, could induce both CA (chromosomal aberrations) and MN (micronuclei) in human blood lymphocytes in vivo. Our earlier observation on sister-chromatid exchanges (SCE) of peripheral blood lymphocytes from this same population showed that the mean SCEs/cell of the workers was significantly higher than that of the controls (p < 0.01) [13]. The results of our studies imply that even if the concentration of the chemical pollutants in the air is low (e.g. F 0.50-0.80 mg/m 3), it may cause damage to genetic material at the chromosomal level... it is suggested that chromosomal abnormalities induced by fluoride could be the results from interaction with the enzymes responsible for DNA synthesis or repair, rather than directly with DNA."


*Our results indicate that there is a significant increase in the frequencies of chromosome aberrations and SCE in one of the village populations exposed to a fluoride concentration higher than the permissible limit. The lymphocytes of these residents were also more susceptible to a clastogen such as Mitomycin-C than the other populations and displayed a significant increase in chromosome aberrations."


Consensus View of In-Vivo Animal Studies - Fluoride's Mutagenicity: (back to top)

*The disagreements among the in vivo tests for chromosome damage in rodents can not yet be reconciled. There are a few reports of positive results for chromosome aberrations in rodent bone marrow and testes, but other studies, using similar protocols and dose ranges, have reported no induced chromosome damage... Therefore, at this time, the in vivo clastogenicity of fluoride should be
considered unresolved."


Excerpts from *In-Vivo Animal Studies* - Fluoride's Mutagenicity: (back to top)

"The results concerning the SCE rate induced by sodium fluoride are shown in Table 1. Although no significant increase was observed with the two low doses tested (from 2 to 4 mg/kg), a significant SCE increase was found with the three highest doses. The cumulative frequency of these data reveals about 70% of cells with four SCE in the group treated with the high dose, a value which is twice the level of the negative control."


"We tested the induction of mutagenic effects by in vivo and in vitro bone marrow micronucleus tests. A significant increase in micronucleated polychromatic erythrocytes was observed 24 H after intraperitoneal injection of sodium fluoride at a dose of 30 mg/kg body weight. In the in vitro micronucleus test, the frequency of micronucleated polychromatic erythrocytes was increased significantly at concentrations of 2 and 4 MM. These results indicate that the micronucleus test may be useful in evaluating the cancer risk of sodium fluoride."


"Genotoxicity of Sodium fluoride was evaluated in mice in vivo with the help of different cytogenetic assays. The frequency of chromosome aberration was dose - and time - dependent but not exactly route-dependent. Fractionated dosing induced less aberration. Incidence of micronucleus and sperm abnormality increased with dose. Relative sensitivity of the three assays has been found to be: Sperm abnormality > Chromosome aberration > Micronucleus. The present results have revealed the mutagenic property of NaF."


"The test animals were fed with low-grade food during 2-5 months under conditions of acute and chronic action of hydrogen phosphide and hydrogen fluoride induced by inhalation, that resulted in the pronounced impairment of the chromosomal apparatus of the bone marrow cells in the rats. A principal possibility has been established of modification of the hydrogen phosphide and hydrogen fluoride cytogenetic effect by the alimentary action. In particular, it has been found that the effect is significantly higher when the rats are fed with a low-grade ration than under conditions of balanced nutrition."


"Cytological studies on bone marrow cell chromosomes and spermatocytes showed that 1-200 ppm F (as sodium fluoride) was able to induce chromosomal changes in a dose-dependent manner. The frequency of the induced chromosomal damage was significantly higher in each treatment than in the controls. The observed abnormalities included translocations, dicentrics, ring chromosomes, and bridges plus fragments, or fragments by themselves. There was a significant correlation between the amount of fluoride in the body ash and the frequency of the chromosomal abnormalities."


"Cryolite concentrations of 3 mg/m3 as well as a mixture of 0.5 mg/m3 of cryolite and 0.35 mg/m3 of hydrogen fluoride increases 3 1/2 to 4 1/2 times (over controls) the percentage of cells with chromosomal aberrations in the bone marrow of rats. The data indicate the need for further study of the mutagenic features of fluoride compounds in relation to their potential for harmful impact on the mechanism of inheritance in humans."
"The mutagenic effect of hydrogen fluoride in concentration 1.0 mg/m-3 was studied in rats and mice. Prolonged inhalation of this compound increased the frequency of cells with chromosome abnormalities in the bone marrow of albino rats. The mutagenic effect was higher in older animals."

"On the grounds of the results obtained during our experiments F compounds are able to produce certain changes in chromosomes from somatic cells of animals treated in vivo by them... Most of the aberrations observed in the case of bone marrow cells were chromatid-type aberrations... [W]e entertain the opinion that the main damage to chromosomes during our experiments with F compounds also took part during the S-phase... [T]hese data enable us to consider as sufficiently established the conclusion that inorganic fluorine compounds may present a mutagenic danger to human beings."

"In 54 tests involving 991 mice bearing transplanted tumors and 58 tests including 1817 tumor-bearing eggs, data were obtained which indicated a statistically significant acceleration of tumor tissue growth in association with comparatively low levels of NaF."

"The effects of fluoride as a mutagen, carcinogen, and antimutagen are inconsistent, but the preponderance of evidence in cultured mammalian cells indicate that sodium fluoride can induce chromosome aberrations and sister chromatid exchanges."

"Fluoride (as sodium fluoride) should be considered capable of inducing chromosomal aberrations, micronuclei, and sister-chromatid exchanges in vitro in mammalian cells, although the results from such studies have been inconsistent."

"Genotoxicity studies are highly dependent on the methods used... Despite the apparently contradictory reports appearing in the published literature, fluoride has not been shown to be mutagenic in bacteria (Ames test). In some studies fluoride has been reported to induce gene mutations in both cultured..."
rodent and human cells. Fluoride has also been reported to transform rodent cells in vitro. Although there is disagreement in the literature concerning the ability of fluoride to be a clastogen (induce chromosome aberrations) in cultured cells, it has been suggested that fluoride can cause chromosome aberrations in rodent and human cells. Fluoride induced primarily chromatid gaps and chromatid breaks, indicating that the cells are most responsive in the G stage of the cell cycle, i.e., after chromosome duplication in preparation for cell division. Negative results reported in some cytogenetic studies are likely the effect of inadequate test protocols.... Although the mechanism(s) by which these cellular effects result from exposure to fluoride is not known, a number of possible mechanisms have been proposed to explain the genetic activity observed. These mechanisms have been based on the observed reactions of fluoride in solution with divalent cations or nucleotides, or the physiological and biochemical responses of cells treated with fluoride. Sodium fluoride inhibits both protein and DNA synthesis in cultured mammalian cells. The inhibition of DNA synthesis may be a secondary effect of the inhibition protein synthesis, or a result of the direct inhibition of DNA polymerase. Fluoride can react with divalent cations in the cell so as to affect enzyme activities that are necessary for DNA or RNA synthesis, or chromosome metabolism or maintenance; it may react directly with DNA as part of a complex; or it ca disrupt other cellular processes such as cell differentiation or energy metabolism.

"Fluoride has displayed mutagenic activity in studies of vegetation, insects, and mammalian oocytes. There is a high correlation between carcinogenicity and mutagenicity of pollutants, and fluoride has been one of the major pollutants in several situations where a high incidence of respiratory cancer has been observed. For these reasons, the relation between airborne fluoride and incidence of lung cancer needs to be investigated."


Excerpts from In-Vitro Laboratory Studies - Fluoride's Mutagenicity: (back to top)

"As cells were exposed to higher doses of fluoride, the percentage of L-02 cells with DNA damage increased. This result is consistent with other studies... Therefore, considering previous studies, we think that fluoride can cause lipid peroxidation, DNA damage and apoptosis, and that there is a positive relationship among these changes."


"For fluoride concentrations of 2 ppm to 35 ppm, non vital cells of less than 10% could be shown. After incubation with 71 ppm and 213 ppm Olaflur, there were 15% and 43% of damaged cells, respectively. Weak genotoxic effects on mucosal cells as well as on lymphocytes could be demonstrated at all concentrations tested. In fluoride concentrations of 213 ppm genotoxicity increased to max."


"To investigate the effects of fluoride on DNA damage as well as the effects of selenium and zinc against fluoride respectively or jointly in pallium neural cells of rats, single cell gel electrophoresis was used to detect the DNA damage of neural cells prepared in vitro. The results showed that the degree of DNA damage in the fluoride group and the selenium group were significantly greater than that in control group(P < 0.01). The damage in the fluoride group was even more serious. The damage in the fluoride + selenium group and fluoride + zinc group was slighter than that in the fluoride group but with no significant difference. The extent of DNA damage in the fluoride + selenium + zinc group was significantly slighter than that in the fluoride group(P < 0.05). It suggested that fluoride and selenium could induce DNA damage in pallium neural cells of rats respectively."

**In the present work, 13 compounds** [chlor dane, Arochlor 1260, di(2-ethylhexyl)phthalate, 1,1,1-trichloro-2, 2-bis(4-chlorophenyl)ethane, limonene, sodium fluoride, ethionine, o-anisidine, benzoil peroxide, o-vanadate, phenobar bital, 12-O-tetradecanoylphorbol 13-acetate and clofibrate] have been tested for their ability to induce morphological transformation and affect intercellular communication in Syrian hamster embryo (SHE) cells... In vitro morphological transformation of SHE cells is now one of the most frequently used cell transformation systems. Around 500 chemicals have been tested in this system, and a good correlation has been obtained with the ability of compounds from different chemical groups to cause tumours in animals and humans. The SHE cell transformation assay also responds to tumour promoters and carcinogens not detected by tests for genotoxicity... [N]ine of the 13 tested substances (TPA, o-vanadate, DEPH, phenobarbital, Arochlor 1260, clofibrate, o-anisidine, limonene and NaF) are considered positive for induction of morphological transformation."


"Significant increases in the frequencies of chromosome aberrations were induced in a dose- and treatment time-dependent fashion when NaF was administered to [rat vertebral bone] cells at 0.5 and 1.0 mM for 24 and 48 h. The results indicate that NaF is genotoxic to rat vertebrae, providing a possible mechanism for the vertebrae, as a target organ of NaF carcinogenesis."


"The genotoxic effects of inorganic fluorides were investigated by treating cultured rat bone marrow cells with varying concentrations (0.1-100 microM) of potassium fluoride (KF) and sodium fluoride (NaF) for different durations (12, 24 and 36 h) and measuring the incidence of cells with aberrations and number of breaks per cell. Both forms of fluoride were found to be weak mutagens relative to the positive control N-methyl-N-nitro-N-nitrosoguanidine (MNNG). A specificity of fluoride ion in inducing chromosome aberrations (CA) was indicated by the observation that both NaF and KF behaved almost equivalently in this study and at significantly higher variations from the results with potassium chloride (KCl) and sodium chloride (NaCl)."


"The testing of hydrogen fluoride (HF) for its mutagenic activity by fumigation of barley seedlings showed that the mutation rate was linear with dose. It was found that the cytogenic effects of gaseous fluoride on grain crops was correlated with the fluoride content in plant tissue.""


"A significant increase in the incidence of chromosome aberrations was observed only in cultures treated with NaF during early and/or middle S phases of cell cycle. These results suggest that cytotoxicity and clastogenicity of NaF to cultured human diploid fibroblasts are cell cycle dependent, and that the cells in early and middle S phases are more sensitive to the effects."


"We show here that NaF is clastogenic not only in human cells but also in great ape cells. The mechanism of NaF clastogenicity is still unknown, but the same profile of chromosomal aberrations in man and chimpanzees suggests that its action on these cells and the response of the cells will be consistent. The different response to NaF among non-human primates might give us a clue to clarify the mechanism of NaF clastogenicity."

"We tested the induction of mutagenic effects by in vivo and in vitro bone marrow micronucleus tests. A significant increase in micronucleated polychromatic erythrocytes was observed 24 H after intraperitoneal injection of sodium fluoride at a dose of 30 mg/kg body weight. In the in vitro micronucleus test, the frequency of micronucleated polychromatic erythrocytes was increased significantly at concentrations of 2 and 4 MM. These results indicate that the micronucleus test may be useful in evaluating the cancer risk of sodium fluoride."


"Sodium fluoride was found to induce gene-locus mutations at the thymidine kinase (tk) and hypoxanthine guanine phosphoribosyl transferase (hgprt) loci in human lymphoblastoid cells."


"Based on these results and those previously reported for NaF and APC, it is proposed that NaF-induced aberrations may occur by an indirect mechanism involving the inhibition of DNA synthesis/repair."


"Inducibility of chromosome aberrations of the cells following treatment with sodium fluoride was also dependent upon the phase of cell cycle. Significant increase in the incidence of chromosome aberrations was observed only in cultures treated during early and/or middle S phases of the cell cycle. These results indicate that cytotoxicity and clastogenicity of sodium fluoride to cultured human diploid fibroblasts are cell phase dependent, and that the cells in early and middle S phases are more sensitive to these effects."


"Sequential treatment of Syrian hamster embryo (SHE) cells with a chemical carcinogen followed by sodium fluoride (NaF) resulted in a higher yield of morphologically transformed cell colonies than treatment of the cells with carcinogen alone... This enhancement/promotion of cell transformation by NaF was only expressed after the cells had been pretreated with either direct-acting carcinogens or procarcinogens. Pretreatment of the cells with noncarcinogens or weakly-acting carcinogens or administration of NaF prior to treatment with the carcinogen failed to enhance the yield of transformation. Transformation was enhanced even when the NaF treatment was delayed for several days after the carcinogen treatment. However, the continued presence of NaF was necessary for maintenance of the increased level of transformation. Removal of NaF prior to termination of the assay resulted in a reversal of the transformed clonal morphologies to a normal phenotype such that the final yield of transformants was decreased, but was still greater than that observed after carcinogen treatment alone."


"Sodium fluoride was found to induce morphological transformation of SHE cells seeded on a feeder layer of X-irradiated cells at high concentrations (75-125 micrograms/ml). When the cells were seeded in the absence of a feeder-layer, the transformation frequencies increased in a dose-dependent manner with the concentrations of sodium fluoride ranging from 0 to the highly toxic concentration of 200 micrograms/ml. In the BALB/3T3 cell system, sodium fluoride was negative in the standard Kakunaga procedure, while through the experiment designed by table L8 (2(7) of the orthogonal method, an initiating-like effect and a weak promoting activity were detected within the concentrations ranging from a 25 micrograms/ml to a 50 micrograms/ml concentration which is highly toxic for BALB/3T3 cells. From these results, it is suggested that, besides a genetic mode of action, sodium fluoride could possibly act through a non-genotoxic mechanism."
"Chromosomal aberrations were recorded for all the concentrations used. Maximum effect at all concentrations was observed after 24 hours of treatment. Several kinds of abnormalities were revealed with the main ones being bridges, double bridges, sidearm bridges, bridges with fragments, tripolar and multipolar anaphases with and without bridges, fragments, and laggards. "Y" and "X" configurations were also noted at metaphase... The authors conclude that sodium-fluoride may be considered to be clastogenic in these cells."


"While the results in this paper demonstrate the ability (of fluoride) to induce genetic damage in cultured mammalian cells, the potential risks to animals or man are not addressed."


"The results are used to illustrate the problems associated with quantitative extrapolation from in vitro tests to human risk, as follows. (1) There appears to be a threshold response (clastogenicity vs. dose) with NaF at around 10 micrograms/ml (48 h exposure) but a more definitive conclusion must await elucidation of the mechanisms of clastogenicity. (2) NaCl is weakly clastogenic at 1000 times the threshold dose for NaF. The mechanisms are unlikely to be similar. (3) No clastogenicity was detected with NaF below about 30% mitotic inhibition but the relationship between clastogenicity and mitotic inhibition was similar for NaF and MMC. (4) There was no obvious threshold in the relationship between clastogenicity and cell killing with NaF. MMC was less clastogenic than NaF at equitoxic doses. Observations 3 and 4 preclude the possibility of regarding the clastogenicity of NaF as a false positive by virtue of associated cytotoxicity."


"These observations, and an analysis of the colony size of trifluorothymidine-resistant mutants in TK+/- cells, suggest that sodium fluoride is clastogenic to dividing cultured mammalian cells at high, toxic concentrations. Further work is desirable to investigate the mechanism by which chromosomes are damaged at high concentrations of fluoride, since without such a mechanistic understanding, extrapolation of our data to the human situation must be insecure."


"The clastogenic effect of NaF has been tested by the use of several cytogenetic assay systems, but the findings on its genotoxicity are not consistent. In this study, the effects of NaF on chromosomes, unscheduled DNA synthesis (UDS) and sister-chromatid exchanges (SCEs) were investigated using cultured human lymphocytes. For clastogenicity testing, cells were treated for 24 h in various concentrations of NaF. At least two donors were tested for each concentration and more than 10,000 cells were totally observed... Sodium fluoride treatment had remarkable effects on the induction of isochromatid gaps and chromosome breaks (NUpds)."


"Mass cultures of cells treated with NaF (75 or 100 micrograms/ml) for 24 hr, followed by continuous cultivation for 35 to 50 passages, developed the ability to grow in soft agar and to produce anaplastic fibrosarcomas when injected into newborn hamsters. In contrast, no morphological and neoplastic transformation was observed in untreated cells. Furthermore, a significant increase in chromosome aberrations at the chromatid level, sister chromatid exchanges, and unscheduled DNA synthesis was induced by NaF in a dose- and time-dependent manner. These results indicate that NaF is genotoxic and capable of inducing neoplastic transformation of Syrian hamster embryo cells in culture. A potential for
carcinogenicity of this chemical, which is widely used by humans, is suggested. However, the carcinogenic risk of this chemical to humans may be reduced by factors regulating in vivo dose levels.”


"A significant increase in the frequency of chromosome aberrations at the chromatid level was observed in treated cells in a dose-dependent manner... These results suggest that NaF causes DNA damage in human diploid fibroblasts in culture.”


"The effect of treatment of cultured human oral keratinocytes with sodium fluoride (NaF) has been investigated with respect to induction of unscheduled DNA synthesis (UDS)... Significant levels of UDS were induced in a dose-related fashion by NaF treatment. The results suggest that NaF causes DNA damage in cultured human oral keratinocytes."


"The study, by light and fluorescent microscopy, of sternal and femoral bone marrow taken from young Swiss mice exposed for period up to 280 days to elevated levels of sodium fluoride in drinking water, has revealed morphologic abnormalities in cell structure and mitotic figure formation in immature leukocytes. Alterations in the content and distribution of RNA and DNA also appear after several weeks of exposure... The results of this investigation indicate that young leukocytes chronically exposed to elevated fluoride levels have the potential for an irreversible shift toward the formation of neoplasm."


"Human leucocytes in the cultures in vitro were exposed to the action of lead and fluorine ions... Both factors caused structural and quantitative aberrations in the chromosome set, which seems to indicate their mutagenic character. It is noteworthy that the smallest of the applied concentrations of fluorine ions (3.15 x 10^-5M) is equal to the concentration of these ions in the running water of Szczecin, given for the prevention of caries.”


"These findings indicate that HF in addition to being a mutagenic agent is also able to reduce crossing over in certain chromosome segments."


"while NaF can be a potent meiotic mutagen in the particular in vitro experimental situations reported here, the variation of in vitro sensitivity between the mouse (which nevertheless showed some oocyte abnormality when tested in vivo) and the higher forms (cow and ewe) would suggest an assessment of abnormal progeny from the latter species for chromosomal abnormalities in NaF-contaminated areas, as a reasonable next step for ascertaining the probability of the mutagenicity of this compound."


"Two strains of Drosophila melanogaster were treated with sub-lethal levels of gaseous hydrogen fluoride for six weeks. Egg samples were collected at various times for hatchability determinations. Adults reared from these samples were evaluated for fecundity and fertility. Treatment with HF caused a marked reduction in hatchability and fecundity in the more sensitive strain. Male fertility was depressed but female fertility remained stable over the test
period. The reduction of these parameters in the offspring of populations subjected to low levels of atmospheric HF contamination for prolonged periods suggests that HF causes genetic damage."


"Genetic differences were observed in the response of the progeny of treated flies. The maintenance of a population at sub-lethal concentrations of HF revealed an apparent accumulation of physiological aberrations resulting in sterility in the treated flies. Results indicate that treatment increased the incidence of genetic aberrations as measured by at least two parameters."


"Maize seedlings of the genotype A1A2C1Wx were fumigated in growth chambers with hydrogen fluoride (HF) at a concentration of about 3 ug/m3. The experiment was run for 10 days, with the first group of treated plants removed from the chambers after 4 days and then at intervals of 2 days. Microsporocyte smears from the treated plants revealed chromosomal aberrations that included asynaptic regions, translocations, inversions, and bridges plus fragments or fragments by themselves. It is believed that these abnormalities were due to the physiological effect of HF causing the chromosomes to become sticky and/or to the occurrence of chromatid breakage followed by reunion to form structural changes. These findings indicate that HF is a mutagenic agent."


"Studies on the effects of HF on meiotic chromosomes of tomatoes indicated a trend toward a higher frequency of chromosomal aberrations with an increase in the fumigation period. It was indicated that HF was capable of inducing paracentric inversions with the possibility of the induction of deficiencies, duplications or even translocations. The progeny obtained from the treated plants produced a number of abnormal phenotypes, the same as, or similar to, known mutations. Further studies in maize microsporocytes for plants treated with HF confirmed the cytological results obtained in tomatoes with clear evidence of the occurrence of inversions, translocations and deficiencies. These results suggest that HF seems to affect primarily the DNA molecule by blocking its replication, probably through its action on the enzymatic system."


"From the results, it is clear that NaF, not being mutagenic by itself, interacts with the mechanism of mutation induction by X-irradiation in fully mature spermatozoa. In fact, the enhancing effect has been observed in 21 out of 23 experiments where pre-treatment with NaF was compared to that with saline."


http://www.fluoridealert.org/health/cancer/mutagen.aspx